Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2022
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission file number 001-38223

RHYTHM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-2159271**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

222 Berkeley Street
12th Floor
Boston, MA 02116
(Address of principal executive offices)
(Zip Code)

(857) 264-4280
(Registrant's telephone number, including area code)

N/A
(Former name, former address and former fiscal year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	RYTM	The Nasdaq Stock Market LLC (Nasdaq Global Market)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15 (d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒	Accelerated filer ☐
Non-accelerated filer ☐	Smaller reporting company ☐
	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒.

The number of shares outstanding of the registrant's Common Stock as of July 28, 2022 was 50,720,570.

RHYTHM PHARMACEUTICALS, INC.

FORM 10-Q

INDEX

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets

(in thousands, except share and per share data)

(Unaudited)

	June 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 113,207	$ 59,248
Short-term investments	122,389	235,607
Accounts receivable, net	1,707	1,025
Prepaid expenses and other current assets	12,029	12,507
Total current assets	249,332	308,387
Property and equipment, net	2,559	2,813
Right-of-use asset	1,359	1,522
Intangible assets, net	8,311	4,658
Restricted cash	328	328
Other long-term assets	15,786	11,815
Total assets	$ 277,675	$ 329,523
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,012	$ 5,737
Accrued expenses and other current liabilities	35,605	30,084
Deferred revenue	2,309	7,000
Lease liability	644	606
Total current liabilities	44,570	43,427
Long-term liabilities:		
Deferred royalty obligation	34,273	—
Lease liability	1,614	1,945
Derivative liability	1,590	—
Total liabilities	82,047	45,372
Stockholders' equity:		
Preferred Stock, $0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding at June 30, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value: 120,000,000 shares authorized; 50,454,170 and 50,283,574 shares issued and outstanding at June 30, 2022 and December 31, 2021, respectively	50	50
Additional paid-in capital	823,188	813,041
Accumulated other comprehensive loss	(906)	(1)
Accumulated deficit	(626,704)	(528,939)
Total stockholders' equity	195,628	284,151
Total liabilities and stockholders' equity	$ 277,675	$ 329,523

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Statements of Operations and Comprehensive (Loss) Income

(in thousands, except share and per share data)

(Unaudited)

	Three months ended June 30,		Six months ended June 30,	
	2022	2021	2022	2021
Product revenue, net	$ 2,312	$ 274	$ 3,810	$ 309
License revenue	6,754	—	6,754	—
Costs and expenses:				
Cost of sales	378	137	608	141
Research and development	31,456	25,104	63,966	45,015
Selling, general, and administrative	22,328	15,465	43,777	29,983
Total costs and expenses	54,162	40,706	108,351	75,139
Loss from operations	(45,096)	(40,432)	(97,787)	(74,830)
Other income:				
Other income	—	—	—	100,000
Interest income, net	95	21	22	175
Total other income, net	95	21	22	100,175
(Loss) income before taxes	(45,001)	(40,411)	(97,765)	25,345
(Benefit from) provision for income taxes	—	(5,022)	—	16,984
Net (loss) income	$ (45,001)	$ (35,389)	$ (97,765)	$ 8,361
Net (loss) income per share				
Basic	$ (0.89)	$ (0.70)	$ (1.94)	$ 0.17
Diluted	$ (0.89)	$ (0.70)	$ (1.94)	$ 0.17
Weighted-average common shares outstanding				
Basic	50,398,003	50,209,484	50,362,512	48,931,127
Diluted	50,398,003	50,209,484	50,362,512	49,644,704
Other comprehensive (loss) income:				
Net (loss) income	$ (45,001)	$ (35,389)	$ (97,765)	$ 8,361
Unrealized (loss) income on marketable securities and other long-term assets	(277)	79	(905)	(28)
Comprehensive (loss) income	$ (45,278)	$ (35,310)	$ (98,670)	$ 8,333

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Statements of Stockholders' Equity

(in thousands, except share data)

(Unaudited)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2021	50,283,574	$ 50	$ 813,041	$ (1)	$ (528,939)	$ 284,151
Stock-based compensation expense	—	—	4,611	—	—	4,611
Issuance of common stock in connection with ESPP	61,518	—	399	—	—	399
Issuance of common stock in connection with exercise of stock options and vesting of restricted stock units	48,639	—	—	—	—	—
Unrealized loss on marketable securities	—	—	—	(628)	—	(628)
Net loss	—	—	—	—	(52,764)	(52,764)
Balance at March 31, 2022	50,393,731	50	818,051	(629)	(581,703)	235,769
Stock-based compensation expense	—	—	5,137	—	—	5,137
Issuance of common stock in connection with exercise of stock options and vesting of restricted stock units	60,439	—	—	—	—	—
Unrealized gain on marketable securities	—	—	—	23	—	23
Unrealized loss on Rarestone equity	—	—	—	(300)	—	(300)
Net loss	—	—	—	—	(45,001)	(45,001)
Balance at June 30, 2022	50,454,170	$ 50	$ 823,188	$ (906)	$ (626,704)	$ 195,628
Balance at December 31, 2020	44,235,903	$ 44	$ 625,762	$ 49	$ (459,327)	$ 166,528
Stock-based compensation expense	—	—	5,191	—	—	5,191
Issuance of common stock in connection with ESPP	17,000	—	388	—	—	388
Issuance of common stock in connection with exercise of stock options and vesting of restricted stock units	198,855	—	3,466	—	—	3,466
Issuance of common stock upon completion of public offering, net of offering costs	5,750,000	6	161,725	—	—	161,731
Unrealized loss on marketable securities	—	—	—	(107)	—	(107)
Net income	—	—	—	—	43,750	43,750
Balance at March 31, 2021	50,201,758	50	796,532	(58)	(415,577)	380,947
Stock compensation expense	—	—	5,669	—	—	5,669
Issuance of common stock in connection with exercise of stock options	24,981	—	383	—	—	383
Unrealized gain on marketable securities	—	—	—	79	—	79
Net loss	—	—	—	—	(35,389)	(35,389)
Balance at June 30, 2021	50,226,739	$ 50	$ 802,584	$ 21	$ (450,966)	$ 351,689

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Statements of Cash Flows

(in thousands)

(Unaudited)

	Six months ended June 30,	
	2022	2021
Operating activities		
Net (loss) income	$ (97,765)	$ 8,361
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	9,748	10,860
Gain on sale of priority review voucher	—	(100,000)
Deferred tax provision	—	16,984
Depreciation and amortization	788	518
Amortization of debt issuance costs	46	—
Non-cash rent expense	(130)	(122)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(580)	(1,374)
Deferred revenue	1,023	—
Other long-term assets	(3,971)	—
Accounts payable, accrued expenses and other current liabilities	(1,600)	(598)
Net cash used in operating activities	(92,441)	(65,371)
Investing activities		
Purchases of short-term investments	(50,440)	(362,469)
Maturities of short-term investments	163,128	135,542
Proceeds from sale of priority review voucher	—	100,000
Milestone obligation under license agreement	(4,000)	(5,000)
Purchases of property and equipment	(187)	(260)
Net cash provided by (used in) investing activities	108,501	(132,187)
Financing activities		
Net proceeds from issuance of common stock	—	161,731
Proceeds from the exercise of stock options	—	3,849
Proceeds from issuance of common stock from ESPP	399	388
Proceeds from royalty financing agreement	37,500	—
Net cash provided by financing activities	37,899	165,968
Net increase (decrease) in cash, cash equivalents and restricted cash	53,959	(31,590)
Cash, cash equivalents and restricted cash at beginning of period	59,576	101,257
Cash, cash equivalents and restricted cash at end of period	$ 113,535	$ 69,667
Supplemental disclosures:		
Deferred financing costs in accrued expenses	$ 1,311	—

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements

Rhythm Pharmaceuticals, Inc.

Notes to Unaudited Condensed Consolidated Financial Statements

(In thousands, except share and per share information)

1. Nature of Business

Rhythm Pharmaceuticals, Inc. (the "Company" or "we") is a global, commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with hyperphagia and severe obesity caused by rare melanocortin-4 receptor (MC4R) pathway diseases. Rhythm's precision medicine, IMCIVREE® (setmelanotide), for which we have exclusive worldwide rights, has the potential to restore dysfunctional MC4R signaling due to impaired MC4R pathway function. MC4R pathway deficiencies result in the disruption of satiety signals and energy homeostasis in the body, which, in turn, leads to intense feelings of hunger and to obesity. In the United States, IMCIVREE is approved for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency as determined by U.S. Food and Drug Administration (FDA) approved test demonstrating variants in *POMC*, *PCSK1* or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS), or Bardet-Biedl syndrome (BBS). In the European Union and Great Britain, IMCIVREE is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. A Type II variation application to the European Medicines Agency seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS also is under review. In July 2022, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending to expand the current indication for IMCIVREE to include the treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS. The European Commission, which has the authority to grant and expand marketing authorizations for medicinal products in the EU, is anticipated to make a final decision on the application to expand the indication for IMCIVREE in the second half of 2022. In addition, we are advancing a broad clinical development program for setmelanotide in patients with hyperphagia and severe obesity caused by additional rare MC4R pathway diseases to expand the approved indications in the United States and Europe. In addition to the United States, European Union and United Kingdom, we and our partners are seeking approval for IMCIVREE to treat patients with these MC4R pathway-related obesities in Israel, China, Hong Kong and Macau.

The Company is a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc., and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. The Company has wholly owned subsidiaries in the United States, Ireland, the United Kingdom, France, Italy, the Netherlands, Germany, Spain and Canada.

The Company is subject to risks and uncertainties common to commercial-stage companies in the biotechnology industry, including but not limited to, risks associated with the commercialization of approved products, completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Commercialization of approved products will require significant resources and in order to market IMCIVREE, the Company must continue to build its sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities.

There are many uncertainties regarding the COVID-19 pandemic, and the Company is closely monitoring the impact of the pandemic on all aspects of its business, including how the pandemic may continue to impact its patients, employees, suppliers, vendors, business partners and distribution channels. While the pandemic did not materially affect the Company's financial results and business operations for the three and six months ended June 30, 2022, the Company is unable to predict the impact that COVID-19 will have on its financial position and operating results in future periods

due to numerous uncertainties. The Company will continue to assess the evolving impact of the COVID-19 pandemic and will make adjustments to its operations as necessary.

Liquidity

The Company has incurred operating losses and negative cash flows from operations since inception. As of June 30, 2022, the Company had an accumulated deficit of $626,704. The Company has primarily funded these losses through the proceeds from the sales of common and preferred stock, asset sales, royalty financing, out-license arrangements, as well as capital contributions received from the former parent company, Rhythm Holdings LLC. To date, the Company has minimal product revenue and management expects operating losses to continue for the foreseeable future. The Company has devoted substantially all of its resources to its drug development efforts, comprising of research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property, pre-commercialization activities and general and administrative functions relating to these operations. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations.

At June 30, 2022, the Company had $235,596 of cash and cash equivalents and short-term investments on hand. In the future, the Company will be dependent on obtaining funding from third parties, such as proceeds from the issuance of debt, sale of equity, product sales and funded research and development programs to maintain the Company's operations and meet the Company's obligations. There is no guarantee that additional equity or other financings will be available to the Company on acceptable terms, or at all. If the Company fails to obtain additional funding when needed, the Company would be forced to scale back, terminate its operations or seek to merge with or be acquired by another company. Management believes that the Company's existing cash and cash equivalents and short term investments will be sufficient to fund the Company’s operations into 2024, and that such existing cash and cash equivalents and short term investments, together with the second investment tranche under the Revenue Interest Financing Agreement, or RIFA, entered into with entities managed by HealthCare Royalty Management, LLC expected in the second half of 2022, will be sufficient to fund the Company's operations into at least the second half of 2024.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's unaudited condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States, or GAAP, and the applicable rules and regulations of the Securities and Exchange Commission, or SEC, regarding interim financial reporting. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification, or ASC, and Accounting Standards Updates, or ASU, of the Financial Accounting Standards Board, or FASB. As permitted under these rules, certain footnotes or other financial information that are normally required by GAAP have been condensed or omitted.

The accompanying condensed consolidated balance sheet as of June 30, 2022, the condensed consolidated statements of operations and comprehensive (loss) income for the three and six months ended June 30, 2022 and 2021, the condensed consolidated statements of stockholders’ equity for the three and six months ended June 30, 2022 and 2021 and the condensed consolidated statements of cash flows for the six months ended June 30, 2022 and 2021 and the related footnote disclosures are unaudited. In management's opinion, the unaudited condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements as of and for the year ended December 31, 2021 and include all adjustments, which are all normal recurring adjustments, necessary for the fair presentation of the interim financial statements. The results for the three and six months ended June 30, 2022 are not necessarily indicative of the results expected for the full fiscal year, any other interim periods, or any future year or period.

The accompanying unaudited condensed consolidated financial statements reflect the application of certain significant accounting policies as described below and elsewhere in these notes to the unaudited condensed consolidated financial statements. As of June 30, 2022, there have been no material changes in the Company's significant accounting

policies from those that were disclosed in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. Significant estimates relied upon in preparing these financial statements include estimates related to determining our net product revenue, license revenue, accruals related to research and development expenses, assumptions used to record stock-based compensation expense, interest expense on our deferred royalty obligation, assumptions used to value the embedded derivative in our deferred royalty obligation, assumptions used to value the common stock received from RareStone Group Ltd., or RareStone, and the valuation allowance on the Company's deferred tax assets. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

Principles of Consolidation

The consolidated financial statements include the accounts of Rhythm Pharmaceuticals, Inc. and its wholly-owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Off-Balance Sheet Risk and Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash and cash equivalents and short-term investments, which are maintained at two federally insured financial institutions. The deposits held at these two institutions are in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

The Company is exposed to risks associated with extending credit to customers related to the sale of products. The Company does not require collateral to secure amounts due from its customers. At June 30, 2022, substantially all of the Company's revenue was generated from a single customer in the United States.

The Company relies on third-party manufacturers and suppliers for the manufacture and supply of its product. The inability of the suppliers or manufacturers to fulfill supply requirements of the Company could materially impact future operating results. A change in the relationship with the suppliers or manufacturer, or an adverse change in their business, could materially impact future operating results.

Segment Information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company currently operates in one business segment, which is the development and commercialization of therapies for patients with rare diseases. A single management team that reports to the Chief Executive Officer comprehensively manages the entire business. The Company does not operate separate lines of business with respect to its product or product candidates. Accordingly, the Company has one reportable segment.

Accounts Receivable, net

Accounts receivable consists of amounts due from customers, net of customer allowances for cash discounts and any estimated expected credit losses. The Company's measurement of expected credit losses is based on relevant information about past events, including historical experience, current conditions, and reasonable and supportable forecasts that affect the collectability of the reported amount. To date, the Company has not experienced any credit losses. The Company's contracts with its customers have standard payment terms that generally require payment within 45 days. The Company analyzes amounts that are past due for collectability, and periodically evaluates the creditworthiness of its customers. At June 30, 2022, the Company determined an allowance for doubtful account was not required based upon our review of contractual payments and our customers' circumstances.

Revenue Recognition

We recognize revenue in accordance with Accounting Standards Codification ASC 606, *Revenue from Contracts with Customers* or ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements, and financial instruments. Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue, net

Subsequent to its regulatory approval, the Company began to sell IMCIVREE in the United States in March 2021 and in France and Germany in March 2022 and June 2022, respectively. The product is distributed through an exclusive third-party logistics, or 3PL, distribution agent that does not take title to the product. Once the product is delivered to the Company's exclusive specialty pharmacy provider, our sole customer in the U.S., the customer, or wholesaler takes title to the product. The wholesaler then distributes the product to health care providers and patients. In our exclusive distribution agreement with the 3PL company, the Company acts as principal because we retain control of the product. The Company generally does not offer returns of product sold to the customer.

Revenue from product sales are recognized when the customer obtains control of our product, which occurs at a point in time, upon transfer of title to the customer because at that point in time we have no ongoing obligations to the customer. There are no other performance obligations besides the sale of product. We classify payments to our customer or other parties in the distribution channel for services that are distinct and priced at fair value as selling, general and administrative expenses in our condensed consolidated statements of operations and comprehensive (loss) income. Otherwise, payments to a customer or other parties in the distribution channel that do not meet those criteria are classified as a reduction of revenue, as discussed further below. Taxes collected from the customer relating to product sales and remitted to governmental authorities are excluded from revenue. Because our payment terms are generally forty-five days, the Company concluded there is not a significant financing component because the period between the transfer of a promised good or service to the customer and when the customer pays for that good or service will be one year or less. The Company expenses incremental costs of obtaining a contract as and when incurred since the expected amortization period of the asset that we would have recognized is one year or less.

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price, or the transaction price, which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates,

co-pay assistance and other allowances that are offered within contracts between us and our customers, health care providers and other indirect customers relating to the sale of IMCIVREE. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is considered probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

The following are the components of variable consideration related to product revenue:

Chargebacks: The Company estimates obligations resulting from contractual commitments with the government and other entities to sell products to qualified healthcare providers and patients at prices lower than the list prices charged to our customers. The government and other entities charge us for the difference between what they pay for the product and the selling price to our customers. The Company records reserves for these chargebacks related to product sold to our customers during the reporting period, as well as our estimate of product that remains in the distribution channel at the end of the reporting period that we expect will be sold to qualified healthcare providers and patients in future periods.

Government rebates: The Company is subject to discount obligations under government programs, including Medicaid programs, Medicare and Tricare in the United States. We estimate Medicaid, Medicare and Tricare rebates based upon a range of possible outcomes that are probability-weighted for the estimated payer mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a liability that is included in accrued expenses and other current liabilities on our condensed consolidated balance sheet. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. On a quarterly basis, we update our estimates and record any adjustments in the period that we identify the adjustments.

Trade discounts and allowances: The Company provides customary invoice discounts on IMCIVREE sales to our U.S. customer for prompt payment that are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we receive and pay for various distribution services from our customer in the distribution channel. For services that are either not distinct from the sale of our product or for which we cannot reasonably estimate the fair value, such fees are classified as a reduction of product revenue.

Product returns: Our customers have limited return rights related to the product's damage or defect. The Company estimates the amount of product sales that may be returned and records the estimate as a reduction of revenue and a refund liability in the period the related product revenue is recognized. Based on the distribution model for IMCIVREE and the price of IMCIVREE, the Company believes there will be minimal returns.

Other incentives: Other incentives include co-payment assistance the Company provides to patients with commercial insurance that have coverage and reside in states that allow co-payment assistance. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue. The estimate is recorded as a reduction of revenue in the same period the related revenue is recognized.

During the three and six months ended June 30, 2022 and 2021, we recorded product revenue, net, of $2,312, $274, $3,810, and $309, respectively. The table that summarizes balances and activity in each of the product revenue allowance and reserve categories has not been included for the three and six months ended June 30, 2022 and 2021, due to the immateriality of the revenue recognized during the periods.

License Agreements

We generate revenue from license or similar agreements with pharmaceutical companies for the development and commercialization of certain of our products and product candidates. Such agreements may include the transfer of intellectual property rights in the form of licenses, transfer of technological know-how, delivery of drug substances, research and development services, and participation on certain committees with the counterparty. Payments made by the customers may include non-refundable upfront fees, payments upon the exercise of customer options, payments based upon the achievement of defined milestones, and royalties on sales of products and product candidates if they are approved and commercialized.

If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize the transaction price allocated to the license as revenue upon transfer of control of the license. We evaluate all other promised goods or services in the agreement to determine if they are distinct. If they are not distinct, they are combined with other promised goods or services to create a bundle of promised goods or services that is distinct. Optional future services where any additional consideration paid to us reflects their standalone selling prices do not provide the customer with a material right and, therefore, are not considered performance obligations. If optional future services are priced in a manner which provides the customer with a significant or incremental discount, they are material rights, and are accounted for as separate performance obligations.

We utilize judgment to determine the transaction price. In connection therewith, we evaluate contingent milestones at contract inception to estimate the amount which is not probable of a material reversal to include in the transaction price using the most likely amount method. Milestone payments that are not within our control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore the variable consideration is constrained. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each reporting period, we re-evaluate the probability of achieving development milestone payments that may not be subject to a material reversal and, if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license and other revenue, as well as earnings, in the period of adjustment.

We then determine whether the performance obligations or combined performance obligations are satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. We evaluate the measure of progress, as applicable, for each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded within deferred revenue. Contract liabilities within deferred revenue are recognized as revenue after control of the goods or services is transferred to the customer and all revenue recognition criteria have been met.

For arrangements that include sales-based royalties, including sales-based milestone payments, and a license of intellectual property that is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of when the related sales occur or when the performance obligation to which some or all of the royalties have been allocated has been satisfied (or partially satisfied).

RareStone Group Ltd.

In December 2021, the Company entered into an Exclusive License Agreement with RareStone Group Ltd., or the RareStone License. Pursuant to the RareStone License, we granted to RareStone an exclusive, sublicensable, royalty-bearing license under certain patent rights and know-how to develop, manufacture, commercialize and otherwise exploit any pharmaceutical product that contains setmelanotide in the diagnosis, treatment or prevention of conditions and diseases in humans in China, including mainland China, Hong Kong and Macao. RareStone has a right of first negotiation in the event that the Company chooses to grant a license to develop or commercialize the licensed product in Taiwan. The arrangement includes a license and an additional performance obligation to supply product upon the request of RareStone.

According to the terms of the RareStone License, RareStone has agreed to seek local approvals to commercialize IMCIVREE for the treatment of obesity and hyperphagia due to biallelic POMC, PCSK1 or LEPR deficiency, as well as Bardet-Biedl and Alström syndromes. Additionally, RareStone has agreed to fund efforts to identify and enroll patients from China in the Company's global EMANATE trial, a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate setmelanotide in four independent sub-studies in patients with obesity due to a heterozygous variant of POMC/PCSK1 or LEPR; certain variants of the SRCI gene, and certain variants of the SH2B1 gene. In accordance with the terms of the RareStone License, RareStone made an upfront payment to Rhythm of $7,000 and issued Rhythm 1,077,586 ordinary shares. The Company is eligible to receive development and commercialization milestones of up to $62,500, as well as tiered royalty payments on annual net sales of IMCIVREE.

As of March 31, 2022, the Company estimated the fair value of the RareStone equity to be $2,440 based on a preliminary valuation. Upon completion of the valuation procedures during the three month period ended June 30, 2022, the Company concluded the initial fair value of the RareStone equity to be $1,040. The $1,400 change in fair value upon finalizing our valuation of the RareStone equity resulted in an adjustment to the contract liability account within our condensed consolidated financial statements. At June 30, 2022, the Company estimated the fair value of the RareStone equity to be $740 based upon a valuation. The $300 decline in fair value is recodered as an a component of other comprehensive (loss) income in our the condensed consolidated statements of operations and other comprehensive (loss) income for the three month period ended June 30, 2022. The Company will remeasure the fair value of the RareStone equity on a quarterly basis.

The Company received total upfront consideration of $8,040 comprised of an upfront payment of $7,000, and the estimated fair value of the RareStone equity of $1,040. The Company determined that the RareStone License contains two performance obligations, the delivery of the license and the supply of clinical and commercial product. The Company further determined the supply of commercial product to RareStone contains a significant future discount and estimates the discount to be $1,286, which is recorded as a component of deferred revenue on the condensed consolidated balance sheet at June 30, 2022. The discount related to commercial manufacturing supply will be deferred and recognized over the commercial supply period.

Based on a relative fair-value allocation between the license and the manufacture of clinical and commercial product, the Company recognized $6,754 of license revenue during the three and six months ended June 30, 2022 as the Company fulfilled its obligations in transferring the license to RareStone.

Deferred Royalty Obligation

We treat the debt obligation to HealthCare Royalty Management, LLC as discussed further in Note 10, "Long-term Obligations", as a deferred royalty obligation, amortized using the effective interest rate method over the estimated life of the revenue streams. We recognize interest expense thereon using the effective rate, which is based on our current estimates of future revenues over the life of the arrangement. In connection therewith, we periodically assess our expected revenues using internal projections, impute interest on the carrying value of the deferred royalty obligation, and record interest expense using the imputed effective interest rate. To the extent our estimates of future revenues are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, we will account for any such changes by adjusting the effective interest rate on a prospective basis, with a corresponding impact to the reclassification of our deferred royalty obligation. The assumptions used in determining the expected repayment term of the deferred royalty obligation and amortization period of the issuance costs requires that we make estimates that could impact the short-term and long-term classification of such costs, as well as the period over which such costs will be amortized.

Cost of Product Sales

Prior to receiving approval from the FDA in November 2020 to sell IMCIVREE in the United States, the Company expensed all costs incurred related to the manufacture of IMCIVREE as research and development expense because of the inherent risks associated with the development of a drug candidate, the uncertainty about the regulatory approval process and the lack of history for the Company of regulatory approval of drug candidates. Subsequent to receiving FDA approval in November 2020, the Company has capitalized a nominal amount of inventory related costs that

were incurred subsequent to FDA approval. At June 30, 2022, the Company had $1,690 of inventory recorded as a component of prepaid and other current assets on the condensed consolidated balance sheet.

Cost of product sales will consist of manufacturing costs, transportation and freight, amortization of capitalized intangibles, royalty payments and indirect overhead costs associated with the manufacturing and distribution of IMCIVREE. Cost of product sales may also include periodic costs related to certain manufacturing services and inventory adjustment charges.

Intangible Assets, Net

Definite-lived intangible assets related to capitalized milestones under license agreements are amortized on a straight-line basis over their remaining useful lives, which are estimated to be the remaining patent life. If our estimate of the product's useful life is shorter than the remaining patent life, then a shorter period is used. Amortization expense is recorded as a component of cost of sales on the consolidated statements of operations and comprehensive loss.

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, which consist primarily of property and equipment and finite lived intangible assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. The Company measures recoverability of assets to be held and used by comparing the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the Company measures the impairment to be recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset, less the cost to sell. No events or changes in circumstances existed to require an impairment assessment during the three or six months ended June 30, 2022 and 2021, respectively.

Fair Value Measurements

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Financial assets and liabilities carried at fair value are classified and disclosed in one of the following three categories:

Level 1 — Quoted market prices in active markets for identical assets or liabilities.

Level 2 — Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's cash equivalents and marketable securities at June 30, 2022 and December 31, 2021 were carried at fair value, determined according to the fair value hierarchy. See Note 4 for further discussion.

The carrying amounts reflected in the consolidated balance sheets for accounts payable and accrued expenses and other current liabilities approximate their fair values due to their short-term maturities at June 30, 2022 and December 31, 2021, respectively.

Net Income (Loss) Per Share

Basic net income (loss) per share is computed by dividing the net income (loss) by the weighted-average number of common shares outstanding during the period, without consideration of potential dilutive securities. Diluted net income

(loss) per common share is computed by adjusting the weighted-average shares outstanding for the potential dilutive effects of common stock equivalents outstanding during the period calculated in accordance with the treasury stock method. For purposes of the diluted net income (loss) per share calculation, 640,318 stock options and 73,259 restricted stock units were considered to be common stock equivalents for the three and six months ended June 30, 2021. For the three and six months ended June 30, 2022, the common stock equivalents have been excluded from the calculation of diluted net income (loss) per share, as their effect would be anti-dilutive for the period presented due to the net loss incurred.

The following table includes the potential common shares that were excluded from the computation of diluted net loss per share as their effect would have been anti-dilutive for the periods indicated:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Stock options	7,176,554	5,151,118	7,176,554	4,691,373
Restricted stock units	718,107	185,176	718,107	133,286
Performance stock units	840,564	—	840,564	—
Potential common shares	8,735,225	5,336,294	8,735,225	4,824,659

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence for certain estimates or to identify matters that require additional disclosure. Subsequent events have been evaluated as required.

Application of New or Revised Accounting Standards

From time to time, new accounting pronouncements are issued by the FASB and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes-Simplifying the Accounting for Income Taxes*, or ASU 2019-12. ASU 2019-12 eliminates certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The standard is effective for annual periods beginning after December 15, 2020 and interim periods within, with early adoption permitted. Adoption of the standard requires certain changes to be made prospectively, with some changes to be made retrospectively. We have adopted ASU 2019-12 as of January 1, 2021 and the adoption of this standard did not have a material impact on the Company's financial position, results of operations and cash flows.

3. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	June 30, 2022	December 31, 2021
Research and development costs	$ 18,380	$ 17,480
Professional fees	6,844	2,163
Payroll related	6,145	8,371
Deferred financing fees	1,311	—
Royalties	116	791
Other	2,809	1,279
Accrued expenses and other current liabilities	$ 35,605	$ 30,084

4. Fair Value of Financial Assets

As of June 30, 2022 and December 31, 2021, the carrying amount of cash and cash equivalents and short-term investments was $235,596 and $294,855, respectively, which approximates fair value. Cash and cash equivalents and short-term investments includes investments in U.S. treasury securities and money market funds that invest in U.S. government securities that are valued using quoted market prices. Accordingly, money market funds and government funds are categorized as Level 1. The financial assets valued based on Level 2 inputs consist of corporate debt securities and commercial paper, which consist of investments in highly-rated investment-grade corporations.

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair value Measurements as of June 30, 2022 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Commercial Paper	$ —	$ 9,993	$ —	$ 9,993
Money Market Funds	61,167	—	—	61,167
Marketable Securities:				
Corporate Debt Securities and Commercial Paper	—	122,389	—	122,389
Other Long-term Assets:				
RareStone Common Stock	—	—	740	740
Total	$ 61,167	$ 132,382	$ 2,140	$ 195,689
Liabilities:				
Derivative on Royalty Financing	$ —	$ —	$ 1,590	$ 1,590
Total	$ —	$ —	$ 1,590	$ 1,590

	Fair value Measurements as of December 31, 2021 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Corporate Debt Securities and Commercial Paper	$ —	$ —	$ —	$ —
Money Market Funds	48,297	—	—	48,297
Marketable Securities:				
Corporate Debt Securities and Commercial Paper	—	235,607	—	235,607
Total	$ 48,297	$ 235,607	$ —	$ 283,904

The estimated fair value of the shares of RareStone equity as of our initial recording date and June 30, 2022, as well as the estimated fair value of the derivative liability related to our RIFA with HealthCare Royalty was determined using Level 3 inputs. The fair value measurement of the RareStone equity as well as the derivative liability are sensitive to changes in the unobservable inputs used to value the financial instrument. Changes in the inputs could result in changes to the fair value of each financial instrument.

The embedded derivative liability associated with our deferred royalty obligation, as discussed further in Note 10, “Long-Term Obligations”, is measured at fair value using an option pricing Monte Carlo simulation model and is included as a component of the deferred royalty obligation. The embedded derivative liability is subject to remeasurement at the end of each reporting period, with changes in fair value recognized as a component of other expense, net. The assumptions used in the option pricing Monte Carlo simulation model include: (1) our estimates of the probability and timing of related events; (2) the probability-weighted net sales of IMCIVREE, including worldwide net product sales, upfront payments, milestones and royalties; (3) our risk-adjusted discount rate that includes a company specific risk premium; (4) our cost of debt; (5) volatility; and (6) the probability of a change in control occurring during the term of the instrument.

Our RareStone equity was valued at $740 at June 30, 2022. The Company determined the estimated fair values using a discounted cash flow model under the income approach and an option pricing allocation model for the period ended June 30, 2022. Inherent in discounted cash flow and option pricing allocation models are assumptions related to the equity value of the entity, expected equity volatility, holding period, risk-free interest rate and discount for lack of marketability. The Company estimated equity volatility based on historical volatility of guideline public companies. The risk-free interest rate was based on the U.S. Treasury rates for a maturity similar to the expected holding period.

Changes in our level 3 securities for the three months ended June 30, 2022 and 2021 are as follows:

	Six months ended June 30,	
	2022	2021
Beginning aggregate estimated fair value of Level 3 securities	$ —	$ —
Initial recording of RareStone equity	1,040	—
Total realized and unrealized gains		
Unrealized gain (loss) included in other comprehensive (loss) income	(300)	—
Ending aggregate estimated fair value of Level 3 securities	$ 740	$ —

Marketable Securities

The following tables summarize the Company's marketable securities:

	June 30, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Corporate debt securities and commercial paper (due within 1 year)	$ 122,994	$ —	$ (605)	$ 122,389
	$ 122,994	$ —	$ (605)	$ 122,389

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Corporate debt securities and commercial paper (due within 1 year)	$ 235,608	$ 50	$ (51)	$ 235,607
	$ 235,608	$ 50	$ (51)	$ 235,607

5. Right Of Use Asset and Lease Liability

The Company has a material operating lease for its head office facility and other immaterial operating leases for certain equipment. The Company’s office lease has a remaining lease term of 3.0 years. The Company measured the lease liability associated with the office lease using a discount rate of 10% at inception. The Company estimated the incremental borrowing rate for the leased asset based on a range of comparable interest rates the Company would incur to borrow an amount equal to the lease payments on a collateralized basis over a similar term in a similar economic environment. As of June 30, 2022, the Company has not entered into any lease arrangements classified as a finance lease.

The Company’s corporate headquarters is located in Boston, Massachusetts. This facility houses the Company’s research, clinical, regulatory, commercial and administrative personnel. The Company’s lease agreement commenced May 2019 and has a term of six years with a five-year renewal option to extend the lease. The Company has not included the five-year renewal option to extend the lease in its measurement of the right-of-use asset or lease liability.

The following table presents the maturities of the Company's operating lease liability related to office space as of June 30, 2022, all of which is under a non-cancellable operating lease:

	Operating Lease
2022	$ 412
2023	834
2024	851
2025	502
Thereafter	—
Total operating lease payments	2,599
Less: imputed interest	341
Total operating lease liability	$ 2,258

6. Intangible Assets, Net

As of June 30, 2022, the Company's finite-lived intangible assets, which totaled $8,311 resulted from the capitalization of certain milestone payments made to Ipsen Pharma, S.A.S., or Ipsen, in accordance with the terms of the Company's license agreement with Ipsen, in connection with the Company's first commercial sale of IMCIVREE in the U.S. in March 2021 and in France in March 2022.

As of June 30, 2022, amortization expense for the next five years and beyond is summarized as follows:

2022	$ 425
2023	855
2024	855
2025	855
2026	855
Thereafter	4,466
Total	$ 8,311

The Company began amortizing its finite-lived intangible assets in April 2021 over an 11 year period based on IMCIVREE's expected patent exclusivity period. Amortization expense totaled $216, $114, $346 and $114 for the three and six months ended June 30, 2022 and 2021, respectively. Amortization expense is included in cost of sales in the condensed consolidated statements of operations and comprehensive (loss) income.

7. Income Taxes

The Company did not record a tax provision for the three and six months ended June 30, 2022 as the Company generated sufficient tax losses during the period. The Company recorded a tax (benefit) of ($5,022) and recorded a tax provision of $16,984 for the three and six month periods ended June 30, 2021, respectively, primarily related to the sale of the Rare Pediatric Disease Priority Review Voucher, or PRV, offset by a tax benefit from ordinary losses generated by the Company during the period. The Company expects to have sufficient tax losses in the current year to offset income and thus no current year liability is expected. The Company expects to maintain a full valuation allowance against its net deferred tax assets for the year.

8. Common Stock

As of June 30, 2022, an aggregate of 13,300,876 shares of common stock were reserved for future issuance under the Company's stock plans, including outstanding stock options, restricted stock units, and performance stock units that have been issued totaling 8,735,225 and 1,404,259 shares are available for future grants under the Company's 2017 Employee Stock Purchase Plan.

On February 9, 2022, the Company's board of directors adopted the Rhythm Pharmaceuticals, Inc. 2022 Employment Inducement Plan or the Inducement Plan, without stockholder approval pursuant to Rule 5635(c)(4) of the Nasdaq Stock Market LLC listing rules or Rule 5635(c)(4). In accordance with Rule 5635(c)(4), awards under the Inducement Plan may only be made to a newly hired employee who has not previously been a member of the Company's board of directors, or an employee who is being rehired following a bona fide period of non-employment by the Company or a subsidiary, as a material inducement to the employee's entering into employment with the Company or its subsidiary. An aggregate of 1,000,000 shares of the Company's common stock have been reserved for issuance under the Inducement Plan. The Company will continue to grant awards under the 2017 Plan pursuant to the terms thereof.

The exercise price of stock options granted under the Inducement Plan will not be less than the fair market value of a share of the Company's common stock on the grant date. Other terms of awards, including vesting requirements, are determined by the Company's board of directors and are subject to the provisions of the Inducement Plan. Stock options granted to employees generally vest over a four-year period but may be granted with different vesting terms. Certain options may provide for accelerated vesting in the event of a change in control. Stock options granted under the Inducement Plan expire no more than 10 years from the date of grant. As of June 30, 2022, 60,565 stock option awards have been issued under the Inducement Plan. As of June 30, 2022, 30,295 restricted stock unit awards have been granted under the Inducement Plan. As of June 30, 2022, 909,140 shares of common stock are available for future grant under the Inducement Plan.

On November 2, 2021, the Company entered into a sales agreement, or the Sales Agreement, with Cowen and Company LLC, or Cowen, as sales agent, pursuant to which the Company may, from time to time, issue and sell common stock with an aggregate value of up to $100,000 in "at-the-market" offerings, or the ATM. Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a) of the Securities Act, including sales made directly through The Nasdaq Global Market or on any other existing trading market for Company's common stock. As of June 30, 2022, there was $100,000 of common stock remaining available for sale under the ATM.

On February 9, 2021 the Company completed a public offering of 5,750,000 shares of common stock at an offering price of $30.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 750,000 additional shares of common stock. The Company received $161,731 in net proceeds after deducting underwriting discounts, commissions and offering expenses.

9. Related-Party Transactions

Expenses paid directly to consultants and vendors considered to be related parties amounted to $498, $487, $978 and $1,097 for the three and six months ended June 30, 2022 and 2021, respectively. Outstanding payments due to these related parties as of June 30, 2022 and December 31, 2021 were $66 and $50, respectively, and were included within accounts payable on the balance sheet.

10. Long-Term Obligations

On June 16, 2022, we entered into a RIFA with entities managed by HealthCare Royalty Management, LLC, collectively referred to as the Investors. Pursuant to the RIFA and subject to customary closing conditions, the Investors have agreed to pay the Company an aggregate investment amount of up to $100,000, or the Investment Amount. Under the terms of the RIFA, we received $37,500 on June 29, 2022 upon FDA approval of IMCIVREE in BBS, referred to as the Initial Investment Amount, and are entitled to receive an aggregate of up to an additional $37,500 of the Investment Amount fifteen business days after IMCIVREE receives EMA approval in BBS, and a remaining $25,000 of the Investment Amount forty-five business days following achievement of a specified amount of cumulative net sales of IMCIVREE between July 1, 2022 and September 30, 2023.

As consideration for the Investment Amount and pursuant to the RIFA, we agreed to pay the Investors a tiered royalty on our annual net revenues, or Revenue Interest, including worldwide net product sales and upfront payments and milestones. The applicable tiered percentage will initially be 11.5% on annual net revenues up to $125,000, 7.5% on annual

net revenues of between $125,000 and $300,000 and 2.5% on annual net revenues exceeding $300,000. If the Investors have not received cumulative minimum payments equal to 60% of the amount funded by the Investors to date by March 31, 2027, or 120% of the amount funded by the Investors to date by March 31, 2029, we must make a cash payment immediately following each applicable date to the Investors sufficient to gross the Investors up to such minimum amounts after giving full consideration of the cumulative amounts paid by us to the Investors through each date, referred to as the Under Performance Payment. As the repayment of the funded amount is contingent upon worldwide net product sales and upfront payments, milestones, and royalties, the repayment term may be shortened or extended depending on actual worldwide net product sales and upfront payments, milestones, and royalties.

The Investors' rights to receive the Revenue Interests will terminate on the date on which the Investors have received payments equal to a certain percentage of the funded portion of the Investment Amount including the aggregate of all payments made to the Investors as of such date, each percentage tier referred to as the Hard Cap, unless the RIFA is earlier terminated. The total Revenue Interests payable by us to the Investors is capped between 185% and 250% of the Investment Amount paid, dependent on the aggregate royalty paid between 2028 and 2032. If a change of control of occurs, the Investors may accelerate payments due under the RIFA up to the Hard Cap plus any other obligations payable under the RIFA.

The repayment period commenced on July 8, 2022 for the Initial Investment Amount, and expires on the earlier of (i) the date at which the Investors received cash payments totaling an aggregate of a Hard Cap ranging from 185% to 250% of the Initial Investment Amount or (ii) the legal maturity date of July 8, 2034. If the Investors have not received payments equal to 250% of the Investment Amount by the twelve-year anniversary of the initial closing date, we will be required to pay an amount equal to the Investment Amount plus a specific annual rate of return less payments previously received by Investors. In the event of a change of control, we are obligated to pay Investors an amount equal to the Hard Cap in effect at the time, ranging from 185% to 250% plus any Under Performance Payment of the Investment Amount less payments previously received by Investors. In addition, upon the occurrence of an event of default, including, among others, our failure to pay any amounts due to Investors under the deferred royalty obligation, insolvency, our failure to pay indebtedness when due, the revocation of regulatory approval of IMCIVREE in the U.S. or our breach of any covenant contained in the RIFA and our failure to cure the breach within the prescribed time frame, we are obligated to pay Investors an amount equal to the Hard Cap in effect at the time of default ranging from 185% to 250% plus any Under Performance Payment of the Investment Amount less payments previously received by Investors. In addition, upon an event of default, Investors may exercise all other rights and remedies available under the RIFA, including foreclosing on the collateral that was pledged to Investors, which consists of all of our present and future assets relating to IMCIVREE.

We have evaluated the terms of the RIFA and concluded that the features are similar to those of a debt instrument. Accordingly, we have accounted for the transaction as long-term debt and presented it as a deferred royalty obligation on our condensed consolidated balance sheets. We have further evaluated the terms of the RIFA and determined that the repayment of the Hard Cap in effect at the time which ranges from 185% to 250% of the Investment Amount, less any payments made to date, upon a change of control is an embedded derivative that requires bifurcation from the debt instrument and fair value recognition. We determined the fair value of the derivative using an option pricing Monte Carlo simulation model taking into account the probability of change of control occurring and potential repayment amounts and timing of such payments that would result under various scenarios, as further described in Note 2, "Summary of Significant Accounting Policies" to our condensed consolidated financial statements. The aggregate fair value of the embedded derivative liability was $1,590 as of June 30, 2022. We will remeasure the embedded derivative to fair value each reporting period until the time the features lapse and/or termination of the deferred royalty obligation. The carrying value of the deferred royalty obligation at June 30, 2022 was $34,273 based on $37,500 of proceeds, net of the fair value of the bifurcated embedded derivative liability upon execution of the RIFA, and debt issuance costs incurred. The carrying value of the deferred royalty obligation approximated fair value at June 30, 2022 and was measured using Level 3 inputs. The estimated fair market value was calculated using an option pricing Monte Carlo simulation model with inputs consistent with those used in determining the embedded derivative values as described in Note 2, "Summary of Significant Accounting Policies." The effective interest rate as of June 30, 2022 was 24%. In connection with the deferred royalty obligation, we incurred debt issuance costs totaling $1,684. Debt issuance costs have been netted against the debt and are being amortized over the estimated term of the debt using the effective interest method, adjusted on a prospective basis for changes in the underlying assumptions and inputs. The assumptions used in determining the expected repayment term

of the debt and amortization period of the issuance costs requires that we make estimates that could impact the short and long-term classification of these costs, as well as the period over which these costs will be amortized.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q. In addition to historical information, some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and is subject to the "safe harbor" created by those sections. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q, including without limitation statements regarding: our financial performance, including our expectations regarding our existing cash, operating losses, expenses and sources of future financing; our ability to hire and retain necessary personnel; patient enrollments and the timing thereof; the timing of announcements regarding results of clinical trials; our ability to protect our intellectual property; ongoing activities under and our ability to negotiate our collaboration and license agreements, if needed; our marketing, commercial sales, and revenue generation; expectations surrounding our manufacturing arrangements; the impact of the novel coronavirus, or COVID-19, pandemic on our business and operations and our future financial results; and other statements identified by words such as "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "might," "likely," "plans," "potential," "predicts," "projects," "seeks," "should," "target," "will," "would," or similar expressions and the negatives of those terms are forward-looking statements. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of known and unknown risks and uncertainties, many of which are beyond our control, and other important factors which could cause actual results to differ materially from those contemplated in such forward-looking statements. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including but not limited to those set forth in Part II, Item 1A under the heading "Risk Factors" of this Quarterly Report on Form 10-Q. Except as may be required by law, we have no plans to update our forward-looking statements to reflect events or circumstances after the date of this Quarterly Report on Form 10-Q. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made.

Overview

We are a global, a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with hyperphagia and severe obesity caused by rare melanocortin 4 receptor (MC4R) pathway diseases. Rhythm's precision medicine, IMCIVREE® (or setmelanotide), for which we have exclusive worldwide rights, has the potential to restore dysfunctional MC4R pathway signaling and MC4R pathway function. MC4R pathway deficiencies result in the disruption of satiety signals and energy homeostasis in the body, which, in turn, leads to intense feelings of hunger and to obesity. IMCIVREE is the first-ever therapy developed for patients with hyperphagia and severe obesity caused by certain rare MC4R pathway diseases that is approved or authorized in the United States, European Union (EU) or Great Britain. In the United States, IMCIVREE is approved for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency as determined by a U.S. Food and Drug Administration (FDA)-approved test demonstrating variants in *POMC*, *PCSK1* or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS), or Bardet-Biedl syndrome (BBS). In the EU and Great Britain, IMCIVREE is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. In the fourth quarter of 2022, the European Commission is anticipated to make a final decision on our Type II variation application the application to expand the indication for setmelanotide to treat obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS. In July 2022, the European Medicines Agency's (EMA) Medicinal Committee for Products for Human Use (CHMP) adopted a positive opinion, recommending this expansion of the current indication for IMCIVREE to include BBS. In addition to United States, EU and UK, we and our partners are seeking approval and or market access for IMCIVREE to treat patients with these MC4R pathway-related obesities in Argentina, Israel, China, Hong Kong and Macau.

Following FDA approval on June 16, 2022, we launched our commercial efforts to bring IMCIVREE to patients in the United States living with BBS. We are advancing efforts to achieve market access for BBS in EU member countries and the UK as well, pending EC authorization and local approvals.

We also are advancing a broad clinical development program evaluating setmelanotide in several ongoing clinical trials, and we are leveraging what we believe is the largest known DNA database focused on obesity - with approximately 45,000 sequencing samples as of December 31, 2021 - to improve the understanding, diagnosis and care of people living with severe obesity due to certain variants in genes associated with the MC4R pathway. In April 2022, we enrolled the first patient in the pivotal Phase 3 EMANATE clinical trial, a randomized, double-blind, placebo-controlled trial to evaluate setmelanotide in four independent sub-studies in patients with obesity due to a heterozygous variant of the *POMC/PCSK1* genes or *LEPR* gene or certain rare variants of the SRC1 gene or the SH2B1 gene. We also have initiated the Phase 2 DAYBREAK clinical trial designed to evaluate setmelanotide in patients who carry a confirmed variant in one or more of 10 additional genes with strong or very strong relevance to the MC4R pathway. Our broad clinical programs evaluating setmelanotide in rare MC4R pathway diseases also includes the ongoing exploratory Phase 2 Basket study, an ongoing Phase 2 study evaluating setmelanotide in patients with hypothalamic obesity, a Phase 3 study in pediatric patients with MC4R pathway deficiencies between the ages of 2 and 6 years old, and a potential registration-enabling study with our once-weekly formulation of setmelanotide. Additionally, as an FDA post-marketing requirement, we are currently evaluating the effects of setmelanotide on the QT interval corrected for heart rate, or QTc interval, in healthy volunteers. We also intend to seek input from the FDA on a pivotal Phase 3 trial in hypothalamic obesity, which we plan to initiate in early 2023.

There are currently no effective or approved treatments for these MC4R pathway related diseases. The FDA has acknowledged the importance of these results by giving setmelanotide Breakthrough Therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4R in the leptin melanocortin pathways. The Breakthrough Therapy designation currently covers indications for POMC deficiency obesity, LEPR deficiency obesity and BBS.

Additional recent clinical, regulatory and commercial updates include:

On August 2, 2022, we announced that more than 35 physicians have written more than 50 prescriptions for IMCIVREE in the first six weeks since IMCIVREE was approved by the FDA on June 16, 2022 for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to BBS.

On August 2, 2022, we announced we had completed enrollment in our Phase 3 study evaluating setmelanotide in pediatric patients with MC4R pathway deficiencies between the ages of 2 and 6 years old.

On July 22, 2022, we announced that the EMA's CHMP adopted a positive opinion, recommending to expand the current indication for IMCIVREE to include the treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS.

On July 19, 2022, we announced that the French National Agency for Medicines and Health Products Safety (ANSM) and Haute Autorité de santé (HAS) granted post-marketing authorization AP1 (autorisation d'accès précoce), or early access authorization, for setmelanotide for chronic weight management in adult and pediatric patients 6 years old and older with monogenic or syndromic obesity due to BBS.

On July 18, 2022, we announced that the National Institute for Health and Care Excellence (NICE)in the United Kingdom has issued guidance that recommends IMCIVREE as an option for treating obesity and controlling hunger caused by POMC, PCSK1 or LEPR deficiency in people 6 years of age and over, which means IMCIVREE will be funded and available for use within 90 days in the National Health Service in England and Wales.

On July 12, 2022, we announced positive interim results from the Phase 2 clinical trial evaluating setmelanotide for the treatment of severe obesity and hyperphagia in people living with hypothalamic obesity. We estimate that there are approximately 5,000 to 10,000 patients living with hypothalamic obesity in the United States.

The Phase 2 clinical trial is a multi-center, open-label, proof-of-concept study that enrolled 18 patients with hypothalamic obesity who are between 6 and 28 years old. The Phase 2 clinical trial consists of 16 weeks of treatment with setmelanotide administered once daily by subcutaneous injection, including an initial period of dose titration. The primary endpoint is the percentage of patients who achieve more than 5 percent reduction in body mass index ("BMI") from baseline after 16 weeks of treatment, compared to a historic control of less than 5 percent in this population. As of the data cutoff date of May 6, 2022, 11 patients were evaluable for assessment, including nine patients who completed 16 weeks of treatment and two patients who discontinued early.

Data highlights from the interim analysis of the full analysis set (n=11) include, as of the cutoff date of May 6, 2022:

- 100 percent of patients achieved a BMI decrease of more than 5 percent;
- 17.2 percent mean percentage change in BMI (range: -37.2 percent, -6.7 percent);
- 15.8 percent mean change (range: -34.9 percent, -6.7 percent) in body weight from baseline weight of 107.1 kgs (range: 39.0, 141.4 kgs) or 236.1 lbs; and
- 15.9 kgs (range: -28.2, -6.7) or -35.1 lbs mean weight loss from baseline.

Data highlights from the interim analysis of completers (n=9) include, as of the cutoff date of May 6, 2022:

- 19.5 mean percent change in BMI (range: -37.2 percent, -10 percent);
- 17.8 mean percent change (range: -34.9 percent, -10.7 percent) in body weight from baseline weight of 107.8 kg (range: 39.0 kgs, 141.4 kgs) or 236.1 lbs; and
- 17.8 kgs (range: -28.2, -9.5) or -37.7 lbs mean weight loss from baseline.

Setmelanotide also achieved a meaningful reduction in hunger scores. The mean change in hunger score for patients older than 12 years old who completed 16 weeks on therapy (n=7) was -2.7 on a scale of 1-10, with 10 being most hungry.

Consistent with prior clinical experience in other rare MC4R pathway diseases, setmelanotide was observed to be generally well tolerated. The most frequently reported treatment-emergent adverse events included nausea, vomiting, COVID-19, diarrhea and injection site reactions.

Of the 18 patients enrolled in this Phase 2 clinical trial, three discontinued due to adverse events, each of whom had achieved a reduction in BMI of more than 5 percent at the time they discontinued, and one patient was discontinued due to documented non-compliance to therapy. In total, 14 of the 18 patients enrolled in this Phase 2 clinical trial remained on setmelanotide therapy as of July 11, 2022. We plan to present the full data from the 18 patients enrolled in this Phase 2 clinical trial at an upcoming medical meeting in the fall of 2022.

Based on the positive interim results from the Phase 2 clinical trial, we intend to proceed to Phase 3 clinical development following consultation with regulatory agencies

On June 22, 2022, we announced the launch of IMCIVREE in Germany for patients with POMC, PCSK1 or LEPR deficiency obesity. IMCIVREE is the first precision medicine designed to induce weight loss and control of hunger that has received a lifestyle exemption from the German Federal Joint Committee, which means it is now eligible for national coverage and reimbursement. The Company also anticipates launching IMCIVREE in the U.K. and Italy for patients with POMC, PCSK1 or LEPR deficiencies.

Also on June 22, 2022, we announced that the EC authorized a variation for IMCIVREE that allows for dosing in patients aged 6 years or older with POMC or LEPR deficiency who have mild, moderate or severe renal impairment.

On June 16, 2022, we announced that the U.S. FDA approved IMCIVREE for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to BBS.

Also on June 16, 2022, we announced a non-dilutive revenue interest financing agreement, or RIFA with HealthCare Royalty Partners, LLC, or HealthCare Royalty, for a total investment amount of up to $100 million. In exchange for the total investment amount to be received by Rhythm, HealthCare Royalty will receive a tiered royalty based on global net product sales generated by IMCIVREE. For additional information, see Note 10, “Long-term Obligations” to the unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

On June 13, 2022, at the Endocrine Society Annual Meeting & Expo (ENDO), we presented new data from our long-term extension (LTE) trial, which showed continued body mass index (BMI) and weight reductions in patients with BBS or POMC or LEPR deficiency obesity (biallelic) receiving between 18 months and three years of setmelanotide therapy. Also at ENDO, we presented initial data from the LTE trial demonstrating continued BMI and weight reductions in patients with SH2B1 or SRC1 deficiency obesity, or with POMC or LEPR insufficiency obesity (heterozygous).

Our operations to date have been limited primarily to conducting research and development activities for setmelanotide. To date, we have generated less than $10.0 million of revenue from product sales and we have financed our operations primarily through the proceeds received from the sales of common and preferred stock, asset sales, as well as capital contributions from the former parent company, Rhythm Holdings LLC. From August 2015 through August 2017, we raised aggregate net proceeds of $80.8 million through our issuance of series A preferred stock. Since our initial public offering, or IPO, on October 10, 2017 and our underwritten follow-on offerings through February 2021, we have raised aggregate net proceeds of approximately $611.4 million through the issuance of our common stock after deducting underwriting discounts, commissions and offering related transaction costs. We also received $100.0 million from an asset sale, specifically in connection with the sale of our PRV. In December 2021, we entered into an Exclusive License Agreement with RareStone Group Ltd., and received $7.0 million in connection with the execution of that agreement. In June 2022, we entered into the RIFA with entities managed by HealthCare Royalty and received proceeds of $37.3 million, net of certain transaction costs at closing.

We will not generate significant revenue from product sales until we are able to successfully establish a marketing and commercialization infrastructure for IMCIVREE. IMCIVREE became commercially available to patients 6 years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency in the U.S. in the first quarter of 2021 and patients 6 years of age and older with obesity due to BBS during June 2022. Following marketing authorizations in the EU and Great Britain, we are pursuing a country-by-country strategy to establish market access and reimbursement for IMCIVREE in several countries. During March 2022, we treated the first patients with IMCIVREE in France under the paid early access program and we treated the first patients with IMCIVREE in Germany during June 2022. We expect to continue to fund our operations through the sale of equity, debt financings or other sources. We intend to build our own marketing and commercial sales infrastructure and we may enter into collaborations with other parties for certain markets outside the United States. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such other arrangements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of setmelanotide.

As of June 30, 2022 we had an accumulated deficit of $626.7 million. Our net (loss) income was ($45.0) million, ($35.4) million, ($97.8) million and $8.4 million for the three and six months ended June 30, 2022 and 2021, respectively. We expect to continue to incur significant expenses and increasing operating losses over the foreseeable future. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- continue to conduct clinical trials for setmelanotide;
- engage contract manufacturing organizations, or CMOs, for the manufacture of clinical and commercial-grade setmelanotide;
- seek regulatory approval for setmelanotide for additional indications;
- expand our clinical, regulatory, commercial and corporate infrastructure and expand operations globally;

- engage in the sales and marketing efforts necessary to support the continued commercial efforts of IMCIVREE globally;
- take into account the levels, timing and collection of revenue earned from sales of IMCIVREE and other products approved in the future, if any; and
- continue to operate as a public company.

As of June 30, 2022, our existing cash and cash equivalents and short-term investments were approximately $235.6 million. We expect that our previously announced changes to the EMANATE and DAYBREAK trials, coupled with a streamlining of our planned global network of clinical trial sites, will result in meaningful cost savings. We expect that our existing cash and cash equivalents and short-term investments will be sufficient to fund our operations into 2024, and that such existing cash and cash equivalents and short-term investments, together with the second investment tranche under the RIFA expected in the second half of 2022, will enable us to fund our operating expenses into at least the second half of 2024.

Corporate Background

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc., and as of October 2015, under the name Rhythm Pharmaceuticals, Inc.

Impact of COVID-19

We are closely monitoring how the continued spread of COVID-19 is affecting our employees, business, preclinical studies and clinical trials. In response to the COVID-19 pandemic, we have limited access to our executive offices with most employees continuing their work outside of our offices and travel has been restricted. Based on current information we do not currently anticipate any disruption in the clinical supply of setmelanotide. Our CMOs have indicated that they have appropriate plans and procedures in place to ensure uninterrupted future supply of clinical and commercial-grade setmelanotide, subject to potential limitations on their operations due to COVID-19. As a result, we do not currently expect that the COVID-19 pandemic will have a material impact on our business, results of operations and financial condition. At this time, however, there is still uncertainty relating to the trajectory of the pandemic and the impact of related responses, and disruptions caused by the COVID-19 pandemic have resulted and may in the future result in difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials and the incurrence of unforeseen costs as a result of disruptions in clinical supply or preclinical study or clinical trial delays. For example, we experienced interruption of key clinical trial activities, such as patient attendance and clinical trial site monitoring, in our Phase 3 clinical trial evaluating setmelanotide for the treatment of insatiable hunger and severe obesity in individuals with BBS or Alström syndrome. The impact of COVID-19 on our future results will largely depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, the impact of variants, evolving travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, the ultimate impact on financial markets and the global economy, the effectiveness of vaccines and vaccine distribution efforts and the effectiveness of other actions taken in the United States and other countries to contain and treat the disease. See “Risk Factors—The COVID-19 pandemic has and may continue to adversely impact our business, including our preclinical studies, clinical trials and our commercialization prospects.” in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Financial Operations Overview

Revenue

To date, we have generated less than $10.0 million of revenue from product sales. Our lead product candidate, IMCIVREE, was approved by the FDA in November 2020 for chronic weight management in adult and pediatric patients six years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency confirmed by genetic testing. IMCIVREE became commercially available in the United States in the first quarter of 2021. We recorded our first sales of IMCIVREE in the United States in March 2021 and we made our first sales in France during March 2022 under the

paid early access program. We expect our initial sales of IMCIVREE will be limited by the ultra-rare nature of the disease and limited number of diagnosed patients in the United States and throughout the rest of the world.

Cost of sales

All of our inventory of IMCIVREE produced prior to FDA approval is available for commercial or clinical use. Most of the manufacturing costs have been recorded as research and development expenses in prior periods. Accordingly, the costs for IMCIVREE included in our cost of sales for the three months ended June 30, 2022 were insignificant. We expect cost of sales to increase in 2022 as we continue to sell inventory that is produced after we began capitalizing IMCIVREE commercial inventory. We continue to evaluate the impact of this previously expensed inventory on the future cost of product sales, however we do not expect there to be a significant impact based on the cost structure of the product.

Research and development expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery and genetic sequencing efforts, and the clinical development of setmelanotide, which include:

- expenses incurred under agreements with third parties, including CROs that conduct research and development and preclinical activities on our behalf, and the cost of consultants and CMOs that manufacture drug products for use in our preclinical studies and clinical trials;
- employee-related expenses including salaries, benefits and stock-based compensation expense;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical and clinical study materials;
- the cost of genetic sequencing of potential patients in clinical studies; and
- facilities, depreciation, and other expenses, which include rent and maintenance of facilities, insurance and other operating costs.

We expense research and development costs to operations as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The following table summarizes our current research and development expenses:

	Three Months Ended June 30,		Six Months Ended June 30,	
Research and development summary	**2022**	**2021**	**2022**	**2021**
Research and development expense	$ 31,456	$ 25,104	$ 63,966	$ 45,015

We are unable to predict the duration and costs of the current or future clinical trials of our product candidates. The duration, costs, and timing of clinical trials and development of setmelanotide will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- the rate of enrollment in clinical trials;
- the safety and efficacy demonstrated by setmelanotide in future clinical trials;
- changes in regulatory requirements;

- changes in clinical trial design; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of our product candidates would significantly change the costs and timing associated with its development and potential commercialization.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our setmelanotide and other development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses to commercialization and there can be no guarantee that we can meet the funding needs associated with these expenses.

Selling, general and administrative expenses

Selling expenses consist of professional fees related to preparation for the commercialization of setmelanotide, as well as salaries and related benefits for commercial employees, including stock-based compensation. As we implement and execute our commercialization plans and start to market setmelanotide and as we explore new collaborations to develop and commercialize setmelanotide, we anticipate that these expenses will materially increase.

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, relating to our full-time employees not involved in R&D or commercial activities. Other significant costs include rent, legal fees relating to patent and corporate matters and fees for accounting, tax and consulting services.

The following table summarizes our current selling, general and administrative expenses:

	Three Months Ended June 30,		Six Months Ended June 30,	
Selling, general and administrative summary	**2022**	**2021**	**2022**	**2021**
Selling, general and administrative expense	$ 22,328	$ 15,465	$ 43,777	$ 29,983

We anticipate that our selling, general and administrative expenses will increase in the future to support continued and expanding development efforts, commercialization of IMCIVREE in the United States and the European Union as well as increased costs of operating as a global commercial stage biopharmaceutical public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, compliance with local rules and regulations in the United States and foreign jurisdictions, exchange listing and Securities and Exchange Commission (SEC) expenses, insurance and investor relations costs, among other expenses.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of revenues and expenses during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances on an ongoing basis, and material changes in these estimates could occur in the future. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

There were no significant changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Results of Operations

Comparison of the three months ended June 30, 2022 and 2021

The following table summarizes our results of operations for the three months ended June 30, 2022 and 2021, together with the changes in those items in dollars and as a percentage:

	Three Months Ended June 30,		Change	
	2022	2021	$	%
	(in thousands)			
Statement of Operations Data:				
Product revenue, net	$ 2,312	$ 274	$ 2,038	NM
License revenue	6,754	—	6,754	NM
Costs and expenses:				
Cost of sales	378	137	241	NM
Research and development	31,456	25,104	6,352	25 %
Selling, general, and administrative	22,328	15,465	6,863	44 %
Total costs and expenses	54,162	40,706	13,456	33 %
Loss from operations	(45,096)	(40,432)	(4,664)	12 %
Other income, net	95	21	74	352 %
Loss before taxes	(45,001)	(40,411)	(4,590)	11 %
Benefit from income taxes	—	(5,022)	5,022	(100)%
Net loss	$ (45,001)	$ (35,389)	$ (9,612)	27 %

NM=Not meaningful

Product revenue, net. Product revenue, net increased to $2.3 million for the three months ended June 30, 2022. There was no significant product revenue in the comparative period. The FDA approved our lead product candidate, IMCIVREE in November 2020 and we recorded our first sales of IMCIVREE in March 2021. We expect our sales of IMCIVREE to continue to increase following the FDA approval for the treatment of patients with BBS in the United States during June 2022. To date, substantially all of our product revenue has been generated in the United States. During March 2022, we completed our first sales of IMCIVREE in France through an early access program. During June 2022, we completed our first sales of IMCIVREE in Germany.

License revenue. License revenue increased to $6.8 million for the three months ended June 30, 2022 and was entirely related to the license we granted to RareStone in December 2021 to develop, manufacture, commercialize and otherwise exploit any pharmaceutical product that contains setmelanotide in the diagnosis, treatment or prevention of conditions and diseases in humans in China, including mainland China, Hong Kong and Macao. We completed our activities required to transfer the license to RareStone during three month period ending June 30, 2022, which resulted in the recognition of the license revenue. We do not expect to recognize additional license revenue related to the RareStone arrangement during 2022.

Cost of sales. Cost of sales increased to $0.4 million for the three months ended June 30, 2022. All of our inventory of IMCIVREE produced prior to FDA approval is available for commercial or clinical use. Most of the manufacturing costs have been recorded as research and development expenses in prior periods. Accordingly, the costs for IMCIVREE included in our cost of sales for the three months ended June 30, 2022 and 2021 were insignificant and primarily reflect the amortization of our capitalized sales based milestone payment made to Ipsen Pharma S.A.S., or Ipsen, upon our first commercial sale in the United States and European Union, as well as a royalty due to Ipsen on our net product sales. We expect cost of sales to increase over time as we sell inventory that is produced after we began capitalizing IMCIVREE commercial inventory.

Research and development expense. Research and development expense increased by $6.4 million to $31.5 million in 2022 from $25.1 million in 2021, an increase of 25%. The increase was primarily due to the following:

- an increase of $4.6 million in our clinical trial costs associated with new and planned clinical trials, including our Phase 2 DAYBREAK and Phase 3 EMANATE trials, Phase 3 pediatrics trial, QTc study, Phase 2 hypothalamic obesity study, and increased enrollment in our long-term extension study; these increases were partially offset by reduced activity due to the winding down of our BBS, Phase 2 Basket and GO-ID studies;

- an increase of $1.3 million in compensation and benefits due to the hiring of additional full-time employees in order to support the growth of our research and development programs and expansion of regulatory affairs operations;

- an increase of $0.7 million due to increased gene sequencing costs to support our expanded clinical programs; and

- an increase of $1.0 million in costs associated with support for regulatory filings and for clinical supply material.

The above increases were partially offset by:

- a decrease of $1.2 million in costs associated with medical affairs.

Selling, general and administrative expense. Selling, general and administrative expense increased by $6.9 million to $22.3 million in 2022 from $15.5 million in 2021, an increase of 44%. The increase was primarily due to the following:

- an increase of $5.0 million related to increased costs associated with commercial operations, sales and marketing activities for IMCIVREE in connection with preparing for the U.S approval for BBS obtained in June 2022;

- an increase of $1.0 million due to increased compensation and benefits related costs associated with additional headcount to support our expanding business operations as well as to build out our commercial operations in the United States and internationally; and

- an increase of $1.0 million due to increased costs associated with office support and insurance costs for our expanding workforce.

Other income, net. Other income increased by $0.1 million for the three months ended June 30, 2022. The increase was primarily due to improving interest rates during the period.

Provision for income taxes. There is no provision for income taxes for the three months ended June 30, 2022, as we project to generate operating losses during the year. We recorded an income tax benefit of $5.0 million as a result of the sale of our PRV during the three months ended June 30, 2021.

Net loss. Net loss increased by $9.6 million to $45.0 million for the three months ended June 30, 2022, from net loss of $35.4 million for the three months ended June 30, 2021. The increase in net loss was a result of higher costs as noted above, offset by current period revenues, and the non recurring nature of the impact of a tax benefit related to the sale of our PRV in the prior year period.

Comparison of the six months ended June 30, 2022 and 2021

The following table summarizes our results of operations for the six months ended June 30, 2022 and 2021, together with the changes in those items in dollars and as a percentage:

	Six Months Ended June 30,		Change	
	2022	2021	$	%
	(in thousands)			
Statement of Operations Data:				
Product Revenue, net	$ 3,810	$ 309	$ 3,501	NM
License revenue	6,754	—	6,754	NM
Costs and expenses:				
Cost of sales	608	141	467	NM
Research and development	63,966	45,015	18,951	42 %
Selling, general, and administrative	43,777	29,983	13,794	46 %
Total costs and expenses	108,351	75,139	33,212	44 %
Loss from operations	(97,787)	(74,830)	(22,957)	31 %
Other income, net	22	100,175	(100,153)	(100)%
(Loss) income before taxes	(97,765)	25,345	(123,110)	(486)%
Provision for income taxes	—	16,984	(16,984)	(100)%
Net (loss) income	$ (97,765)	$ 8,361	$ (106,126)	(1,269)%

NM=Not meaningful

Product revenue, net. Product revenue, net increased to $3.8 million for the six months ended June 30, 2022. There was no significant product revenue in the comparative period. The FDA approved our lead product candidate, IMCIVREE in November 2020 and we recorded our first sales of IMCIVREE in March 2021. We expect our sales of IMCIVREE to continue to increase following the FDA approval for the treatment of patients with BBS in the United States during June 2022. To date, substantially all of our product revenue has been generated in the United States. During March 2022, we completed our first sales of IMCIVREE in France through an early access program. During June 2022, we completed our first sales of IMCIVREE in Germany.

License revenue. License revenue increased to $6.8 million for the three months ended June 30, 2022 and was entirely related to the RareStone license. We completed our activities required to transfer the license to RareStone during six month period ending June 30, 2022 which resulted in the recognition of the license revenue. We do not expect to recognize additional license revenue related to the RareStone arrangement during 2022.

Cost of sales. Cost of sales increased to $0.6 million for the six months ended June 30, 2022. All of our inventory of IMCIVREE produced prior to FDA approval is available for commercial or clinical use. Most of the manufacturing costs have been recorded as research and development expenses in prior periods. Accordingly, the costs for IMCIVREE included in our cost of sales for the six months ended June 30, 2022 were insignificant and primarily reflect the amortization of our capitalized sales based milestone payment made to Ipsen Pharma S.A.S., or Ipsen, upon our first commercial sale in the United States and European Union, as well as a royalty due to Ipsen on our net product sales. We expect cost of sales to increase overtime as we sell inventory that is produced after we began capitalizing IMCIVREE commercial inventory.

Research and development expense. Research and development expense increased by $19.0 million to $64.0 million in the six months ended June 30, 2022 from $45.0 million in the six months ended June 30, 2021, an increase of 42%. The increase was primarily due to the following:

- an increase of $14.0 million in our clinical trial costs associated with new and planned clinical trials, including our Phase 2 DAYBREAK and Phase 3 EMANATE trials, Phase 3 pediatrics trial, QTc study, Phase 2 hypothalamic obesity study, and increased enrollment in our long-term extension study. These

increases were partially offset by reduced activity due to the completion and winding down of our BBS, Phase 2 Basket, renal and GO-ID studies;

- an increase of $4.2 million due to increased purchases of clinical supply material;
- an increase of $1.5 million in compensation and benefits due to the hiring of additional full-time employees in order to support the growth of our research and development programs and expansion of regulatory affairs operations;
- an increase of $1.2 million due to increased gene sequencing costs;
- an increase of $1.0 million in development milestones earned by Camurus AB, or Camurus, related to development milestone achieved related to our weekly formulation; and
- an increase of $0.5 million to support regulatory filings.

The above increases were partially offset by:

- a decrease of $3.2 million in costs associated with medical affairs.

Selling, general and administrative expense. Selling, general and administrative expense increased by $13.8 million to $43.8 million in the six months ended June 30, 2022 from $30.0 million in the six months ended June 30, 2021, an increase of 46%. The increase was primarily due to the following:

- an increase of $7.3 million related to increased costs associated with commercial operations, sales and marketing activities for IMCIVREE in connection with preparing for the U.S approval for BBS obtained in June 2022;
- an increase of $4.4 million due to increased compensation and benefits related costs associated with additional headcount to support our expanding business operations as well as to build out our commercial operations in the United States and internationally; and
- an increase of $2.0 million due to increased costs associated with information technology, international office space, sponsorships and general corporate travel related expenses for our expanding workforce.

Other income, net. Other income decreased by $100.1 million in the six months ended June 30, 2022. The decrease was primarily due to the sale of our PRV in February 2021. The sale of our PRV in the prior year was a non-recurring transaction.

Provision for income taxes. There is no provision for income taxes for the six months ended June 30, 2022, as we project to generate operating losses during the year. We recorded a provision for income taxes of $17.0 million as a result of the sale of our PRV during the six months ended June 30, 2021.

Net (loss) income. Net loss increased by $106.1 million to $97.8 million for the six months ended June 30, 2022, from net income of $8.4 million for the six months ended June 30, 2021. The increase in net loss was primarily a result of the non-recurring nature of our PRV sale in 2021, which resulted in $100.0 million of other income during the prior year period, as well as higher costs in the current year as noted above.

Liquidity and Capital Resources

As of June 30, 2022, our cash and cash equivalents and short-term investments were approximately $235.6 million.

Cash flows

The following table provides information regarding our cash flows for the six months ended June 30, 2022 and 2021:

	Six Months Ended June 30,	
	2022	2021
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (92,441)	$ (65,371)
Investing activities	108,501	(132,187)
Financing activities	37,899	165,968
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 53,959	(31,590)

Net cash used in operating activities

The use of cash in all periods resulted primarily from our net (loss) income adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was $92.4 million for the six months ended June 30, 2022 and consisted primarily of a net loss of $87.3 million adjusted for non-cash items, which consisted of non-cash stock-based compensation, depreciation and amortization and rent expense. The change in operating assets and liabilities reflected a total use of cash of approximately $4.5 million from a decrease in other long-term assets, prepaid expenses and other current assets coupled with a $0.6 million decrease in accounts payable, deferred revenue and accrued expenses and other current liabilities.

Net cash used in operating activities was $65.4 million for the six months ended June 30, 2021 and consisted primarily of a net loss of $63.4 million adjusted for non-cash items, which consisted of non-cash stock-based compensation, the gain on the sale of the PRV, a deferred provision for income taxes, depreciation and amortization and rent expense. The change in operating assets and liabilities reflected a total use of cash of approximately $0.6 million from an increase in accounts payables and accrued expenses associated with our CROs, CMOs, and consultants due to the timing of payments, coupled with an increase of $1.2 million in prepaid expenses.

Net cash provided by (used in) investing activities

Net cash provided by investing activities was $108.5 million for the six months ended June 30, 2022 and relates to $163.1 million of maturities of short-term investments, partially offset by $50.4 million of purchases of short-term investments, a $4.0 million milestone obligation payment under our license agreement with Ipsen and $0.2 million related to the purchase of property plant and equipment.

Net cash used in investing activities was $132.2 million for the six months ended June 30, 2021 and relates to $226.9 million of net purchases of short-term investments and $5.0 million for the acquisition of an intangible asset, partially offset by the $100.0 million in proceeds from the sale of the PRV.

Net cash provided by financing activities

Net cash provided by financing activities was $37.9 million for the six months ended June 30, 2022, which represents the net proceeds from the RIFA coupled with the net proceeds of the issuance of common stock from our 2017 Employee Stock Purchase Plan, or the ESPP.

Net cash provided by financing activities was $166.0 million for the six months ended June 30, 2021, which represents the net proceeds of $161.7 million from our common stock offering in February 2021 and $4.2 million of cash proceeds from the exercise of stock options and the issuance of common stock from the ESPP.

Revenue Interest Financing Agreement

On June 16, 2022, we announced a non-dilutive revenue interest financing agreement, or RIFA, with HealthCare Royalty Partners, LLC, or HealthCare Royalty, for a total investment amount of up to $100 million. In exchange for the total investment amount to be received by Rhythm, HealthCare Royalty will receive a tiered royalty based on global net product sales generated by IMCIVREE. For additional information, see Note 10, “Long-term Obligations” to the unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q .

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical development of and seek marketing approval for setmelanotide for future indications, and build out our global organization. In addition, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. We also expect to incur additional costs associated with operating as a public company.

We expect that our existing cash and cash equivalents and short-term investments will be sufficient to fund our operations into 2024, and that such existing cash and cash equivalents and short-term investments, together with the second investment tranche under the RIFA expected in the second half of 2022, will enable us to fund our operating expenses into at least the second half of 2024. We may need to obtain substantial additional funding in connection with our research and development activities and any continuing operations thereafter. If we are unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the cost to commercialize setmelanotide, by building an internal sales force or entering into collaborations with third parties and providing support services for patients;
- the scope, progress, results and costs of clinical trials for our setmelanotide program;
- the costs, timing and outcome of regulatory review of our setmelanotide program;
- the obligations owed to Ipsen, Camurus and Takeda pursuant to our license agreements;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain additional collaborations on favorable terms, if at all; and
- the costs of operating as a public company, including those resulting from losing our emerging growth company status.

Although IMCIVREE has been approved by the FDA and authorized by the EC and Great Britain in certain indications, IMCIVREE may not achieve commercial success. In addition, developing our setmelanotide program is a time-consuming, expensive and uncertain process that may take years to complete, and we may never generate the necessary data or results required to obtain future marketing approvals and achieve product sales. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

In addition, the magnitude and duration of the COVID-19 pandemic and its impact on our liquidity and future funding requirements is uncertain as of the filing date of this Quarterly Report as this continues to evolve globally. See "Impact of COVID-19" above and "Risk Factors— The COVID-19 pandemic has and may continue to adversely impact our business, including our preclinical studies, clinical trials and our commercialization prospects." in Part II, Item 1A of this Quarterly Report for a further discussion of the possible impact of the COVID-19 pandemic on our business.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, involves agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties or other means, we may have to relinquish valuable rights to our setmelanotide program on terms that may not be favorable to us. If we are unable to raise additional funds through equity, debt financings or other means, when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our setmelanotide program that we would otherwise prefer to develop and market ourselves.

Contractual obligations

As of June 30, 2022, apart from additional contractual obligations under our RIFA as disclosed in Note 10, "Long-Term Obligations", to the unaudited condensed consolidated financial statements included under Part I, Item 1 of this Quarterly Report on Form 10-Q, there were no other material changes to our principal contractual obligations and commitments as reported in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Recent Accounting Pronouncements

For a discussion of pending and recently adopted accounting pronouncements, see Note 2 to our unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

As of June 30, 2022, there were no material changes to our quantitative and qualitative disclosures about market risks as reported in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Item 4. Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their cost.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a- 15(e) and 15d- 15(e) under the Securities Exchange Act of 1934, as amended), as of the end of the period covered by this Quarterly Report on Form

10-Q. Based on such evaluation, our principal executive officer and principal financial officer have concluded that as of June 30, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the most recent fiscal quarter covered by this Quarterly Report on Form 10-Q that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 1A. Risk Factors

Our operations and financial results are subject to various risks and uncertainties, including those described below, which could adversely affect our business, financial condition, results of operations, cash flows, and the trading price of our common stock. Additional risks and uncertainties that we currently do not know about or that we currently believe to be immaterial may also impair our business. You should carefully consider the risks described below and the other information in this Annual Report, including our audited consolidated financial statements and the related notes thereto, and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Risks Related to Our Financial Position and Need for Capital

We are a commercial stage biopharmaceutical company with a limited operating history and have not generated significant revenue from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability.

We are a commercial stage biopharmaceutical company with a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in February 2013. Our operations to date have been primarily on acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting research and development activities, including clinical trials, for setmelanotide. To date we have generated less than $10.0 million of revenue from product sales. We have obtained FDA approval for IMCIVREE for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin, or POMC, proprotein convertase subtilisin/kexin type 1, or PCSK1, or leptin receptor, or LEPR, deficiency confirmed by FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, and due to Bardet-Biedl syndrome, or BBS. IMCIVREE has also received marketing authorization from the European Commission and Great Britain's Medicines and Healthcare Products Regulatory Agency, or MHRA for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. A variation of IMCIVREE has also received marketing authorization from the European Commission for dosing in patients with POMC or LEPR deficiency who have mild, moderate or severe renal impairment. We have not obtained any other regulatory approvals for setmelanotide. We first commercialized IMCIVREE in the U.S. in the first quarter of 2021 and therefore do not have a long history operating as a commercial company. We are continuing to transition from a company with a research and development focus to a company capable of supporting commercial activities and we may not be successful in such transition. We are still at the early stages of demonstrating our ability to manufacture at commercial scale, or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Since our inception, we have focused substantially all of our efforts and financial resources on the research and development of setmelanotide, which is approved by the FDA and authorized by the European Commission and the MHRA, as noted above, and is in development to address patients affected by several other indications. We have funded our operations to date primarily through the proceeds from the sales of common stock and preferred stock, asset sales, as well as capital contributions from our former parent, Rhythm Holdings LLC, and have incurred losses in each year since our inception.

Our net (loss) income was ($45.0) million, ($35.4) million, ($97.8) million and $8.4 million for the three and six months ended June 30, 2022 and 2021, respectively. As of June 30, 2022, we had an accumulated deficit of $626.7 million. Substantially all of our operating losses have resulted from costs incurred in connection with our development programs and from commercial and general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of setmelanotide and development of any other product candidates we may choose to pursue. In addition, having obtained marketing approval for IMCIVREE, we expect to continue to incur significant sales, marketing and outsourced manufacturing expenses. We have and will continue to incur additional costs associated with operating as a public company, including as a result of no longer qualifying as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date we have generated less than $10.0 million of revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- continue to commercialize setmelanotide by building a commercial organization and/or entering into collaborations with third parties;
- ensure setmelanotide is available to patients;
- continue to achieve market acceptance of setmelanotide in the medical community and with third-party payors;
- continue to initiate and successfully complete later-stage clinical trials that meet their clinical endpoints;
- continue to initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approvals for setmelanotide as a treatment for obesity caused by genetic deficiencies affecting the MC4R pathway; and
- successfully manufacture or contract with others to manufacture setmelanotide.

Absent our entering into collaboration or partnership agreements, we have and expect to continue to incur significant sales and marketing costs as we prepare to commercialize setmelanotide. Even though IMCIVREE is FDA approved for chronic weight management in patients 6 years of age and older with monogenic or syndromic obesity due to POMC, PCSK1, or LEPR, deficiency confirmed by FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, and due to BBS and authorized in the EU and Great Britain for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above, and authorized in the EU for treatment of patients with POMC or LEPR deficiency who have mild, moderate or severe renal impairment, and even if we successfully complete our pivotal and other clinical trials and setmelanotide is approved for commercial sale in additional indications, setmelanotide may not be a commercially successful drug. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate

significant product revenue, we will not become profitable and will be unable to continue operations without continued funding.

We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently in the early stages of commercializing IMCIVREE for chronic weight management in patients with obesity due to POMC, PCSK1 or LEPR deficiencies in the U.S. and the EU and Great Britain and advancing setmelanotide through clinical development for additional indications in the United States and for potential approvals in other countries. Developing peptide therapeutic products is expensive and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance setmelanotide in additional clinical trials. We intend to use our available cash resources to advance the clinical development of setmelanotide, for disease-education and community-building activities, patient identification, and commercialization activities related to IMCIVREE. Depending on the status of additional regulatory approvals and commercialization of setmelanotide, as well as the progress we make in any sales of IMCIVREE, we may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter. We may also need to raise additional funds if we choose to pursue additional indications and/or geographies for setmelanotide or otherwise expand more rapidly than we presently anticipate.

From August 2015 through August 2017, we raised aggregate net proceeds of $80.8 million through our issuance of series A preferred stock. In connection with our initial public offering, or IPO, in October 2017 and our underwritten follow-on offerings through February 2021, we raised aggregate net proceeds of approximately $611.4 million through the issuance of our common stock after deducting underwriting discounts, commissions and offering related transaction costs. Since inception, we have received a further $100.0 million from asset sales, specifically in connection with the sale of our Rare Pediatric Disease Priority Review Voucher, or PRV, to Alexion Pharmaceuticals, Inc. In June 2022, we entered into the RIFA with HealthCare Royalty for a total investment amount of up to $100 million, conditioned upon our achievement of certain clinical development and sales milestones. As of June 30, 2022, our cash and cash equivalents and short-term investments were approximately $235.6 million. We expect that our existing cash and cash equivalents and short-term investments will be sufficient to fund our operations into 2024, and that such existing cash and cash equivalents and short-term investments, together with the second investment tranche under the RIFA expected in the second half of 2022, will enable us to fund our operating expenses into at least the second half of 2024. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. We will also require additional capital to obtain additional regulatory approvals for, and to continue to commercialize, setmelanotide. Raising funds in the current economic environment, particularly in light of ongoing uncertainty related to the COVID-19 pandemic, supply chain issues and labor shortages, rising inflation and international turmoil due to the Russian invasion of Ukraine, may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize setmelanotide. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or other third parties at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to setmelanotide or technologies or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of setmelanotide or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations.

Our Revenue Interest Financing Agreement with Healthcare Royalty Partners could restrict our ability to commercialize IMCIVREE, limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations.

On June 16, 2022, we entered into the RIFA, with entities managed by HealthCare Royalty Management, collectively referred to as the Investors. Pursuant to the RIFA and subject to customary closing conditions, the Investors have agreed to pay the Company an aggregate investment amount of up to $100.0 million, or the Investment Amount. Under the terms of the RIFA, we received $37.5 million on June 29, 2022 upon FDA approval of IMCIVREE in BBS, and are entitled to receive an aggregate of up to an additional $37.5 million of the Investment Amount fifteen business days after IMCIVREE receives EMA approval in BBS, and a remaining $25.0 million of the Investment Amount forty-five business days following achievement of a specified amount of cumulative net sales of IMCIVREE between July 1, 2022 and September 30, 2023.

As consideration for the Investment Amount and pursuant to the RIFA, we agreed to pay the Investors a tiered royalty on our annual net revenues, or Revenue Interest, including worldwide net product sales and upfront payments and milestones. The applicable tiered percentage will initially be 11.5% on annual net revenues up to $125 million, 7.5% on annual net revenues of between $125 million and $300 million and 2.5% on annual net revenues exceeding $300 million. If the Investors have not received cumulative minimum payments from equal to 60% of the amount funded by the Investors to date by March 31, 2027 or 120% of the amount funded by the Investors to date by March 31, 2029, we must make a cash payment immediately following each applicable date to the Investors sufficient to gross the Investors up to such minimum amounts after giving full consideration of the cumulative amounts paid by us to the Investors through each date.

The Investors' rights to receive the Revenue Interests will terminate on the date on which the Investors have received payments equal to a certain percentage of the funded portion of the Investment Amount including the aggregate of all payments made to the Investors as of such date, each percentage tier referred to as the Hard Cap, unless the RIFA is earlier terminated. The total Revenue Interests payable by us to the Investors is capped between 185% and 250% of the Investment Amount paid to us, dependent on the aggregate royalty paid between 2028 and 2032. If a change of control of occurs, the Investors may accelerate payments due under the RIFA up to the Hard Cap plus any other obligations payable under the RIFA.

Our obligations under the RIFA could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing or enter into IMCIVREE partnership agreements;
- requiring the dedication of a portion of our cash flow from operations to service our indebtedness, which will reduce the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital; and
- if we fail to comply with the terms of the RIFA, resulting in an event of default that is not cured or waived, Investors could seek to enforce their security interest in our cash and cash equivalents and all assets relating to IMCIVREE that secures such indebtedness.

To the extent we incur additional debt (including without limitation additional amounts under the Revenue Interest Financing Agreement), the risks described above could increase.

Risks Related to the Development of Setmelanotide

Positive results from early clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for, and commercialize additional indications for setmelanotide.

Positive results from any of our Phase 1, Phase 2, or Phase 3 clinical trials of setmelanotide, or initial results from other clinical trials of setmelanotide, may not be predictive of the results of later clinical trials. The duration of effect of setmelanotide tested in our Phase 1 and Phase 2 clinical trials was often for shorter periods than in our pivotal Phase 3 clinical trials. The duration of effect of setmelanotide has only been studied in long-term durations for a small number of patients in our Phase 2 and Phase 3 clinical trials and safety or efficacy issues may arise when more patients are studied in longer trials and on commercial drug. It is possible that the effects seen in short-term clinical trials will not be replicated in long-term or larger clinical trials. In addition, not all of our trials demonstrated statistically significant weight loss and there can be no guarantee that future trials will do so.

Positive results for one indication are not necessarily predictive of positive results for other indications. We have demonstrated statistically significant and clinically meaningful reductions in weight and hunger in Phase 3 clinical trials in obesity due to POMC, PCSK1 or LEPR deficiencies and BBS, and believe we have demonstrated proof of concept in Phase 2 clinical trials in impairments due to a variant in one of the two alleles in the *POMC*, *PCSK1*, or *LEPR* genes (HET obesity), as well as the SRC1 and SH2B1 genes, all genetic diseases of extreme and unrelenting appetite and obesity. We hypothesize that patients with other upstream genetic variants in the MC4R pathway may also respond with reductions in weight and hunger after treatment with setmelanotide. However, patients with other upstream genetic variants may not have a similar response to setmelanotide, and until we obtain more clinical data in other genetic variants, we will not be sure that we can achieve proof of concept in such indications.

We are actively working to advance additional genetic variants related to the MC4R pathway through our clinical development program. Our continued development efforts are focused on obesity related to several single gene related, or monogenic, MC4R pathway impairments: BBS; HET obesity due to a genetic variant in one of the two alleles of the *POMC*, *PCSK1* or *LEPR* gene, or HETs; obesity due to steroid receptor coactivator 1, or SRC1, variants; obesity due to SH2B adapter protein 1, or SH2B1; hypothalamic obesity; and MC4R deficiency obesity. For example, in April 2022 we enrolled the first patient our pivotal Phase 3 EMANATE clinical trial of setmelanotide. The trial is a randomized, double-blind, placebo-controlled study with four independent sub-studies evaluating setmelanotide in patients with: heterozygous POMC/PCSK1 obesity; heterozygous LEPR obesity; certain variants of the SRC1; or certain variants of SH2B1 genes. After receiving feedback from the FDA in April 2022 that indicated that additional clinical trials to support potential registration for non-rare patient populations would likely be required, we eliminated a fifth sub-study intended to evaluate setmelanotide in patients with a PCSK1 N221D variant. Each of the four sub-studies will be entirely independent of the others and, if successful, is designed to support separate regulatory submissions to the FDA and EMA in each studied indication. However, the FDA and EMA may not view positive results in one sub-study, even if such results are statistically significant and clinically meaningful, as being sufficient for approval for any given indication.

Success in a basket trial, or any trial in one indication, may not predict success in another indication. In contrast, in the event of an adverse safety issue, clinical hold, or other adverse finding in one or more indications being tested, such event could adversely affect our trials in the other indications and may delay or prevent completion of such clinical trials.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials after achieving positive results in early stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway.

Additionally, setbacks may be caused by new safety or efficacy observations made in clinical trials, including previously unreported adverse events, or AEs. Moreover, preclinical and clinical data are often susceptible to varying

interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA approval or a marketing authorization from the European Commission or foreign regulatory authorities. If we fail to obtain positive results in our Phase 3 clinical trials of setmelanotide, the development timeline and regulatory approval and commercialization prospects for setmelanotide and, correspondingly, our business and financial prospects, would be materially adversely affected.

Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published or reported. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

The number of patients suffering from each of the MC4R pathway variants we are targeting is small and has not been established with precision. If the actual number of patients is smaller than we estimate, our revenue and ability to achieve profitability may be materially adversely affected.

Due to the rarity of our target indications, there is no comprehensive patient registry or other method of establishing with precision the actual number of patients with MC4R pathway deficiencies. As a result, we have had to rely on other available sources to derive clinical prevalence estimates for our target indications. In addition, we have internal genetic sequencing results from individuals with severe obesity that provide another approach to estimating prevalence. As of December 31, 2021, our database had approximately 45,000 sequencing samples. Since the published epidemiology studies for these genetic variants are based on relatively small population samples, and are not amenable to robust statistical analyses, it is possible that these projections may significantly exceed the addressable population, particularly given the need to genotype patients to definitively confirm a diagnosis.

Based on multiple epidemiological methods, we have estimated the potential addressable patient populations with these MC4R pathway deficiencies based on the following sources and assumptions:

- *POMC Deficiency Obesity*. POMC Deficiency Obesity is defined by the presence of biallelic variants in the *POMC* or *PCSK1* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS). Our addressable patient population estimate for POMC deficiency obesity is approximately 100 to 500 patients in the United States, with a comparable addressable patient population in Europe. Our estimates are based on:
  - approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency obesity is often unavailable and currently is rarely performed;
  - our belief, based on discussions with experts in rare diseases, that the number of diagnosed cases could increase several-fold with increased awareness of this deficiency and the availability of new treatments;
  - U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for adults with severe obesity (body mass index, or BMI, greater than 40 kg/m2) and for children with severe early-onset obesity (99th percentile at ages two to 17 years old); and
  - our internal sequencing yield for POMC deficiency obesity patients (including both *POMC* and *PCSK1* gene diseases), defined as patients having biallelic variants in the *POMC* or *PCSK1* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS), of approximately 0.05%.
- *LEPR Deficiency Obesity*. LEPR Deficiency Obesity is defined by the presence of biallelic variants in the *LEPR* gene that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS). Our addressable patient population estimate for LEPR deficiency obesity is approximately 500 to 2,000 patients in the United States, with a comparable addressable patient population in Europe. Our estimates are based on:
  - epidemiology studies on LEPR deficiency obesity in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity;
  - U.S. Census Bureau figures for adults and children and CDC prevalence numbers for adults with severe obesity (BMI, greater than 40 kg/m2) and for children with severe early-onset obesity (99th percentile at ages two to 17 years old);
  - with wider availability of genetic testing expected for LEPR deficiency obesity and increased awareness of new treatments, our belief that up to 40% of patients with these diseases may eventually be diagnosed; and
  - our internal sequencing yield for LEPR deficiency obesity patients, defined as patients having biallelic variants in the *LEPR* gene that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS), of approximately 0.09%.

- *Bardet-Biedl Syndrome*. Our addressable patient population estimate for BBS is approximately 1,500 to 2,500 patients in the United States based on:
  - published prevalence estimates of one in 100,000 in North America, which projects to approximately 3,250 people in the United States. We believe the majority of these patients are addressable patients; and
  - our belief that with wider availability of genetic testing expected for BBS and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.
- *POMC, PCSK1, or LEPR Heterozygous Obesities; SRC1 and SH2B1 Obesities*. Our potential setmelanotide-responsive patient population estimate for POMC, PCSK1, or LEPR heterozygous, SRC1 and SH2B1 obesity patients with at least one variant interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS) suspected pathogenic is approximately 53,000 patients in the United States. Our estimates are based on:
  - U.S. Census Bureau population data and CDC prevalence numbers for early onset obesity (120% the 95th percentile between the ages of 2-5 years);
  - our internal sequencing yield of patients with POMC, PCSK1, or LEPR heterozygous, SRC1 or SH2B1 variants interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS) of approximately 10-15%; and
  - a clinical response rate of 40% for patients carrying pathogenic or likely pathogenic variants, and 20% for patients carrying a variant of uncertain significance (VUS).

The clinical response rate used in this calculation is based on the clinical data currently available to us from our trials and may change as more data become available.

- *MC4R Deficiency Obesity*. Our addressable patient population estimate for MC4R-rescuable deficiency obesity is approximately 10,000 patients in the United States. This estimate is based on:
  - U.S. Census Bureau population data and CDC prevalence numbers for early onset obesity (120% the 95th percentile between the ages of 2-5 years);
  - a comprehensive ongoing biochemical screening study indicating there may be a defined subset of individuals who carry MC4R variants that may be rescued by an MC4R agonist; and
  - our internal sequencing yield for MC4R deficiency obesity patients of approximately 2.0% prior to application of functional filters.
- *Hypothalamic obesity*. Our addressable patient population estimate for hypothalamic obesity (HO) is 5,000 to 10,000 patients in the United States. This estimate is based on:
  - diagnosis of an underlying HO etiology such as craniopharyngioma (CP), astrocytoma, or other brain tumors with CP accounting for approximately 50% of HO etiologies;
  - an annual incidence of craniophryngioma (CP) of approximately 1.3 million to 2.2 million per year in the United States, which projects to approximately 600 cases of CP per year based on a United States population of approximately 329 million;
  - approximately 50% (based on a published range of 6% to 91%) of CP patients develop HO;
  - published estimates of overall survival (OS) after CP diagnosis, with a 20-year OS of 84%;

- allowing for patients that develop HO due to other factors besides CP, results in an estimated HO prevalence after CP diagnosis in the United States exceeding 2,500-7,500 patients; and

- internal Company estimate is based on reported incidence of hypothalamic obesity following craniophryngioma and long-term survival rates.

We believe that the patient populations in the EU are at least as large as those in the United States. However, we do not have comparable epidemiological data from the EU and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

Defining the exact genetic variants that result in MC4R pathway diseases is complex, so if any approval that we obtain is based on a narrower definition of these patient populations than we had anticipated, then the potential market for setmelanotide for these indications will be smaller than we originally believed. In either case, a smaller patient population in our target indications would have a materially adverse effect on our ability to achieve commercialization and generate revenues.

If we experience delays or difficulties in the enrollment and/or retention of patients in clinical trials, our regulatory submissions or receipt of additional marketing approvals could be delayed or prevented.

We may not be able to initiate or continue our planned clinical trials on a timely basis or at all for our product candidates if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these trials through completion of such trials as required by the FDA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

Our clinical trials will compete with other clinical trials that are in the same therapeutic areas as our product candidates, including general obesity, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. In addition, there are limited patient pools from which to draw for clinical studies. In addition to the rarity of genetic diseases of obesity, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. Patient enrollment for our current or any future clinical trials may be affected by other factors, including:

- size and nature of the patient population;

- severity of the disease under investigation;

- availability and efficacy of approved drugs for the disease under investigation;

- patient eligibility criteria for the trial in question as defined in the protocol;

- perceived risks and benefits of the product candidate under study;

- clinicians’ and patients’ perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or future product candidates being investigated for the indications we are investigating;

- clinicians’ willingness to screen their patients for genetic markers to indicate which patients may be eligible for enrollment in our clinical trials;

- delays in or temporary suspension of the enrollment of patients in our planned clinical trial due to the COVID-19 pandemic;
- ability to obtain and maintain patient consents;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion, including as a result of contracting COVID-19 or other health conditions or being forced to quarantine, or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials.

In addition, the pediatric population is an important patient population for setmelanotide, and our addressable patient population estimates include pediatric populations. However, it may be more challenging to conduct studies in younger participants, and to locate and enroll pediatric patients. These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may also result in increased development costs for setmelanotide and any future product candidates and jeopardize our ability to obtain additional marketing approvals for the sale of setmelanotide. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

Failures or delays in the commencement or completion of our planned clinical trials of setmelanotide could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

Successful completion of our ongoing and planned clinical trials is a prerequisite to submitting an NDA or NDA supplement to the FDA, an MAA to the EMA, and other applications for marketing authorization to equivalent competent authorities in foreign jurisdictions, and consequently, successful completion of such trials, at a minimum will be required for regulatory approvals and the commercial marketing of setmelanotide.

We do not know whether our planned clinical trials will begin or whether any of our clinical trials will be completed on schedule, if at all, as the commencement and successful completion of clinical trials can be delayed or prevented for a number of reasons, including but not limited to:

- inability to generate sufficient preclinical or other in vivo or *in vitro* data to support the initiation of clinical studies;
- delays in the completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA's good laboratory practice requirements and other applicable regulations;
- the FDA or other equivalent competent authorities in foreign jurisdictions may deny permission to proceed with our ongoing or planned trials or any other clinical trials we may initiate, or may place a clinical trial on hold or be suspended;
- delays in filing or receiving authorization to proceed under an additional investigational new drug application, or IND, or similar foreign application if required;
- delays in reaching a consensus with the FDA and other regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials;

- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- difficulties in obtaining Institutional Review Board, or IRB, and/or ethics committee approval to conduct a clinical trial at a prospective site or sites;

- since many already diagnosed patients are at academic sites, delays in conducting clinical trials at academic sites due to the particular challenges and delays typically associated with those sites, as well as the lack of alternatives to these sites which have already diagnosed patients;

- inadequate quantity or quality of setmelanotide or other materials necessary to conduct clinical trials, including delays in the manufacturing of sufficient supply of finished drug product;

- challenges in identifying, recruiting and training suitable clinical investigators;

- challenges in recruiting and enrolling suitable patients to participate in clinical trials;

- severe or unexpected drug related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials;

- difficulty collaborating with patient groups and investigators;

- failure by our CROs, other third parties or us to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements, or GCPs, or applicable regulatory guidelines in other countries;

- occurrence of adverse events associated with setmelanotide that are viewed to outweigh its potential benefits, or occurrence of adverse events in trial of the same or similar class of agents conducted by other companies;

- changes to the clinical trial protocols;

- clinical sites deviating from trial protocol or dropping out of a trial;

- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;

- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;

- the cost of clinical trials of our product candidates being greater than we anticipate;

- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates; and

- development of antibodies to the drug or adjuvants may result in loss of efficacy or safety events.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial

may be suspended or terminated by us, the FDA or other equivalent competent authorities in foreign jurisdictions, the IRB at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board, or DSMB, or Safety Monitoring Committee, or SMC, overseeing the clinical trial at issue or other equivalent competent authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other equivalent competent authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical trial supply materials; and
- lack of adequate funding to continue the clinical trial.

Delays in the completion of any preclinical studies or clinical trials of setmelanotide will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of a regulatory approval for setmelanotide. Any delays to our preclinical studies or clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize setmelanotide and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

The COVID-19 pandemic has and may continue to adversely impact our business, including our preclinical studies, clinical trials and our commercialization prospects.

The COVID-19 pandemic has spread to multiple countries and regions, including the United States, Canada, Europe, and China, where we have planned or ongoing preclinical studies and clinical trials. Governments from many countries have established stay at home measures including, among other things, the prohibition of public gatherings and restrictions on domestic and international travel. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. In response to the spread of COVID-19, we have limited access to our principal executive office with most employees continuing their work outside of our office and restricted travel. In addition, we experienced interruption of key clinical trial activities, such as patient attendance and clinical trial site monitoring, in our Phase 3 clinical trial evaluating setmelanotide for the treatment of insatiable hunger and severe obesity in individuals with BBS or Alström syndrome. If the COVID-19 pandemic continues for a significant length of time, we may experience additional disruptions that could severely impact our business, preclinical studies, clinical trials and our commercialization prospects, including:

- delays in receiving approval from local regulatory authorities to initiate or conduct our planned clinical trials;
- further delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;

- further delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- further interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruptions or delays in preclinical studies due to restricted or limited operations at our research and development laboratory facility;
- interruptions or delays in manufacturing activities due to restricted or limited operations at our CMOs;
- delays in global shipping of raw materials, API, and/or finished goods between locations;
- interruptions or delays in delivery of clinical trial ancillary supplies, due to restricted or limited operations;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- continued limitations in employee resources that would otherwise be focused on the start-up or conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people, or due to increased hiring and/or retention or other staffing issues;
- refusal of the FDA or foreign regulatory authorities to accept data from clinical trials in affected geographies;
- impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans; and
- delays in the receipt of marketing authorizations for our product candidates, which could materially affect our commercialization plans.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the pandemic impacts our business, preclinical studies, clinical trials and our commercialization prospects will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration and severity of the pandemic, the impact of the variants, travel restrictions and social distancing recommendations and regulations in the United States and other countries, business closures or business disruptions, the effectiveness of vaccines, vaccine distribution efforts and treatments, and the effectiveness of other actions taken in the United States and other countries to contain and treat the disease. While the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, the recession or economic downturn resulting from the spread of COVID-19 could materially affect our business.

Setmelanotide may cause undesirable side effects that could delay or prevent additional regulatory approvals, limit the commercial profile of approved labeling, or result in significant negative consequences following marketing approval.

First generation MC4R agonists were predominantly small molecules that failed in clinical trials due to significant safety issues, particularly increases in blood pressure, and had limited efficacy. Undesirable side effects caused by setmelanotide could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive labeling or the delay or denial of additional regulatory approvals by the FDA or other equivalent competent authorities in foreign jurisdictions. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may adversely affect our business, financial condition and prospects significantly.

Setmelanotide is an MC4R agonist. Potential side effects of MC4R agonism, which have been noted either with setmelanotide or with other MC4R agonists in clinical trials and preclinical studies, may include:

- adverse effects on cardiovascular parameters, such as increases in heart rate and blood pressure;
- erections in males and similar effects in women, such as sexual arousal, clitoral swelling and hypersensitivity;
- nausea and vomiting;
- reduced appetite;
- headache;
- effects on mood, depression, anxiety and other psychiatric manifestations; and
- other effects, for which most investigators reported as unrelated to setmelanotide and for which no increased incidence or pattern is currently evident.

In addition, injection site reactions have been seen in subcutaneous, or SC, injections with setmelanotide. In addition, setmelanotide has likely off target effects on the closely related MC1 receptor, which mediates tanning in response to sun exposure. Other MC1 receptor mediated effects include darkening of skin blemishes, such as freckles and moles, and hair color change. The cosmetic effects are not tolerated by all patients, as a small number of patients have withdrawn from treatment due to skin darkening. These effects have generally been reversible in clinical trials after discontinuation of setmelanotide, but it is still unknown if they will be reversible with long term exposure. The MC1 receptor mediated effects may also carry risks. The long term impact of MC1 receptor activation has not been tested in clinical trials, and could potentially include increases in skin cancer, excess biopsy procedures and cosmetic blemishes. These skin changes may also result in unblinding, which could make interpretation of clinical trial results more complex and possibly subject to bias. We have also initiated trials of setmelanotide in potential new indications that include patients who might have more serious underlying conditions, such as Alström syndrome and other indications. It is possible that the underlying conditions in these patients, such as congestive heart failure and potentially other conditions, may confound the understanding of the safety profile of setmelanotide.

If these or other significant adverse events or other side effects are observed in any of our ongoing or planned clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, other comparable regulatory authorities or an IRB may also suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude setmelanotide from maintaining marketing approval or obtaining additional approvals, undesirable side

effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially adversely affect our business, financial condition and prospects.

Further, if we or others identify undesirable side effects caused by the product, or any other similar product, before or after regulatory approvals, a number of potentially significant negative consequences could result, including:

- regulatory authorities may request that we withdraw the product from the market or may limit or vary their approval of the product through labeling or other means;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- the FDA, the EU competent authorities and other equivalent competent authorities in foreign jurisdictions may require the addition of a Risk Evaluation and Mitigation Strategy, or REMS, or other specific obligations as a condition for marketing authorization due to the need to limit treatment to rare patient populations, or to address safety concerns;
- we may be required to change the way the product is distributed or administered or change the labeling of the product;
- we may be required to conduct additional studies and clinical trials or comply with other post-market requirements to assess possible serious risks;
- we may be required to conduct long term safety follow-up evaluations, including setting up disease and drug based registries;
- we may decide to remove the product from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking the product; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of setmelanotide and could substantially increase the costs of commercializing setmelanotide and significantly impact our ability to successfully commercialize setmelanotide and generate revenues.

We may not be able to obtain or maintain orphan drug designations for setmelanotide or to obtain or maintain exclusivity in any use. Even with exclusivity, competitors may obtain approval for different drugs that treat the same indications as setmelanotide.

The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Federal Food, Drug and Cosmetic Act, or FDCA, as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of seven years of marketing exclusivity, which precludes the FDA from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances.

The exclusivity period in the United States can be extended by six months if the NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. Orphan drug exclusivity may be revoked if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Other potential benefits of orphan drug designation and/or approval of a designated drug include eligibility for: exemption from certain prescription drug user fees, tax credits for certain qualified clinical testing expenses, and waivers from the pediatric assessment requirements of the Pediatric Research Equity Act.

In the EU, orphan drug designation is granted by the European Commission based on a scientific opinion of the EMA's Committee for Orphan Medicinal Products. A medicinal product may be designated as orphan if its sponsor can establish that (i) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the medicinal product will be of significant benefit to those affected by the condition. The application for orphan designation must be submitted before the application for marketing authorization.

Grant of orphan designation by the European Commission also entitles the holder of this designation to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Orphan drug designation must be requested before submitting an application for marketing authorization. In addition to a range of other benefits during the development and regulatory review, orphan medicinal products are, upon grant of marketing authorization, entitled to ten years of exclusivity in all EU member states for the approved therapeutic indication, which means that the EMA and European Commission cannot accept another marketing authorization application, grant a marketing authorization, or accept an application to extend a marketing authorization for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed Pediatric Investigation Plan, or PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Marketing authorization may, however, be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities.

The ten-year market exclusivity in the EU may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan designation, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Additionally granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time: (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant cannot supply enough orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. Orphan drug designation does not, in itself, convey any advantage in, or shorten the duration of, the regulatory review and authorization process.

In connection with IMCIVREE's approval, the FDA granted us seven years of orphan drug exclusivity for setmelanotide for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1, or LEPR deficiency and BBS confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, and in the EU, we obtained ten years of market exclusivity for setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.

We have also been granted orphan drug designation for setmelanotide for the treatment of BBS and Alström syndrome in both the United States and the EU. Setmelanotide has also been granted orphan designation for setmelanotide in treating Prader-Willi syndrome in the EU. There can be no assurance that we will be able to maintain the benefits orphan

drug exclusivity, or that the FDA or the European Commission will grant orphan designations for setmelanotide for other uses. In addition, orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Even though we have obtained orphan drug exclusivity for certain uses of setmelanotide, such exclusivities may not effectively protect setmelanotide from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. As discussed above, similar rules apply in the EU.

Although we have obtained PRIME designation in the EU for setmelanotide for the treatment of obesity and the control of hunger associated with deficiency disorders of the MC4R receptor pathway and Breakthrough Therapy designation for setmelanotide for the treatment of obesity associated with certain genetic defects upstream of the MC4R in the leptin melanocortin pathway, which includes POMC deficiency obesity, LEPR deficiency obesity, Bardet- Biedl syndrome and Alström syndrome in the United States, the FDA may rescind the Breakthrough Therapy Designation and we may be unable to obtain Breakthrough Therapy designation for other uses. In addition, Breakthrough Therapy designation by the FDA or PRIME designation by the EMA may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that setmelanotide will receive additional marketing approvals in the United States or additional marketing authorizations in the EU.

The FDA is authorized under the FDCA to give certain product candidates "Breakthrough Therapy designation." A Breakthrough Therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of Breakthrough Therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross disciplinary review. In addition, the FDA may consider reviewing portions of an NDA before the sponsor submits the complete application, or rolling review. Product candidates designated as breakthrough therapies by the FDA may be eligible for other expedited programs, such as priority review, if supported by clinical data.

Designation as Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe setmelanotide meets the criteria for designation as Breakthrough Therapy, the FDA may disagree. In any event, the receipt of Breakthrough Therapy designation for a product candidate, or acceptance for one or more of the FDA's other expedited programs, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not guarantee ultimate approval by the FDA. Regulatory standards to demonstrate safety and efficacy must still be met. Additionally, the FDA may later decide that the product candidate no longer meets the conditions for designation and may withdraw designation at any time or decide that the time period for FDA review or approval will not be shortened.

The PRIME scheme was launched by the EMA in 2016. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. In late June 2018, setmelanotide was granted eligibility to PRIME by the CHMP for the treatment of obesity and the control of hunger associated with deficiency disorders of the MC4R receptor pathway. Acknowledging that setmelanotide targets an unmet medical need, the EMA offers enhanced support in the development of the medicinal product through enhanced interaction and early dialogue to optimize our development plans and speed up regulatory evaluation in the EU. As part of this designation, the EMA has provided guidance to us concerning the development of setmelanotide. The PRIME designation does not, however,

guarantee that the regulatory review process in the EU will be shorter or less demanding. Neither does the PRIME designation guarantee that the European Commission will grant additional marketing authorizations for setmelanotide.

We may not be able to translate the once-daily formulations of setmelanotide for methods of delivery that would be acceptable to the FDA or other equivalent competent authorities in foreign jurisdictions or commercially successful.

Setmelanotide is currently administered by once-daily SC injection using small insulin type needles and syringes. SC injection is generally less well received by patients than other methods of administration, such as oral administration. Considerable additional resources and efforts, including potential studies, may be necessary in order to translate the once-daily formulation of setmelanotide into a once-weekly formulation that may be well received by patients.

We have entered into a license agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology, FluidCrystal, to formulate once-weekly setmelanotide. This formulation, if successfully developed for setmelanotide, and approved by the FDA and other regulatory authorities, will be delivered subcutaneously, similar to our once-daily formulation, except that we anticipate it will be injected once weekly. In addition, we have initiated development of an auto-injector device designed to make administration of our once-weekly product candidate easier and more convenient for our patients.

While we have started consultations with regulatory authorities about the potential path for approval of the once-weekly formulation, we cannot yet estimate the requirements for non-clinical and clinical data, manufacturing program, time, cost, and probability of success for approval. Regulatory authorities have limited experience evaluating Camurus' formulations, which further complicates our understanding regarding the information that may be required to obtain approval of a once-weekly formulation.

We received FDA approval of the once-daily formulation in the initial NDA submission for setmelanotide, and plan to seek approval of the once-weekly formulation at a later time. While we plan to develop the once-weekly formulation, or to develop other new and useful formulations and delivery technology for setmelanotide, we cannot estimate the probability of success, nor the resources and time needed to succeed. If we are unable to gain approval and utilize the once-weekly formulation, or to develop new formulations, setmelanotide may not achieve significant market acceptance and our business, financial condition and results of operations may be materially harmed.

Our approach to treating patients with MC4R pathway deficiencies requires the identification of patients with unique genetic subtypes, for example, POMC genetic deficiency. The FDA or other equivalent competent authorities in foreign jurisdictions could require the clearance, approval or certification of an in vitro companion diagnostic device to ensure appropriate selection of patients as a condition of approving setmelanotide in additional indications. The requirement that we obtain clearance, approval or certification of an in vitro companion diagnostic device will require substantial financial resources, and could delay or prevent the receipt of additional regulatory approvals for setmelanotide, or adversely affect those we have already obtained.

We have focused our development of setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4R pathway. To date, we have employed *in vitro* genetic diagnostic testing to select patients for enrollment in our clinical trials, including our clinical trials for IMCIVREE and for other potential indications for setmelanotide. If the safe and effective use of any of our product candidates depends on an *in vitro* diagnostic that is not otherwise commercially available, then the FDA may require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time as, or in connection with, the FDA approval of such product candidates.

In the EU, until May 25, 2022, in vitro diagnostic medical devices were regulated by Directive 98/79/EC, or the IVDD, which has been repealed and replaced by Regulation (EU) No 2017/746, or the IVDR. Unlike the IVDD, the IVDR is directly applicable in EU member states without the need for member states to implement into national law. The regulation of companion diagnostics is now subject to further requirements set forth in the IVDR. However on October 14, 2021, the European Commission proposed a "progressive" roll-out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. The European Parliament and Council adopted the proposed regulation on December 15, 2021. The IVDR will fully apply on May 26, 2022 but there will be a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation. For

instance, class C devices (including devices that are intended to be used as companion diagnostics) will have until May 26, 2026 to comply with the new requirements. The IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue a CE certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a marketing authorization application for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA. Compliance with the new requirements may impact our development plans for setmelanotide.

If the FDA or a comparable regulatory authority requires clearance, approval or certification of a companion diagnostic for setmelanotide, any delay or failure by us or our current and future collaborators to develop or obtain regulatory clearance or approval of, or certification of, such tests, if necessary, could delay or prevent us from obtaining additional approvals for setmelanotide, or adversely affect the approvals we have already obtained. For example, in November 2020, the FDA approved IMCIVREE for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1, or LEPR deficiencies confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. Although the FDA did not require that we obtain approval of a companion diagnostic prior to approving the New Drug Application, or NDA, for IMCIVREE, in connection with the NDA approval we agreed as a post-marketing commitment to conduct adequate analytical and clinical validation testing to develop and establish an *in vitro* companion diagnostic device to accurately and reliably detect patients with variants in the *POMC*, *PCSK1*, and *LEPR* genes that may benefit from setmelanotide therapy. In September 2020, our collaboration partner, Prevention Genetics, submitted a *de novo* request seeking FDA authorization to market such an *in vitro* companion diagnostic device for IMCIVREE as a Class II medical device. In January 2022, the FDA granted the *de novo* request for classification for the POMC/PCSK1/LEPR CDx Panel for market authorization as a Class II device. In June 2022, the FDA approved our supplemental NDA for the use of IMCIVREE to treat chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to BBS. If the FDA or a comparable regulatory authority requires clearance, approval or certification of a companion diagnostic when we seek additional approvals for setmelanotide, any delay or failure by us or our current and future collaborators to develop or obtain regulatory clearance or approval of, or certification of, such tests, if necessary, could delay or prevent us from obtaining such additional approvals for setmelanotide, or adversely affect the approvals we have already obtained.

We rely, and expect that we will continue to rely, on third parties to conduct clinical trials for setmelanotide. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain additional regulatory approvals for or commercialize setmelanotide and our business could be substantially harmed.

We have agreements with third party CROs to operationalize, provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for the execution of clinical trials for setmelanotide and control only certain aspects of their activities. As a result, we have less direct control over the start-up, conduct, timing and completion of these clinical trials, and the management of data developed through the clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. However, we remain responsible for the conduct of these trials and are subject to enforcement which may include civil and criminal liabilities for any violations of FDA rules and regulations and the comparable foreign regulatory provisions during the conduct of our clinical trials. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- devote inadequate resources to our clinical trials;

- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form more favorable relationships with other entities, some of which may be our competitors.

These factors, among others, may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are guidelines enforced by the FDA, the competent authorities of the EU member states and equivalent competent authorities in foreign jurisdictions for any products in clinical development. The FDA and foreign regulatory authorities enforce these regulations and GCP guidelines through periodic inspections of clinical trial sponsors, principal investigators, and trial sites, and IRBs. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other equivalent competent authorities in foreign jurisdictions may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA or foreign regulatory authorities will determine that any of our clinical trials comply with GCPs. In addition, our clinical trials must be conducted with products produced under current Good Manufacturing Practices, or cGMPs and similar foreign requirements. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

If any of our relationships with these third party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any such clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, setmelanotide. As a result, our financial results and the commercial prospects for setmelanotide in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Risks Related to the Commercialization of IMCIVREE (setmelanotide)

The successful commercialization of IMCIVREE and any other product candidates for which we obtain approval will depend in part on the extent to which governmental authorities, private health insurers, and other third-party payors provide coverage and adequate reimbursement levels. Failure to obtain or maintain coverage and adequate reimbursement for IMCIVREE or our other product candidates, if any and if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Our ability to successfully commercialize IMCIVREE or any other product candidates for which we obtain approval will depend in part on the extent to which coverage and reimbursement for these product candidates and related treatments will be available from government authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

Increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products, such as IMCIVREE, and, as a result, they may not cover or provide adequate payment. Even if we show improved efficacy or improved convenience of administration, third-party payors may deny or revoke the reimbursement status of our product candidates, if approved, or establish prices for our product candidates at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize IMCIVREE or other product candidates, and may not be able to obtain a satisfactory financial return. Further, as we continue to grow as an organization, previously-established prices may no longer be sufficient and could create additional pricing pressure for us.

No uniform policy for coverage and reimbursement for products exist among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that may require us to provide scientific and clinical support for the use of IMCIVREE to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

In some foreign countries, particularly in Canada, Great Britain and in the EU member states, the pricing and reimbursement of prescription only medicinal products is subject to strict governmental control which varies widely between countries. In these countries, pricing negotiations with governmental authorities can take six to twelve months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of IMCIVREE with other available therapies. If reimbursement for IMCIVREE is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

In the EU, in particular, each EU member state can restrict the range of medicinal products for which its national health insurance system provides reimbursement and can control the prices of medicinal products for human use marketed in its territory. As a result, following receipt of marketing authorization in an EU member state, through any application route, an applicant is required to engage in pricing discussions and negotiations with the competent pricing authority in the individual EU member states. Some EU member states operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. Other EU member states approve a specific price for the medicinal product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, we may face competition for IMCIVREE from lower priced products in foreign countries that have placed price controls on pharmaceutical products.

Health Technology Assessment, or HTA, of medicinal products, however, is becoming an increasingly common part of the pricing and reimbursement procedures in the United Kingdom and some EU member states, including France, Germany, Italy, Spain, the Netherlands, Belgium, Norway and Sweden. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU member states. In addition, pursuant to Directive 2011/24/EU on the application of patients' rights in cross border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU member states and in pricing and reimbursement decisions and may negatively affect price in at least some EU member states.

On January 15, 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be

responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell IMCIVREE, we may not be able to generate any revenue.

In order to market IMCIVREE, we must continue to build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. Although we have received FDA approval for IMCIVREE, for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency and BBS, from the European Commission and MHRA granted marketing authorization to IMCIVREE, for the treatment of obesity and the control of hunger associated with confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above, and from the European Commission for dosing in patients with POMC or LEPR deficiency who have mild, moderate or severe renal impairment, we are early in our commercialization efforts and have not yet established a full-scale commercial infrastructure. Therefore, you should not compare us to commercial-stage biotechnology companies, and you should not expect that we will generate substantial revenues or become profitable in the near term. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects would be materially adversely affected.

We may never receive regulatory approval to market setmelanotide outside of the United States, the European Union and Great Britain.

We intend to seek marketing authorizations in various countries worldwide. In order to market any product outside of the United States, the EU or Great Britain, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Marketing authorization procedures vary among countries and can involve additional setmelanotide testing and additional administrative review periods. The time required to obtain marketing authorization in other countries might differ from that required to obtain FDA approval or marketing authorization from the European Commission or the MHRA. The marketing authorization processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States and Europe, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Grant of marketing authorization in one country does not ensure grant of marketing authorization in another country, but a failure or delay in obtaining marketing authorization in one country may have a negative effect on the regulatory process or commercial activities in others. Failure to obtain marketing authorization in other countries or any delay or other setback in obtaining such authorizations would impair our ability to market setmelanotide in such foreign markets. Any such impairment would reduce the size of our potential market share and could have a material adverse impact on our business, results of operations and prospects.

We may not achieve market acceptance for IMCIVREE, which would limit the revenue that we generate from the sale of IMCIVREE.

The commercial success of IMCIVREE will also depend upon the awareness and acceptance of IMCIVREE within the medical community, including physicians, patients and third party payors. If IMCIVREE does not achieve an adequate level of acceptance by patients, physicians and third party payors, we may not generate sufficient revenue to become or remain profitable. Before granting reimbursement approval, third party payors may require us to demonstrate that, in addition to treating obesity caused by certain genetic deficiencies affecting the MC4R pathway, IMCIVREE also provides incremental health benefits to patients. Our efforts to educate the medical community and third party payors about the benefits of IMCIVREE may require significant resources and may never be successful. All of these challenges may impact our ability to ever successfully market and sell IMCIVREE.

Market acceptance of IMCIVREE will depend on a number of factors, including, among others:

- the ability of IMCIVREE to provide chronic weight management in patients with obesity caused by certain genetic deficiencies affecting the MC4R pathway and, if required by any competent authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available treatments, therapies, devices or surgeries;
- the complexities of genetic testing, including obtaining genetic results that support patient treatment with IMCIVREE;
- the relative convenience and ease of SC injections as the necessary method of administration of IMCIVREE, including as compared with other treatments for patients with obesity;
- the prevalence and severity of any adverse side effects associated with IMCIVREE;
- limitations or warnings contained in the labeling approved for IMCIVREE by the FDA or the specific obligations imposed as a condition for marketing authorization imposed by other equivalent competent authorities in foreign jurisdictions, particularly by the European Commission;
- availability of alternative treatments, including a number of obesity therapies already approved or expected to be commercially launched in the near future;
- our ability to increase awareness of these diseases among our target populations through marketing and other cross-functional efforts;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the ability of IMCIVREE to treat the maximum range of pediatric patients, and any limitations on its indications for use;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning IMCIVREE or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of IMCIVREE through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- the likelihood that competent authorities in foreign jurisdictions may require development of a REMS or other specific obligations as a condition of approval or post-approval, may not agree with our proposed REMS or other specific obligations, or may impose additional requirements that limit the promotion, advertising, distribution or sales of IMCIVREE.

Our industry is intensely competitive. If we are not able to compete effectively against current and future competitors, we may not be able to generate revenue from the sale of IMCIVREE, our business will not grow and our financial condition and operations will suffer.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds that could make IMCIVREE obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. In addition, payers may require that patients try other medications known as step therapy or a "step-edit," including medications approved for treatment of general obesity, before receiving reimbursement for IMCIVREE. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to IMCIVREE. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

Currently, IMCIVREE is the only approved treatment for providing chronic weight management in patients with obesity due to BBS or POMC, PCSK1 or LEPR deficiencies, and there are no approved treatments for chronic weight management in patients with Alström syndrome, or with deficiencies due to a variant in one of the two alleles in the *POMC, PCSK1, or LEPR* genes (HET obesity), SRC1 deficiency obesity, SH2B1 deficiency obesity, MC4R deficiency obesity, and hypothalamic obesity. Bariatric surgery is not a good treatment option for these genetic diseases of obesity because the severe obesity and hyperphagia associated with these diseases are considered to be risk factors for bariatric surgery. Also, existing therapies indicated for general obesity, including glucagon-like peptide-1 (GLP-1) receptor agonists, such as Wegovy®, and glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) agonists, such as tirzepatide which is being investigated as a treatment for obesity, do not specifically restore function impaired by genetic deficiencies in the MC4R pathway, which we believe is the root cause of hyperphagia and obesity in patients with MC4R genetic variants. Based on search results from ClinicalTrials.gov, we are unaware of any competitive products in therapeutic clinical studies for the obesity and hyperphagia caused by upstream MC4R pathway deficiencies specifically, however LG Chem has represented it is in early-stage clinical development of an MC4R agonist. New competitors may emerge which could limit our business opportunity in the future.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The use of setmelanotide in clinical trials and the sale of IMCIVREE exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with IMCIVREE. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design or a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws and any equivalent laws in foreign countries. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for IMCIVREE or any future product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;
- litigation costs;

- distraction of management's attention from our primary business;
- loss of revenue; and
- the inability to successfully commercialize IMCIVREE or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials and commercial product with a $10.0 million annual aggregate coverage limit. Our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

We rely completely on third party suppliers to manufacture our clinical and commercial drug supplies of setmelanotide, and we intend to rely on third parties to produce preclinical, clinical and commercial supplies of any future product candidate.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to manufacture our clinical and commercial drug supply internally for setmelanotide, or any future product candidates, for use in the conduct of our preclinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidate on a clinical or commercial scale. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture the active pharmaceutical ingredient, or API, and final drug product must pass inspection by the FDA and other equivalent competent authorities in foreign jurisdictions pursuant to inspections that have been and will be conducted following submission of our NDAs or relevant foreign regulatory submission to the other equivalent competent authorities in foreign jurisdictions. Our failure or the failure of our CMOs to pass preapproval inspection of the manufacturing facilities of setmelanotide could delay the regulatory approval process. In addition, our clinical trials must be conducted with products produced under GMP and similar foreign regulations. Our failure or the failure of our CROs or CMOs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action, including civil and criminal penalties. When we import any drugs or drug substances, we would be subject to FDA, United States Department of Agriculture, and U.S. Bureau of Customs and Border Patrol import regulation requirements. Such enforcement for our failure or our CROs or CMOs' failure to comply with these regulations could result in import delays, detention of products, and, depending on criteria such as the history of violative activities, the FDA could place a foreign firm or certain drug substances or products on Import Alert and require that all such drug substances or products be subject to detention without physical examination which could significantly impact the global supply chain for setmelanotide. With the exception of those on the FDA's drug shortage list or properly imported by individuals, the FDCA prohibits the importation of prescription drug products for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly.

We currently contract with third parties for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into process development and manufacturing service agreements with our CMOs, Corden Pharma Switzerland, LLC, or Corden, (formerly Peptisyntha SA prior to its acquisition by Corden), and Neuland Laboratories for certain process development and manufacturing services for regulatory starting materials and/or raw materials in connection with the manufacture of setmelanotide. We have entered into long-term commercial supply agreements with PolyPeptide Group and Recipharm Monts S.A.S. for manufacturing of drug substance and drug product for IMCIVREE. Under our agreements, we pay these third parties for services in accordance with the terms of mutually agreed upon work orders, which we may enter into from time to time. We may need to engage additional third party suppliers to manufacture our clinical and/or commercial (subject to approval) drug supplies. We also have engaged other third parties to assist in, among other things, distribution, post-approval safety reporting and pharmacovigilance activities. We cannot be certain that we can engage third party suppliers on terms as favorable as those that are currently in place.

We do not perform the manufacturing of any drug products and are completely dependent on our CMOs to comply with GMPs and similar foreign requirements for manufacture of both drug substance, or API and finished drug product. We recognize that we are ultimately responsible for ensuring that our drug substances and finished drug product are manufactured in accordance with GMPs and similar foreign requirements, and, therefore, the company's management practices and oversight, including routine auditing, are critical. If our CMOs cannot successfully manufacture material that conform to our specifications and the strict regulatory requirements of the FDA or other equivalent competent authorities in foreign jurisdictions, they may be subject to administrative and judicial enforcement for non-compliance and the drug products would be deemed misbranded or adulterated and prohibited from distribution into interstate commerce. Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those other company materials and products may affect the regulatory clearance of our CMOs' facilities generally. In addition, satisfying the regulatory requirements for production of setmelanotide with multiple suppliers, while assuring more robust drug availability in the future, adds additional complexity and risk to regulatory approval. If the FDA or another equivalent competent foreign regulatory agency does not approve these facilities for the manufacture of setmelanotide or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market setmelanotide.

We are manufacturing finished drug product for use in our upcoming or ongoing clinical trials and for commercial supply. We believe we currently have a sufficient amount of finished setmelanotide and placebo to complete our ongoing and planned clinical trials, and for commercial supply. However, these projections could change based on delays encountered with manufacturing activities, equipment scheduling and material lead times. Any such delays in the manufacturing of finished drug product could delay our planned clinical trials of setmelanotide and our commercial supply, which could delay, prevent or limit our ability to generate revenue and continue our business.

Moreover, as a result of the COVID-19 pandemic and ongoing global supply chain issues, certain of our suppliers and CMOs in Europe have been affected, which has disrupted their activities. As a result, we could face difficulty sourcing key components necessary to produce supply of setmelanotide, which may negatively affect our clinical development and commercialization activities. If the COVID-19 coronavirus further impacts business operations, including our CMOs and suppliers, we could face additional disruption to our supply chain that could affect the supply of drug product for preclinical, clinical trial and commercial use. Additionally, as our CMOs are producers of drug substances and drug products, including vaccines and therapeutics, they could be compelled by a national government, or choose themselves, to shift their resources to the production of a COVID-19 vaccine and/or therapeutics for COVID-19, which could disrupt any scheduled drug substance or drug product batches we may have and may prevent us from obtaining supplies for our programs in a timely manner to meet our development timelines.

We do not have long term supply agreements in place with all of our contractors involved with the manufacturing of our weekly formulation of setmelanotide. We currently place individual batch or campaign orders with the CMOs/suppliers that are individually contracted under existing master services and quality agreements for the weekly formulation of setmelanotide. If we engage new contractors, such contractors must be approved by the FDA and other equivalent competent authorities in foreign jurisdictions. We will need to submit information to the FDA and other equivalent competent authorities in foreign jurisdictions describing the manufacturing changes. If manufacturing changes occur post-approval, the FDA and foreign regulatory authorities may have to approve these changes. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of setmelanotide. Our current scale of manufacturing appears adequate to support all of our current needs for clinical trial and initial commercial supplies for setmelanotide. Going forward, we may need to identify additional CMOs or partners to produce setmelanotide on a larger scale.

The exclusive license agreement with RareStone Group Ltd., or RareStone, is important to our business. If we or RareStone fail to adequately perform under the agreement, or if we or RareStone terminate the agreement, the development of setmelanotide in certain indications and commercialization of IMCIVREE in certain markets would be delayed or terminated and our business would be adversely affected.

In December 2021, we entered into an Exclusive License Agreement with RareStone, or the RareStone License. Pursuant to the RareStone License, we granted to RareStone an exclusive, sublicensable, royalty-bearing license under certain patent rights and know-how to develop, manufacture, commercialize and otherwise exploit any pharmaceutical product that contains setmelanotide in the diagnosis, treatment or prevention of conditions and diseases in humans in China, including mainland China, Hong Kong and Macao. RareStone has a right of first negotiation in the event that the Company chooses to grant a license to develop or commercialize the licensed product in Taiwan.

Termination of this RareStone License could cause significant delays in our product development and commercialization efforts for setmelanotide and could prevent us from commercializing IMCIVREE in the markets covered by the RareStone License without first expanding our internal capabilities or entering into another agreement with a third party. Any alternative collaboration or license could also be on less favorable terms to us. In addition, under the agreement, RareStone agreed to provide funding for certain clinical development activities. If the agreement were terminated, we may need to refund those payments and seek additional financing to support the research and development of any terminated products or discontinue any terminated products, which could have a material adverse effect on our business.

Under the RareStone License, we are dependent upon RareStone to successfully commercialize any applicable collaboration products in China, including mainland China, Hong Kong and Macao. We cannot directly control RareStone's commercialization activities or the resources it allocates to setmelanotide. Our interests and RareStone's interests may differ or conflict from time to time, or we may disagree with RareStone's level of effort or resource allocation. RareStone may internally prioritize setmelanotide differently than we do or it may not allocate sufficient resources to effectively or optimally commercialize setmelanotide. If these events were to occur, our business would be adversely affected.

Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology or maintain issued patents that are sufficient to protect setmelanotide, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our commercial success will depend in part on our success in obtaining and maintaining issued patents and other intellectual property rights in the United States and elsewhere and protecting our proprietary technology. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect setmelanotide. Other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty.

Although an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and such patent may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Patents, if issued, may be challenged, deemed unenforceable, invalidated or circumvented. U.S. patents and patent applications or the patents and patent application obtained or submitted pursuant to

comparable foreign laws, may also be subject to interference proceedings, *ex parte* reexamination, *inter partes* review proceedings, post-grant review proceedings, supplemental examination and challenges in court. Patents may be subjected to opposition or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize setmelanotide.

Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering setmelanotide are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered setmelanotide, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect setmelanotide;
- any of our pending patent applications will issue as patents;
- we will be able to successfully commercialize IMCIVREE before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- any of our patents will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

We rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with employees, consultants, collaborators and vendors. We also have agreements with employees and selected consultants that obligate them to assign their inventions to us. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such an agreement. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, collaborators, vendors, former employees and current employees.

Furthermore, if the parties to our confidentiality agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the attention of our management and key personnel from our business operations. Even if we prevail in any lawsuits that we initiate, the damages or other remedies awarded may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing IMCIVREE.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. For example, numerous third party U.S. and non U.S. patents and pending applications exist that cover melanocortin receptor analogs and methods of using these analogs.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that setmelanotide or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced or choose to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing IMCIVREE.

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion.

In addition, in order to avoid infringing the intellectual property rights of third parties and any resulting intellectual property litigation or claims, we could be forced to do one or more of the following, which may not be possible and, even if possible, could be costly and time consuming:

- cease development and commercialization of setmelanotide;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, rename setmelanotide and/or its trade name IMCIVREE.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Issued patents covering setmelanotide could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners threatened or initiated legal proceedings against a third party to enforce a patent covering setmelanotide, the defendant could claim that the patent covering setmelanotide is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any one of several statutory requirements, including novelty, non-obviousness and enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld material information from the U.S. PTO, or made a misleading statement, during patent prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions, for example, opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover setmelanotide or competitive products. The outcome following legal assertions of invalidity and/or unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on setmelanotide. Such a loss of patent protection would have a material adverse impact on our business.

We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on setmelanotide in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as

that in the United States. These products may compete with our product and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, an April 2017 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing setmelanotide.

We have licensed our rights to setmelanotide from Ipsen Pharma SAS, or Ipsen. Our license with Ipsen imposes various obligations on us, and provides Ipsen the right to terminate the license in the event of our material breach of the license agreement, our failure to initiate or complete development of a licensed product, or our commencement of an action seeking to have an Ipsen licensed patent right declared invalid. Termination of our license from Ipsen would result in our loss of the right to use the licensed intellectual property, which would materially adversely affect our ability to develop and commercialize setmelanotide, as well as harm our competitive business position and our business prospects.

We also have licensed from Camurus its drug delivery technology, FluidCrystal, to formulate setmelanotide. Our license with Camurus imposes various obligations on us, and provides Camurus the right to terminate the license in the event of our material breach of the license agreement. Termination of our license from Camurus would result in our inability to use the licensed intellectual property.

We may enter into additional licenses to third party intellectual property that are necessary or useful to our business. Future licensors may also allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensors may have the right to terminate our license at will. Any termination could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize setmelanotide, as well as harm our competitive business position and our business prospects.

While we have registered trademarks for the commercial trade name IMCIVREE (setmelanotide) in the United States and the EU, we have not yet obtained trademark protection for IMCIVREE in certain foreign jurisdictions and failure to secure such registrations could adversely affect our business.

While we have received registered trademarks for the commercial trade name IMCIVREE (setmelanotide) and its logo in the United States and the EU, we have not yet obtained trademark protection for IMCIVREE in certain foreign jurisdictions and are pursuing trademark registrations in other jurisdictions. Our trademark applications may be rejected during trademark registration proceedings. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome them. In addition, in the U.S. PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive those proceedings.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining product exclusivity for setmelanotide, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval for setmelanotide, one or more of the U.S. patents we license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent term restoration of up to five years as compensation for patent term lost during product development and the FDA regulatory review process, and we have applied to the U.S. PTO for patent term extension. However, we may not be granted an extension because of, for example, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

Because setmelanotide contains active ingredients that the FDA has determined to be a new chemical entity, it has been afforded five years of marketing exclusivity by the FDA. Following the expiration of this marketing exclusivity, the FDA may approve generic products. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for setmelanotide. Recent legislation enacted by Congress created, among other things, new causes of action against innovator companies that refuse to offer samples of drugs for purposes of testing and developing generic or biosimilar products or to allow companies to participate in a shared Risk Evaluation and Mitigation Strategy (REMS). Competition that setmelanotide may face from generic versions could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in setmelanotide.

In the EU, the grant of orphan designation for setmelanotide means that this medicinal product would be entitled, upon grant of marketing authorization by the European Commission, to ten years of exclusivity in all EU member states. Marketing authorization may, however, be granted to a similar medicinal product with the same orphan indication during the ten year period if we are unable to supply sufficient quantities of setmelanotide. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to setmelanotide. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that setmelanotide is sufficiently profitable not to justify maintenance of market exclusivity.

If we fail to obtain an extension of patent protection under similar foreign legislation, where applicable, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected in the foreign countries concerned.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product.

The United States has enacted and is currently implementing the America Invents Act of 2011, wide ranging patent reform legislation. Further, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents or future patents.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees.

Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize setmelanotide, which would materially adversely affect our commercial development efforts.

Risks Related to Regulatory Approval and Marketing of Setmelanotide and Other Legal Compliance Matters

Even if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining additional approvals for the commercialization of setmelanotide beyond FDA approval for obesity due to POMC, PCSK1 or LEPR deficiencies, or BBS in the United States, the marketing authorizations granted by the European Commission and the MHRA for the treatment of obesity and the control of hunger associated with confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above in the EU and Great Britain, respectively, and the marketing authorizations granted in the European Commission for the patients with POMC or LEPR deficiency who have mild, moderate or severe renal impairment.. We depend primarily on the success of setmelanotide, and we cannot be certain that we will be able to obtain additional regulatory approvals for, or successfully commercialize, setmelanotide. If we are not able to obtain, or if there are delays in obtaining, required additional regulatory approvals, we will not be able to commercialize setmelanotide in additional indications in the United States or in foreign jurisdictions, and our ability to generate revenue will be materially impaired.

We currently have only one product candidate, setmelanotide, in clinical development, and our business depends entirely on its successful clinical development, regulatory approval and commercialization. Setmelanotide (IMCIVREE), which is currently approved by FDA for chronic weight management in patients with monogenic or syndromic obesity due to POMC, PCSK1, or LEPR deficiency confirmed by FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, or due to BBS, and by the European Commission for patients with POMC or LEPR deficiency who have mild, moderate or severe renal impairment, will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence commercialization in indications beyond those currently approved for IMCIVREE in the United States, the EU and Great Britain. The clinical trials, manufacturing and marketing of setmelanotide are subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market setmelanotide.

Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through nonclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and approval, if any, may be conditional on postmarketing studies and surveillance, and will require the expenditure of substantial resources beyond our existing cash resources. Of the large number of drugs in development in the United States and in other countries, only a small percentage will successfully complete the FDA regulatory approval process or the equivalent process in foreign jurisdictions and will be commercialized. In addition, we have not discussed all of our proposed development programs with the FDA or the competent authorities of foreign jurisdictions. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure you that setmelanotide will be successfully developed or commercialized.

In addition, obtaining FDA approval of an NDA for additional indications and the approval of an MAA from the European Commission for additional indications is a complex, lengthy, expensive and uncertain process, and the FDA, EMA or equivalent competent authorities in foreign jurisdictions may delay, limit or deny approval of setmelanotide for many reasons, including, among others:

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;

- we may not be able to demonstrate to the satisfaction of the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions that setmelanotide is safe and effective in treating obesity caused by certain genetic deficiencies affecting the MC4R pathway;

- the results of our clinical trials may not be interpretable or meet the level of statistical or clinical significance required by the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions for marketing approval. For example, the potential unblinding of setmelanotide studies due to easily identifiable AEs may raise the concern that potential bias has affected the clinical trial results;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with the number, size, conduct or implementation of our clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may require that we conduct additional clinical trials or pre-clinical studies;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not consider that our diagnostic strategy supports approval;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may decide that additional assays or data to understand any risks for anti-drug antibodies may need to be available for approval;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may decide that the toxicology program, including any parts of carcinogenicity studies that are filed, do not meet the requirements for approval;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions or the applicable foreign regulatory agency may identify deficiencies in our chemistry, manufacturing or controls of setmelanotide, or in the commercial production of setmelanotide to support product approval;

- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may find the data from preclinical studies and clinical trials insufficient to demonstrate that clinical and other benefits of setmelanotide outweigh its safety risks;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from our preclinical studies and clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not approve the formulation, labeling or specifications of setmelanotide;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not accept data generated at our clinical trial sites;

- the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions may require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- as part of our NDA approval, we were required to complete certain post-market requirements and commitments, which we may not be able to meet;

- the FDA may require development of a REMS as a condition of additional approvals or may impose additional requirements that limit the promotion, advertising, distribution, or sales of setmelanotide;

- the European Commission may grant only conditional approval marketing authorization or based on the EMA's opinion impose specific obligations as a condition for marketing authorization, or may require us to conduct post authorization safety studies as a condition of grant of marketing authorization;

- the FDA or other equivalent competent foreign regulatory agencies may deem our manufacturing processes or our facilities or the facilities of our CMOs inadequate to preserve the identity, strength, quality, purity, or potency of our product; or

- the FDA or the equivalent competent authorities in foreign jurisdictions may change its approval policies or adopt new regulations and guidance.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain additional regulatory approvals for and successfully market IMCIVREE. Moreover, because our business is entirely dependent upon setmelanotide, any such setback in our pursuit of regulatory approvals would have a material adverse effect on our business and prospects.

Future regulatory legislation or regulation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates.

The EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is expected to be adopted by the European Commission by the end of 2022. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024), may have a significant impact on the pharmaceutical industry in the long term.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's and foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA began conducting voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities in circumstances where the FDA determines that such remote evaluation would be appropriate based on mission needs and travel limitations. In July 2021, the FDA

resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Our failure to obtain marketing approval in foreign jurisdictions would prevent setmelanotide from being marketed abroad, and any current or future approvals we have been or may be granted for setmelanotide in the United States would not assure approval of setmelanotide in foreign jurisdictions.

In order to market and sell setmelanotide and any other product candidate that we may develop in the EU and many other jurisdictions, we or our third party collaborators must obtain separate marketing authorizations and comply with numerous and varying regulatory requirements. The marketing authorization procedure varies among countries and can involve additional testing. The time required to obtain marketing authorization may differ substantially from that required to obtain FDA approval. The marketing authorization process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or these third parties may not obtain marketing authorization from competent authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure grant of marketing authorization by competent authorities in other countries or jurisdictions, and grant of marketing authorization by one competent authority outside the United States does not ensure grant of marketing authorization by competent authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing authorizations and may not receive necessary marketing authorization to commercialize setmelanotide in any market. Additionally, the United Kingdom's withdrawal from the EU, commonly referred to as Brexit, has resulted in the relocation of the EMA from the United Kingdom to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and the MHRA, including delays in granting clinical trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of setmelanotide, or any other product candidates in the EU and/or the United Kingdom. Although we have obtained FDA approval and marketing authorization from the European Commission and the MHRA for setmelanotide, any delay in obtaining, or an inability to obtain, any marketing authorization, for any of our other product candidates, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek marketing authorization in the United Kingdom and/or EU for any of our other product candidates, which could significantly and materially harm our business.

The terms of our current and future potential marketing approvals for setmelanotide and ongoing regulation may limit how we manufacture and market setmelanotide, and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Regulatory authorities may impose significant restrictions on setmelanotide's indicated uses or marketing or impose ongoing requirements for potentially costly post approval studies. We and setmelanotide will also be subject to ongoing requirements by the FDA and foreign regulatory authorities, governing labeling, packaging, storage, advertising, promotion, marketing, distribution, importation, exportation, post-approval changes, manufacturing, recordkeeping, and submission of safety and other post market information. Advertising and promotional materials must comply with the FDCA and implementing regulations and foreign regulations, and are subject to FDA and foreign regulatory authorities oversight and post-marketing reporting obligations, in addition to other potentially applicable federal and state laws. The FDA and the other competent foreign authorities have significant post market authority, including, for example, the authority to require labeling changes based on new safety information and to require post market studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA and foreign regulatory authorities also has the

authority to require, as part of an NDA or similar foreign application or post approval, the submission of a REMS or other specific obligations, which may include Elements to Assure Safe Use. Any REMS or other specific obligations required by the FDA or foreign regulatory authorities may lead to increased costs to assure compliance with new post approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. The holder of an approved NDA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process, or adding new manufacturers. Similar requirements apply in foreign jurisdictions.

Manufacturers of drug products and their facilities may be subject to payment of application and program fees and are subject to continual review and periodic inspections by the FDA and other equivalent competent authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with setmelanotide, such as AEs of unanticipated severity or frequency, or problems with the facility where setmelanotide is manufactured or disagrees with the promotion, marketing or labeling of the product, a regulatory agency may impose restrictions on setmelanotide, the manufacturer or us, including requiring withdrawal of setmelanotide from the market or suspension of manufacturing. If we or the manufacturing facilities for setmelanotide fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- vary, suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain setmelanotide, refuse to permit the import or export of setmelanotide, or request that we initiate a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects.

Accordingly, we and our CMOs will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for setmelanotide withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

In addition, a sponsor’s responsibilities and obligations under the FDCA and FDA regulations, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Similar to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states, both before and after grant of the manufacturing and marketing authorizations. This oversight includes control of compliance with GMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third party manufacturers would be required to ensure that all of our processes, methods, and equipment are compliant with GMP. Failure by us or by any of our third party partners, including suppliers, manufacturers, and distributors to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, revocation or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

In addition, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, AE management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time consuming and expensive and could impact our profitability. Noncompliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions there have been, and continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, restrict or regulate post-approval activities with respect to IMCIVREE and affect our ability, or the ability of any future collaborators, to profitably sell our products. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States and elsewhere, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for IMCIVREE or any product candidates approved for sale.

In March 2010, Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was signed into law. The ACA substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affects the U.S. pharmaceutical industry. Among the provisions of the ACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any product candidates that are approved for sale, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer’s Medicaid rebate liability;

- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs, revising the "average manufacturer price" definition, and extending rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well as Medicaid managed care;

- expansion of the list of entity types eligible for participation in the Public Health Service 340B drug pricing program, or the 340B program, to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers, and sole community hospitals, but exempting "orphan drugs," such as IMCIVREE, from the 340B ceiling price requirements for these covered entities;

- establishment of the Medicare Part D coverage gap discount program, which requires manufacturers to provide a 70% point of sale discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and

- establishment of the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, including prescription drug spending.

Since its enactment, certain provisions of the ACA have been subject to judicial, executive, and legislative challenges. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. It is unclear how healthcare reform measures enacted by Congress or implemented by the Biden administration or other challenges to the ACA, if any, will impact the ACA or our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, beginning April 1, 2013, Medicare payments to providers were reduced by 2% under the sequestration required by the Budget Control Act of 2011, which will remain in effect through 2030, with the exception of a temporary suspension due to the COVID-19 pandemic from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments varies from 1% from April 1, 2022 through June 30, 2022, to up to 3% in the final fiscal year of the sequester. Additionally, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Moreover, the federal government and the individual states in the United States have become increasingly active in developing proposals, passing legislation and implementing regulations designed to control drug pricing, including price or patient reimbursement constraints, discounts, formulary flexibility, marketing cost disclosure, drug price increase reporting, and other transparency measures. These types of initiatives may result in additional reductions in Medicare, Medicaid, and other healthcare funding, and may otherwise affect the prices we may obtain for IMCIVREE or the frequency with which IMCIVREE is prescribed or used.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which was fully implemented in 2019. At this time, it is unclear how the introduction of this Medicare quality payment program will impact overall physician reimbursement. The cost of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States. There have been several Congressional inquiries, as well as legislative and regulatory initiatives and executive orders designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Members of Congress and the Biden Administration have indicated they will continue to pursue legislative or administrative measures to control prescription

drug costs, although the likelihood of such measures being adopted remains uncertain. For example, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation. We cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage and payment criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of setmelanotide to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired. For more details concerning the risks related to pricing and reimbursement in the EU, please refer to the discussion in the risk factor "*The successful commercialization of setmelanotide and our other product candidates will depend in part on the extent to which governmental authorities, private health insurers, and other third-party payors provide coverage and adequate reimbursement levels. Failure to obtain or maintain coverage and adequate reimbursement for setmelanotide or our other product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue*" in this Annual Report.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in which we participate, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Medicaid is a joint federal and state program administered by the states for low income and disabled beneficiaries. We participate in and have certain price reporting obligations under the Medicaid Drug Rebate Program, or the MDRP, as a condition of having covered outpatient drugs payable under Medicaid and, if applicable, under Medicare Part B. The MDRP requires us to pay a rebate to state Medicaid programs for each unit of our covered outpatient drugs dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. These rebates are based on pricing data that we must report on a monthly and quarterly basis to the Centers for Medicare & Medicaid Services, or CMS, the federal agency that administers the MDRP and other governmental healthcare programs. These data include the average manufacturer price for each drug and, in the case of innovator products, the best price, which in general represents the lowest price available from the manufacturer to certain entities in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. If we become aware that our MDRP government price reporting submission for a prior quarter was incorrect or has changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. If we fail to provide information timely or are found to have knowingly submitted false information to the government, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP. In the event that CMS terminates our rebate agreement pursuant to which we participate in the MDRP, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs. Our failure to comply with our MDRP price reporting and rebate payment obligations could negatively impact our financial results.

The ACA made significant changes to the MDRP, as described under the risk factor "*Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations*," above. In addition, in March 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other things, eliminated the statutory cap on drug manufacturers' MDRP rebate liability, effective January 1, 2024. Under current law enacted as part of the ACA, drug manufacturers' MDRP rebate liability is capped at 100% of the average manufacturer price for a covered outpatient drug. Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the MDRP. Additional legislation or the issuance of regulations relating to the MDRP could have a material adverse effect on our results of operations.

Federal law requires that any company that participates in the MDRP also participate in the Public Health Service's 340B drug pricing program in order for federal funds to be available for the manufacturer's drugs under Medicaid and, if applicable, Medicare Part B. We participate in the 340B program, which is administered by the Health Resources and Services Administration, or HRSA, and requires us to charge statutorily defined covered entities no more than the 340B "ceiling price" for our covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The ACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs," such as IMCIVREE, from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the MDRP, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes those prices to 340B covered entities. In addition, HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs. Our failure to comply 340B program requirements could negatively impact our financial results. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA or other legislation or regulation could affect our 340B ceiling price calculations and also negatively impact our financial results. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

In order for IMCIVREE or any product candidates, if approved, to be paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we also participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. As part of this program, we are required to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (VA, U.S. Department of Defense, or DOD, Public Health Service, and U.S. Coast Guard). The FCP is based on the Non-Federal Average Manufacturer Price, or Non-FAMP, which we must calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information. The FSS pricing and contracting obligations also contain extensive disclosure and certification requirements.

We also participate in the Tricare Retail Pharmacy program, under which we are required to pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. We are required to list our innovator products on a Tricare Agreement in order for them to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges could result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action,

would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation. Requirements of pharmaceutical manufacturers under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. CMS, the Department of Health & Human Services Office of Inspector General, and other governmental agencies have pursued manufacturers that were alleged to have failed to report these data to the government in a timely or accurate manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that any submissions we are required to make under the MDRP, the 340B program, the VA/FSS program, the Tricare Retail Pharmacy Program, and other governmental drug pricing programs will not be found to be incomplete or incorrect.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

In the United States, the FDA strictly regulates marketing, labeling, advertising and promotion of prescription drugs. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet and off-label promotion. Any regulatory approval that the FDA grants is limited to those specific diseases and indications for which a product is deemed to be safe and effective by the FDA. For example, the FDA-approved label for IMCIVREE is limited to chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due POMC, PCSK1, or LEPR, deficiency confirmed by FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, and due to BBS. In addition to the FDA approval required for new formulations, any new indication for an approved product also requires FDA approval. If we are not able to obtain FDA approval for any desired future indications for our drugs and drug candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians in the United States may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote the products is narrowly limited to those indications that are specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. For example, we are actively evaluating IMCIVREE in subjects with other forms of obesity caused by defects in the MCR4 pathway. We are not currently permitted to, and do not, market or promote setmelanotide for these uses.

Regulatory authorities in the United States generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on the subject of off-label use. Although recent court decisions suggest that certain off-label promotional activities may be protected under the First Amendment, the scope of any such protection is unclear. If our promotional activities fail to comply with the FDA's regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, bring an enforcement action against us, suspend or withdraw an approved product from the market, require a recall or institute fines or civil fines, or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution, any of which could harm our reputation and our business.

In the EU, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off label promotion. The off label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU member states also prohibit the direct to consumer advertising of prescription only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

We may be subject to federal, state and foreign healthcare laws and regulations. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, substantial civil penalties, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of setmelanotide, if approved. Our arrangements and interactions with healthcare professionals, third party payors, patients and others will expose us to broadly applicable fraud and abuse, antikickback, false claims and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute setmelanotide, if we obtain marketing approval. The U.S. federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- The United States federal healthcare Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, (anything of value), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease order or arranging for or recommending the purchase, lease or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers, formulary managers, and patients on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals or patients as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exception or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product and patient support programs.

- The federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Such private individuals may share in amounts paid by the entity to the government in recovery or settlement. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non-reimbursable uses, inflating prices reported to private price publication

services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false or fraudulent claim or statement for violations. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may be awarded in litigation proceedings. Settlements may require companies to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, including private third-party payors, and also imposes obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. Penalties for failure to comply with a requirement of HIPAA vary significantly and include civil monetary penalties as well as criminal penalties for knowingly obtaining or disclosing individually identifiable health information in violation of HIPAA. The criminal penalties increase if the wrongful conduct involves false pretenses or the intent to sell, transfer or use identifiable health information for commercial advantage, personal gain or malicious harm. HIPAA also prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal healthcare Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

- The federal Physician Payments Sunshine Act, implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies to report payments and other transfers of value to physicians for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, Centers for Medicare and Medicaid Services, information related to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse-midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Manufacturers must submit reports on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payer, including private insurers. Some state laws require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-related activities including the provision of gifts, meals, or other items to certain health care providers. Some states restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Some states require the posting of information relating to clinical studies and their outcomes. Other states and cities require identification or licensing of sales representatives. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes of conduct.

- Analogous foreign laws and regulations, including restrictions imposed on the promotion and marketing of medicinal products in the EU member states and other countries, restrictions on interactions with healthcare professionals and requirements for public disclosure of payments made to physicians. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we may decide not to directly promote or market our products, inappropriate activity by our international distribution partners could have implications for us.

Ensuring that our business arrangements and interactions with healthcare professionals, third party payors, patients and others comply with applicable healthcare laws and regulations will require substantial resources. Various state, federal and foreign regulatory and enforcement agencies continue actively to investigate violations of health care laws and regulations, and the United States Congress continues to strengthen the arsenal of enforcement tools.

It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse, privacy, or other healthcare laws and regulations. If our operations, including our engagements with healthcare professionals, researchers and patients, or our disease awareness and/or patient identification initiatives including genetic testing programs, or anticipated activities to be conducted by our field teams, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to costly investigations, significant civil, criminal and administrative monetary penalties, imprisonment, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could substantially disrupt our operations or financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and generate negative publicity, which could harm our financial condition and divert our management's attention from the operation of our business.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non U.S. regulators, provide accurate information to the FDA and applicable non U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and any precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. Some of these laws and related risks are described under the risk factor "*We may be subject to federal and state healthcare laws and regulations. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, substantial civil penalties, reputational harm and diminished profits and future earnings"* of this Annual Report.

Actual or perceived failure to comply with data protection, privacy and security laws, regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of

personal information. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our financial performance, business and operating results.

In the United States, numerous federal and state laws and regulations, including HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and regulations implemented thereunder, collectively HIPAA, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws, including Section 5 of the Federal Trade Commission Act, which govern the collection, use, disclosure and protection of health-related and other personal information, may apply to our operations and the operations of current and future collaborators. We may obtain health information from third parties, such as research institutions with which we collaborate, that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA, other than potentially with respect to providing certain employee benefits, we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA. In addition, state laws govern the privacy and security of health, research and genetic information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Further, we may also be subject to other state laws governing the privacy, processing and protection of personal information. For example, the California Consumer Privacy Act of 2018, or CCPA, went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act, or CPRA, recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Utah and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In addition, some of our research activities involve minors, which may be subject to additional laws and can require specialized consent processes, privacy protections, and compliance procedures. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Furthermore, the Federal Trade Commission, or FTC, and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security practices that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, in Europe, the collection and use of personal data, including health and genetic data, is governed by the provisions of the GDPR. The GDPR became effective on May 25, 2018, and imposes strict requirements for the processing of the personal data of individuals within the European Economic Area, or EEA, including health data from clinical trials and AE reporting. In particular, these requirements include certain obligations concerning the consent of the individuals to

whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EU, the EEA and the United Kingdom, security breach notifications, and security and confidentiality of the personal data, and violations of these requirements could result in substantial fines, up to the greater of 20 million Euros or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease/change our processing of our data, enforcement notices, and/or assessment notices for a compulsory audit. We may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm. Data protection authorities from the different EU and EEA member states may also interpret the GDPR and national laws differently and impose additional requirements, which adds to the complexity of processing personal data in the EU and the EEA.

Additionally, from January 1, 2021, we have had to comply with the GDPR and also the United Kingdom GDPR, or UK GDPR, which, together with the amended United Kingdom Data Protection Act 2018, retains the GDPR in United Kingdom national law following Brexit. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term.

Among other requirements, the GDPR and UK GDPR also regulate transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States; in July, 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-US Privacy Shield Framework, or the Privacy Shield, under which personal data could be transferred from the EEA to US entities who had self-certified under the Privacy Shield scheme and imposed further restrictions on the use of the standard contractual clauses, or SCCs. These restrictions include a requirement for companies to carry out a transfer impact assessment which, among other things, assesses the laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under SCCs will need to be implemented to ensure an essentially equivalent level of data protection to that afforded in the EEA. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. The revised SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom. The United Kingdom's Information Commissioner's Office has also published new data transfer standard contracts for transfers from the UK under the UK GDPR. This new documentation will be mandatory for relevant data transfers from September 21, 2022; existing standard contractual clauses arrangements must be migrated to the new documentation by March 21, 2024. We will be required to implement the latest UK data transfer documentation for data transfers subject to the UK GDPR, in relation to relevant existing contracts and certain additional contracts and vendor/ customer arrangements, within the relevant time frames. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. The European Commission has adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/extends that decision, and remains under review by the European Commission during this period. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of UK data protection laws following Brexit and the response to this consultation was published in June 2022. There is a risk that any material changes which are made to the UK data protection regime could result in the European Commission reviewing the UK adequacy decision, and the UK losing its adequacy decision if the European Commission deems the UK to no longer provide adequate protection for personal data.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Our failure to comply with our obligations under the GDPR, including any failure to adopt measures to ensure that we can continue to conduct the data processing activities that we initiated in the EU before the GDPR entered into application could adversely impact our ability to use the data generated in our studies. And any actual or perceived failure to comply with these data protection laws or adequately address privacy and security concerns could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

Our future growth depends, in part, on our ability to continue to penetrate foreign markets, where we will be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability will depend, in part, on our ability to continue to commercialize setmelanotide in foreign markets for which we intend to rely on collaborations with third parties, including RareStone. As we continue to commercialize setmelanotide in foreign markets, we will be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for setmelanotide in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of setmelanotide could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling setmelanotide outside of the United States and require us to develop and implement costly compliance programs.

If we continue to expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act of 1977, or the FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of such third party in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the

company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

The results of the United Kingdom's referendum on withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business.

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the EU on January 31, 2020 and ratified a trade and cooperation agreement governing its future relationship (commonly referred to as "Brexit"). The agreement, which was applied provisionally from January 1, 2021 and entered into force on May 1, 2021, addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. Because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the EU as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

Since January 1, 2021, however, the United Kingdom operates under a separate regulatory regime to the EU. EU laws regarding medicinal products only apply in respect of the United Kingdom to Northern Ireland (as set out in the Protocol on Ireland/Northern Ireland). The EU laws that have been transposed into United Kingdom law through secondary legislation remain applicable. While the United Kingdom has indicated a general intention that new laws regarding the development, manufacture and commercialization of medicinal products in the United Kingdom will align closely with EU law, there are limited detailed proposals for future regulation of medicinal products. The trade and cooperation agreement includes specific provisions concerning medicinal products, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued (such mutual recognition can be rejected by either party in certain circumstances), but does not foresee wholesale mutual recognition of United Kingdom and EU pharmaceutical regulations. For example, it is not clear to what extent the United Kingdom will adopt legislation aligned with, or similar to, the EU CTR which became applicable on January 31, 2022 and which significantly reforms the assessment and supervision processes for clinical trials throughout the EU. Therefore, there remains political and economic uncertainty regarding to what extent the regulation of medicinal products will differ between the United Kingdom and the EU in the future. Any divergences will increase the cost and complexity of running our business, including with respect to the conduct of clinical trials. Brexit also materially impacted the regulatory regime with respect to the approval of our product candidates. Great Britain is no longer covered by the EU's procedures for the grant of marketing authorizations (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). As of January 1, 2021, all existing centralized marketing authorizations were automatically converted into United Kingdom marketing authorizations effective in Great Britain and issued with a United Kingdom marketing authorization number on January 1, 2021 (unless marketing authorization holders opted out of this

scheme). A separate marketing authorization is now required to market drugs in Great Britain. It is currently unclear whether the regulator in the United Kingdom, the MHRA is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in Great Britain and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in Great Britain for our product candidates, which could significantly and materially harm our business. The United Kingdom's withdrawal from the EU and the associated uncertainty has had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Any of these factors could have a significant adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel.

We are highly dependent on our executive leadership team. We have employment agreements with these individuals but any individual may terminate his or her employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives. We also do not have any key-person life insurance on any of these key employees. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us and may not be subject to non-compete agreements. Recruiting and retaining qualified scientific personnel and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

We expect to increase our number of employees and the scope of our operations. In particular, we will need to transition from a research and development company to a commercial company. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business and commercial opportunities, loss of employees and reduced productivity among remaining employees. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy.

The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of setmelanotide. Many of our suppliers and collaborative and clinical trial relationships are located outside the United States, and we may in the future seek to hire employees located outside of the United States. Accordingly, our business may become subject to economic, political, regulatory and other risks associated with international operations, such as compliance with tax, employment, immigration and labor laws for employees living or traveling abroad, workforce uncertainty in countries where labor unrest is more common than in the United States, as well as difficulties associated with staffing and managing international operations, including differing labor relations. Any of these factors could materially affect our business, financial condition and results of operations. Our future financial

performance and our ability to commercialize setmelanotide, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

Our internal computer systems, or those of our third party CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of setmelanotide development programs, regulatory investigations, enforcement actions and lawsuits.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers, as well as personally identifiable information of employees. Similarly, our third-party CROs, CMOs and other contractors and consultants possess certain of our sensitive data. The secure maintenance of this information is material to our operations and business strategy. Despite the implementation of security measures, our internal computer systems and those of our third-party CROs, CMOs and other contractors and consultants are vulnerable to attacks by hackers, damage from computer viruses, unauthorized access, breach due to employee error, malfeasance or other disruptions, natural disasters, terrorism and telecommunication and electrical failures. Any such attack, incident or breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost, corrupted or stolen. Further, attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification, some also require implementation of reasonable security measures and provide a private right of action in the event of a breach. Costs of breach response, mitigation, investigation, remediation, notice and ongoing assessments can be considerable. Thus, any access, disclosure, damage or other loss of information, including our data being breached at our partners or third-party providers, could result in legal claims or proceedings and liability under state, federal and international privacy laws, disruption of our operations, and damage to our reputation, which could adversely affect our business.

If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for setmelanotide or other product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of setmelanotide and our product candidates could be delayed.

Risks Related to Our Common Stock

Our directors and executive officers and their affiliated entities own a significant percentage of our stock and, if they choose to act together, will be able to exert significant influence over matters subject to stockholder approval.

Our executive officers and directors and their respective affiliates, in the aggregate, hold shares representing approximately 11.9% of our outstanding voting stock as of June 30, 2022. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders could significantly influence elections of directors, any amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

We are a Delaware corporation. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively will provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. Any provision in our amended and restated certificate of incorporation and amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Market volatility may affect our stock price and the value of your investment.

The market price for our common stock has been volatile and may continue to fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of, or results from preclinical studies and clinical trials of setmelanotide;
- the failure of the FDA or EMA to approve IMCIVREE for additional indications;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other weight loss therapies and companies targeting rare diseases and orphan drug treatment;
- regulatory or legal developments in the United States and other countries;
- failure of setmelanotide, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;

- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting setmelanotide;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- the achievement and timing of milestone payments under our existing collaboration and license agreements; and
- if setmelanotide receives regulatory approval, the level of underlying demand for that product and customers' buying patterns.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our ability to use certain net operating loss carryovers and other tax attributes may be limited.

Under the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year, and can use such NOLs to offset future taxable income, if any, until such losses are used or, for NOLs arising in taxable years ending on or before December 31, 2017, until such NOLs expire. Other unused tax attributes, such as research tax credits may also be carried forward to offset future taxable income, if any, until such attributes are used or expire. As of December 31, 2021, we had approximately $422.3 million and $385.1 million of unused federal and state NOL carryforwards, respectively, and approximately $9.3 million and $4.2 million of unused federal and state carryforwards of research tax credits, respectively. Of the federal NOL carryforwards at December 31, 2021, $349.2 million can be carried forward indefinitely, while $73.2 million will begin to expire in 2033. Additionally, as of December 31, 2021, we had federal orphan drug credits related to qualifying research of $15.4 million.

If a corporation undergoes an "ownership change," very generally defined as a greater than 50% change by value in its equity ownership by certain shareholders or groups of shareholders over a rolling three-year period, Sections 382 and 383 of the Code limit the corporation's ability to use carryovers of its pre-change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to prior public offerings may have resulted in a limitation under Code Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. Future changes in our stock ownership, some of which are outside of our control, could also result in an ownership change under Sections 382 and 383 of the Code. In addition, for taxable years beginning after December 31, 2020, utilization of federal NOLs generated in tax years beginning after December 31, 2017 are limited to a maximum of 80% of the taxable income for such year, after taking into account utilization of NOLs generated in years beginning before January 1, 2018 and determined without regard to such NOL deduction. Further regulatory changes could also limited our ability to utilize our NOLs. As a result, our ability

to use carryovers of NOLs and credits to reduce our future U.S. federal income tax liability may be subject to limitations. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. Any such limitation could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 or 383 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods. We do not expect to generate positive taxable income in the near future and we may never achieve tax profitability.

Substantial future sales or perceived potential sales of our common stock in the public market could cause the price of our common stock to decline significantly.

Sales of our common stock in the public market, or the perception that these sales could occur, could cause the market price of our common stock to decline significantly. As of June 30, 2022, we had 50,454,170 shares of common stock outstanding.

The holders of an aggregate of approximately 6.0 million shares of our common stock, or approximately 11.9% of our total outstanding common stock as of June 30, 2022, are entitled to rights with respect to the registration of their shares under the Securities Act, subject to specified conditions, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the investors' rights agreement between us and such holders. We have also registered and intend to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares under the Securities Act, the shares become freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividends on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

Provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our certificate of incorporation and bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things:

- establish a classified board of directors so that not all members of our board are elected at one time;

- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan (also known as a "poison pill");
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting;
- authorize our board of directors to amend the bylaws;
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and
- require a super-majority vote of stockholders to amend some provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our certificate of incorporation, bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders and our bylaws designate the federal district courts of the United States as the exclusive forum for actions arising under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of fiduciary duty; (iii) any action asserting a claim against us arising under the DGCL, our certificate of incorporation or our bylaws; and (iv) any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to the provisions of our certificate of incorporation and bylaws described above. These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find these provisions of our certificate of incorporation or bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

General Risk Factors

We may acquire businesses or products, form strategic alliances or create joint ventures in the future, and we may not realize their benefits.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance, joint venture or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

An active market for our common stock may not be maintained.

Our stock began trading on the Nasdaq Global Market in October 2017 and we can provide no assurance that we will be able to continue to maintain an active trading market on the Nasdaq Global Market or any other exchange in the future. If an active market for our common stock is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration.

If securities or industry analysts do not continue to publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not control these analysts. If we lose securities or industry analysts coverage of our company, the trading price for our stock would be negatively impacted. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts issues unfavorable commentary or ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, a stockholder's ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to setmelanotide, our intellectual property or future revenue streams, or grant licenses on terms that are not favorable to us.

Unfavorable global political or economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the recent global financial crisis has caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn or recession and a continued increase in inflation rates or interest rates could result in a variety of risks to our business, including weakened demand for setmelanotide and our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further

deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Increased inflation rates and related increases in interest rates can adversely affect us by increasing our costs, including labor and employee benefit costs. In addition, the current military conflict between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U.S., the EU or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We have incurred and will continue to incur substantial costs as a result of operating as a public company, our management will continue to devote substantial time to new compliance initiatives and corporation governance policies, and we will need to hire additional qualified accounting and financial personnel with appropriate public company experience.

As a public company, and particularly now that we are no longer an emerging growth company, we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will continue to devote a substantial amount of time to these compliance initiatives and we will need to continue to hire additional accounting and financial personnel with appropriate public company experience and technical accounting knowledge. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development efforts. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and make some activities more time consuming and costly.

These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in future uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. To continue to achieve compliance with Section 404, we continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective as required by Section 404.

In addition, because we no longer qualify as an emerging growth company, we are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. If we are unable to maintain effective internal control over financial reporting, we may not have adequate, accurate or timely financial information, our independent registered public accounting firm may issue a report that is adverse, and we may be unable to meet our reporting obligations as a public company or comply with the requirements of the SEC or Section 404. This could result in a restatement of our financial statements, the imposition of sanctions, including the inability of registered broker dealers to make a market in our common stock, or investigation by regulatory authorities. Any such action or other negative results caused by our inability to meet our reporting requirements or comply with legal and regulatory requirements or by disclosure of an accounting, reporting or control issue could adversely affect the trading price of our securities and our business. Material weaknesses in our internal control over financial reporting could also reduce our ability to obtain financing or could increase the cost of any financing we obtain. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.

There has been increasing public focus by investors, customers, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. We may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have a materially adverse impact on our business and financial condition.

In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

Unregistered Sales of Equity Securities

None.

Use of Proceeds

Not applicable.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosure

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference		
		Form	Date	Number
3.1	Amended and Restated Certificate of Incorporation.	10-Q	05/04/2020	3.1
3.2	Amended and Restated Bylaws.	8-K	12/11/2020	3.1
10.1*†	Revenue Interest Financing Agreement, dated June 16, 2022, by and between the Company and entities managed by HealthCare Royalty Management, LLC			
31.1*	Certification of the Principal Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
31.2*	Certification of the Principal Financial Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
32.1**	Certification of the Principal Executive Officer, as required by Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
32.2**	Certification of the Principal Financial Officer, as required by Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
101.INS*	Inline XBRL Instance Document - the Instance Document does not appear in the interactive data file because its XBRL tags are embedded within the Inline XBRL document.			
101.SCH*	Inline XBRL Taxonomy Extension Schema Document.			
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document.			
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.			
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document.			
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document.			
104*	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).			

* Filed herewith.

** Furnished herewith.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

RHYTHM PHARMACEUTICALS, INC.

Dated: August 3, 2022

By: /s/ David P. Meeker, M.D.
Name: David P. Meeker, M.D.
Title: President and Chief Executive Officer
(Principal Executive Officer)

Dated: August 3, 2022

By: /s/ Hunter C. Smith
Name: Hunter C. Smith
Title: Chief Financial Officer and Treasurer
(Principal Financial Officer)

[***] Certain information in this document has been omitted pursuant to Regulation S-K, Item (601)(b)(10). Such omitted information is both (i) not material and (ii) the type that the Registrant customarily and actually treats as private or confidential.

EXECUTION VERSION

Exhibit 10.1

REVENUE INTEREST FINANCING AGREEMENT

by and among

RHYTHM PHARMACEUTICALS, INC.,

as the Company,

ENTITIES MANAGED BY HEALTHCARE ROYALTY MANAGEMENT, LLC, as the Investors,

and

HCR COLLATERAL MANAGEMENT, LLC, as the Investor Representative

Dated June 16, 2022

TABLE OF CONTENTS

ARTICLE V
REPRESENTATIONS AND WARRANTIES OF THE INVESTOR

ARTICLE VI
AFFIRMATIVE COVENANTS

ARTICLE VII
NEGATIVE COVENANTS

ARTICLE VIII
THE CLOSINGS

ARTICLE IX
CONFIDENTIALITY

ARTICLE X
INDEMNIFICATION

ARTICLE XI
EVENTS OF DEFAULT AND REMEDIES

ARTICLE XII
MISCELLANEOUS

REVENUE INTEREST FINANCING AGREEMENT

This REVENUE INTEREST FINANCING AGREEMENT (this "Agreement") dated as of June 16, 2022 (the "Effective Date") is by and among RHYTHM PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), the entities managed by HEALTHCARE ROYALTY MANAGEMENT, LLC listed on the signature pages hereto (the "Investors"), and HCR COLLATERAL MANAGEMENT, LLC, a Delaware limited liability company (the "Investor Representative"), solely in its capacity as agent for, and representative of, the Investors. Each of the Company and the Investors are referred to in this Agreement as a "Party" and collectively as the "Parties".

W I T N E S S E T H:

WHEREAS, the Company is developing Imcivree (defined in Section 1.1) for the purposes of sale throughout the world;

WHEREAS, the Company desires to secure financing from the Investors, and the Investors have indicated their willingness to provide financing, upon and subject to the terms and conditions set forth in this Agreement; and

NOW, THEREFORE, in consideration of the premises and the mutual agreements, representations and warranties set forth herein and for other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, intending to be legally bound, the parties hereto covenant and agree as follows:

ARTICLE I
DEFINED TERMS AND RULES OF CONSTRUCTION

Section 1.1 Defined Terms. The following terms, as used herein, shall have the following respective meanings:

"Acquired Debt" means Indebtedness (1) of a Person existing at the time such Person becomes a Subsidiary (which is not also a Guarantor) through the acquisition of the Equity Interests in such Subsidiary, (2) assumed by a Subsidiary (which is not also a Guarantor) in connection with the acquisition by such Subsidiary of assets from such Person or (3) of a Person at the time such Person merges or amalgamates with or into or consolidates or otherwise combines with any Subsidiary (which is not also a Guarantor), in each case so long as (i) such Indebtedness was not incurred in connection with, or in anticipation or contemplation of, such Person becoming a Subsidiary or such acquisition, merger, amalgamation or consolidation, as the case may be, (ii) no Special Termination Event, Default or Event of Default shall have occurred and be continuing or would result from such acquisition, merger, amalgamation or consolidation, as the case may be and (iii) the Company does not guarantee or assume any such Indebtedness.

"Additional Amounts" has the meaning set forth in Section 3.1(h).

"Affiliate" means, with respect to any Person, any other Person that, directly or indirectly, controls, is controlled by or is under common control with such Person. For purposes of this definition, "control" of a Person means the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of such Person, whether through the ownership of securities entitled to elect the Board of Directors or management board, by Contract or otherwise, and the terms "controlled" and "controlling" have meanings correlative to the foregoing.

"Agreement" has the meaning set forth in the preamble.

"Annual Net Revenues" means, with respect to any Calendar Year, the aggregate amount of worldwide Net Revenues for that Calendar Year.

"Anti-Corruption Laws" means all Laws of any jurisdiction applicable to the Company or any of its Affiliates from time to time concerning or relating to bribery or corruption, including without limitation the United States Foreign Corrupt Practices Act of 1977, as amended, the UK Bribery Act 2010 and other similar legislation in any other jurisdictions.

"Anti-Terrorism Laws" means any Laws relating to terrorism or money laundering, including without limitation Executive Order No. 13224 (effective September 24, 2001), the USA PATRIOT Act, the Laws comprising or implementing the Bank Secrecy Act, the Trading with the Enemy Act, as amended, and each of the foreign assets control regulations of the United States Treasury Department (31 CFR, Subtitle B, Chapter V, as amended) and any other enabling legislation or executive order relating thereto.

"Applicable Law" means, with respect to any Person, all Laws, rules, regulations and orders of Governmental Authorities applicable to such Person or any of its properties or assets.

"Applicable Tiered Percentage" means the percentage based on the applicable portion of Annual Net Revenues, as set forth in the chart below:

Payment Tiers based on Annual Net Revenues	Applicable Tiered Percentage
A. Portion of Annual Net Revenues less than or equal to $125,000,000	11.5%
B. Portion of Annual Net Revenues exceeding $125,000,000 and less than or equal to $300,000,000	7.5%
C. Portion of Annual Net Revenues in excess of $300,000,000	2.5%

"Audited Financial Statements" means the audited consolidated balance sheets of the Company and its Subsidiaries for the fiscal year ended December 31, 2021, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for such fiscal year of the Company and its Subsidiaries, including the notes thereto, audited by independent public accountants of recognized national standing and prepared in conformity with GAAP.

"Bankruptcy Event" means the occurrence of any of the following in respect of a Person: (a) such Person shall generally not, shall be unable to, or an admission in writing by such Person of its inability to, pay its debts as they come due or a general assignment by such Person for the benefit of creditors; (b) the filing of any petition or answer by such Person seeking to adjudicate itself as bankrupt or insolvent, or seeking for itself any liquidation, winding-up, reorganization, arrangement, adjustment, protection, relief or composition of such Person or its debts under any Applicable Law relating to bankruptcy, insolvency, receivership, winding-up, liquidation, reorganization, examination, relief of debtors or other similar Applicable Law now or hereafter in effect, or seeking, consenting to or acquiescing in the entry of an order for relief in any case under any such Applicable Law, or the appointment of or taking possession by a receiver, trustee, custodian, liquidator, examiner, assignee, sequestrator or other similar official for such Person or for any substantial part of its property; (c) corporate or other entity action taken by such Person to authorize any of the actions set forth in clause (a) or clause (b) above; or (d) without the consent or acquiescence of such Person, the commencement of an action seeking entry of an order for relief or approval of a petition for relief or reorganization or any other petition seeking any reorganization, arrangement, composition, readjustment, liquidation, dissolution or other similar relief under any present or future bankruptcy, insolvency or similar Applicable Law, or the filing of any such petition against such Person, or, without the consent or acquiescence of such Person, the commencement of an action seeking entry of an order appointing a trustee, custodian, receiver or liquidator of such Person or of all or any substantial part of the property of such Person, in each case where such petition or order shall remain unstayed or shall not have been stayed or dismissed within 90 days from entry thereof.

"Board of Directors" means (a) with respect to a company or corporation, the board of directors of the company or corporation or any committee thereof duly authorized to act on behalf of such board, (b) with respect to a partnership, the board of directors or similar governing body of the general partner of the partnership, (c) with respect to a limited liability company, the managing member or members or any controlling committee of managing members thereof, and (d) with respect to any other Person, the board or committee of such Person serving a similar function.

"Business Day" means any day that is not a Saturday, Sunday or other day on which commercial banks in New York City are authorized or required by Applicable Law to remain closed.

"Calendar Quarter" means, for the first calendar quarter, the period beginning on the Initial Closing Date and ending on the last day of the calendar quarter in which the Initial Closing Date falls, and thereafter each successive period of three consecutive calendar months ending on March 31, June 30, September 30 or December 31.

"Calendar Year" means (a) for the first such Calendar Year, the period beginning on the Initial Closing Date and ending on December 31 of the calendar year in which the Initial Closing Date occurs, (b) for each calendar year of the Payment Term thereafter, each successive period beginning on January 1 and ending 12 consecutive calendar months later on December 31, and (c) for the last year of the Payment Term, the period beginning on January 1 of the year in which this Agreement expires or terminates and ending on the effective date of expiration or termination of this Agreement.

"Camurus License Agreement" means that certain License Agreement, dated as of January 4, 2016, by and between the Company and Camurus AB, a limited liability company organized under the Laws of Sweden, as may be amended, supplemented, restated or otherwise modified from time to time.

"CDA" means that certain letter agreement, dated as of December 3, 2021, by and between HealthCare Royalty Management, LLC and the Company.

"Change of Control" means the occurrence of any of the following events:

(a) any reorganization, recapitalization, consolidation or merger (or similar transaction or series of related transactions) of the Company or issuance, sale or exchange of Equity Interests (or similar transaction or series of related transactions) of the Company in which the holders of the Company's outstanding Equity Interests immediately before consummation of such transaction or series of related transactions do not, immediately after consummation of such transaction or series of related transactions, retain Equity Interests representing more than 50.0% of the voting power of the surviving entity of such transaction or series of related transactions (or the parent of such surviving entity if such surviving entity is wholly owned by such parent), in each case without regard to whether the Company is the surviving entity,

(b) the sale, transfer, assignment or other disposition of all or substantially all of the assets of the Company;

(c) during any period of 12 consecutive months, a majority of the members of the Board of Directors of the Company cease to be composed of individuals (i) who were members of that Board of Directors on the first day of such period, (ii) whose election, appointment or nomination to that Board of Directors was approved by individuals referred to in clause (i) above constituting at the time of such election, appointment or nomination at least a majority of that Board of Directors (either by a specific vote or by approval of the proxy statement of the Company in which such member was named as a nominee for election as a director, without objection to such nomination) or (iii) whose election or nomination to that Board of Directors was approved by individuals referred to in clauses (i) and (ii) above constituting at the time of such election, appointment or nomination at least a majority of that Board of Directors;

(d) any "change of control", "fundamental change" or any comparable term shall occur under the Permitted Debt Facility Document; or

(e) the Company or any of its Subsidiaries grants or transfers the right to Commercialize Imcivree to any Person, other than a Permitted Licensee or as otherwise expressly permitted hereunder.

"Change of Control Payment" means, as of any date of determination, the amount equal to the sum of (i) the Hard Cap less the aggregate of all of the payments of the Company in respect of the Revenue Interests (including any Under Performance Payment) made to the Investors prior to such date, plus (ii) any other Obligations payable by the Company Parties under this Agreement and the other Transaction Documents (if any).

"Closing" has the meaning set forth in Section 8.1.

"Closing Date" means the Initial Closing Date, the Second Closing Date or the Third Closing Date, as applicable.

"Collateral" means all of each Company Party's right, title and interest in, to and under the following, whether now owned or hereafter acquired:

(a) Imcivree;

(b) the Material Contracts and any other contracts relating to Imcivree to which any Grantor is a party;

(c) the Intellectual Property rights relating to Imcivree throughout the world (including, for the avoidance of doubt, the Imcivree Patent Rights);

(d) the supplemental New Drug Application relating to Imcivree and any other Drug Applications in other countries or regions relating to Imcivree (including all Drug Applications relating to Imcivree filed with the EMA or the MHRA);

(e) gross receivables of the Company and its Subsidiaries with respect to Imcivree;

(f) the Lockbox Accounts, Collection Account and all rights (contractual and otherwise and whether constituting accounts, contract rights, financial assets, cash, investment property or general intangibles) arising under, connected with or in any way related to the Collection Account and the Lockbox Account, in each case to the extent holding any receivables with respect to Imcivree;

(g) all of the Equity Interests in the Guarantors;

(h) to the extent that any Subsidiary that owns any portion of any asset relating to Imcivree is organized as a Massachusetts Securities Corporation, all of the Equity Interests in such Subsidiary;

(i) any asset or property relating to Imcivree in any material respect that is now owned or may be acquired by any Grantor after the Initial Closing Date that is necessary for the Commercialization of Imcivree; and

(j) all proceeds resulting from the assets described in each of the foregoing clauses.

For the avoidance of doubt, "Collateral" does not include any product other than Imcivree that may be developed or marketed by the Company or any of its Subsidiaries in the future, or any Material Contract relating to such other product.

"Collateral Documents" has the meaning ascribed thereto in the Security Agreement.

"Collection Account" means one Deposit Account per Company or Guarantor, as applicable, established and maintained at any Depositary Bank solely for the purpose of receiving remittances from the Lockbox Account of proceeds of accounts and royalty receivables of the Company arising from sales of the Included Products or Other Royalty Payments and disbursement thereof as provided herein, and any successor Collection Account entered into in accordance with Section 3.2(d).

"Commercialization" means, on a country by country basis, any and all activities with respect to the manufacture, distribution, marketing, detailing, promotion, selling and securing of reimbursement of Included Products accordance with the Product Plans in a country after Marketing Authorization for an Included Product in that country has been obtained, which shall include, as applicable, post-marketing approval studies, post-launch marketing, promoting, detailing, marketing research, distributing, customer service, selling the Included Product, importing, exporting or transporting the Included Product for sale, and regulatory compliance with respect to the foregoing, in each case in accordance with the Product Plans. When used as a verb, "Commercialize" means to engage in Commercialization.

"Commercially Reasonable and Diligent Efforts" means, with respect to the efforts to be expended with respect to Imcivree in any country or regulatory jurisdiction, such efforts and resources normally used by a reasonably prudent company in the biotechnology industry of a size and product portfolio comparable, and with similar resources available, to the Company and its Affiliates in the biopharmaceutical industry, taken as a whole, in such applicable country or

jurisdiction, which pharmaceutical product is owned or licensed in the same manner as Imcivree, which pharmaceutical product is at a similar stage in its product life and of similar market and profit potential as Imcivree, taking into account efficacy, safety, approved labeling, the competitiveness of alternative products in such country or jurisdiction, pricing/reimbursement for the pharmaceutical product in such country or jurisdiction relative to other countries and jurisdictions, the Intellectual Property and regulatory protection of the pharmaceutical product in such country or jurisdiction, the regulatory structure in such country or jurisdiction and the profitability of the pharmaceutical product in such country or jurisdiction, all as measured by the facts and circumstances in existence at the time such efforts are due.

"Company" has the meaning set forth in the preamble.

"Company Account" means any account established by the Company or its Subsidiaries that is not subject to the Deposit Agreement.

"Company Indemnification Cap" has the meaning set forth in Section 10.6(a).

"Company Indemnification Obligations" has the meaning set forth in Section 10.1.

"Company Indemnified Party" has the meaning set forth in Section 10.2.

"Company Party" means any of the Company, the Guarantors and the Pledged Subsidiaries.

"Comparable Yield" has the meaning set forth in Section 6.22(a).

"Compliance Certificate" means a certificate substantially in the form of Exhibit B.

"Confidential Information" means any and all technical and non-technical non-public information provided by either Party to the other (including, without limitation, the reports provided pursuant to Section 3.4 and any notices or other information provided pursuant to Section 6.3), either directly or indirectly, and including any materials prepared on the basis of such information, whether in graphic, written, electronic or oral form, and marked or identified at the time of disclosure as confidential, or which by its context would reasonably be deemed to be confidential, including without limitation information relating to a Party's technology, products and services, and any business, financial or customer information relating to a Party. The existence and terms of this Agreement shall be deemed the Confidential Information of both Parties. For clarity, this Agreement shall supersede the CDA and the CDA shall cease to be of any force and effect following the execution of this Agreement; provided, however, that all information falling within the definition of "Confidential Information" set forth in the CDA shall also be deemed Confidential Information disclosed pursuant to this Agreement, and the use and disclosure of such Confidential Information following the date of this Agreement shall be subject to the provisions of ARTICLE IX.

"Contract" means any contract, agreement, commitment, instrument, license, sublicense, subcontract, real or personal property lease or sublease, note, indenture, mortgage, bond, letter of credit, guarantee, purchase order, or other legally binding business arrangement,

whether written or oral, together with any amendments, restatements, supplements or other modifications thereto.

"Contractual Obligation" means, as to any obligation arising under any Contract.

"Copyright License" means any agreement, whether written or oral, providing for the grant of any right to use any Work under any Copyright.

"Copyrights" means (a) all proprietary rights afforded Works pursuant to Title 17 of the United States Code, including, without limitation, all rights in mask works, copyrights and original designs, and all proprietary rights afforded such Works by other countries for the full term thereof (and including all rights accruing by virtue of bilateral or international treaties and conventions thereto), whether registered or unregistered, including, but not limited to, all applications for registration, renewals, extensions, reversions or restorations thereof now or hereafter provided for by Law and all rights to make applications for registrations and recordations, regardless of the medium of fixation or means of expression; and (b) all copyright rights under the copyright Laws of the United States and all other countries for the full term thereof (and including all rights accruing by virtue of bilateral or international copyright treaties and conventions), whether registered or unregistered, including, but not limited to, all applications for registration, renewals, extensions, reversions or restorations of copyrights now or hereafter provided for by Law and all rights to make applications for copyright registrations and recordations, regardless of the medium of fixation or means of expression.

"Debtor Relief Laws" means the Bankruptcy Code of the United States, and all other liquidation, conservatorship, bankruptcy, assignment for the benefit of creditors, moratorium, rearrangement, receivership, insolvency, reorganization, or similar debtor relief Laws of the United States or other applicable jurisdictions from time to time in effect.

"Default" means any event or condition that constitutes an Event of Default or that, with the giving of any notice, the passage of time, or both, would be an Event of Default.

"Deposit Account" means a "deposit account" (as defined in Article 9 of the UCC), investment account or other account in which funds are held or invested to or for the credit or account of any Party.

"Deposit Agreement" means the deposit account control agreement entered into by the Depositary Bank, the Investor Representative and the Company (and any Permitted Debt Creditors, if applicable), which shall be in form and substance reasonably acceptable to the Investor Representative and the Company, as amended, supplemented or otherwise modified from time to time and any replacements thereof.

"Depositary Bank" means such bank account specified to Investor Representative in writing by the Company on or prior to the Closing Date or such other bank or financial institution approved by the Investor Representative and the Company, including any successor Depositary Bank appointed pursuant to Section 3.2(d).

"Designated Jurisdiction" means any country, territory or region to the extent that such country, territory or region is the subject of any Sanction.

"Disposition" or "Dispose" means the sale, transfer, out-license, lease or other disposition (including any sale and leaseback transaction or any issuance by any Subsidiary of its Equity Interests other than to a Company Party) of any property included in the Collateral (or owned by any Pledged Subsidiary and relating to Imcivree) or any economic interest in the Collateral by any Company Party or any Affiliate of the Company, including any sale, assignment, transfer or other disposal, with or without recourse, of any notes or accounts receivable or any rights and claims associated therewith, but excluding the following (collectively, the "Permitted Transfers"): (a) the sale, lease, license, transfer or other disposition of inventory in the ordinary course of business, (b) the sale, lease, license, transfer or other disposition in the ordinary course of business of surplus, obsolete or worn out property no longer used or useful in the conduct of the business of the Company and its Affiliates, (c) any sale, lease, license, transfer or other disposition of property to any Company Party, (d) the abandonment or other disposition of Intellectual Property that is not material or are no longer used or useful in any material respect to the business of the Company and its Affiliates, (e) licenses, sublicenses, leases or subleases (other than relating to Intellectual Property, in each case) granted to third parties in the ordinary course of business and not interfering with the business of the Company and its Affiliates, (f) any Involuntary Disposition or any sale, lease, license or other disposition of property (other than, for the avoidance of doubt, Intellectual Property) in settlement of, or to make payment in satisfaction of, any property or casualty insurance, (g) dispositions consisting of the sale, transfer, assignment or other disposition of unpaid and overdue accounts receivable in connection with the collection, compromise or settlement thereof in the ordinary course of business and not as part of a financing transaction, (h) Permitted Licenses, (i) sales, leases, licenses, transfers or other dispositions of property to the extent that (i) such property is exchanged for credit against the purchase price of similar replacement property or (ii) the proceeds of such sale, lease, license, transfer or other disposition are promptly applied to the purchase price of similar replacement property, (j) the sale, transfer, issuance or other disposition of a *de minimis* number of shares of the Equity Interests of a Foreign Subsidiary of a Company Party in order to qualify members of the governing body of such Subsidiary if required by Applicable Law, (k) dispositions of cash and cash equivalents, in each case, in the ordinary course of business and (l) the sale, lease, license, transfer or other disposition of any asset among non-Company Parties. It is understood and agreed that, notwithstanding anything to the contrary set forth in this definition, in no event shall a "Permitted Transfer" include any license of Imcivree or owned by any Pledged Subsidiary and relating to Imcivree (or any Intellectual Property associated therewith) other than Permitted Licenses.

"Disputes" has the meaning set forth in Section 4.10(k).

"Disqualified Capital Stock" means any Equity Interests that (i) by its terms, (ii) by the terms of any security into which it is convertible or for which it is exchangeable, or (iii) by Contract or otherwise, is, or upon the happening of any event or passage of time would be, required to be redeemed, or is redeemable at the option of the holder thereof, in any such case on or prior to the date that is 91 days after the Legal Maturity Date; provided that only the portion of Equity Interests (or portion of security into which it is convertible or for which it is exchangeable) which is, or upon the happening of any event or passage of time would be, required to be redeemed, or is redeemable at the option of the holder thereof, on or prior to such date will be deemed to be Disqualified Capital Stock; and provided further that if such Equity Interests are issued to any plan for the benefit of directors, managers, employees, officers or consultants of the Company or its Subsidiaries or by any such plan to such directors, managers, employees, officers or consultants,

such Equity Interests shall not constitute Disqualified Capital Stock solely because it may be required to be repurchased by the Company or its Subsidiaries in order to satisfy applicable statutory or regulatory obligations. Notwithstanding the preceding sentence, any Equity Interests that would constitute Disqualified Capital Stock solely because the holders thereof have the right to require the redemption or repurchase of such Equity Interests upon the occurrence of a Change of Control, fundamental change or an asset sale will not constitute Disqualified Capital Stock if the "asset sale," "fundamental change" or "Change of Control" provisions applicable to such Equity Interests provide that the issuer thereof will not redeem or repurchase any such Equity Interests pursuant to such provisions prior to all other Obligations (other than contingent indemnification obligations for which no claim has been asserted) having been irrevocably paid in full in cash.

"Dollar" or the sign "$" means United States dollars.

"Domain Names" means all domain names and URLs that are registered and/or owned by or licensed to the Company or any Subsidiary or with respect to which the Company or any Subsidiary is authorized or granted rights under or to.

"Domestic Subsidiary" means any Subsidiary that is organized under the Laws of the United States, any state of the United States or the District of Columbia.

"Drug Application" means an application for Regulatory Approval to market, sell and distribute a drug or product in a country or region, including (a) a New Drug Application, (b) any corresponding foreign application in any country or jurisdiction in the world, including, with respect to the EEA, an application for a Marketing Authorization filed with the EMA, the MHRA or with the applicable Regulatory Agency of a country in the European Union with respect to the mutual recognition or any other national approval procedure, and (c) all supplements, amendments, variations, extensions and renewals thereof that may be filed with respect to the foregoing.

"EEA" means the European Economic Area and the United Kingdom.

"EEA Financial Institution" means (a) any credit institution or investment firm established in any EEA Member Country which is subject to the supervision of an EEA Resolution Authority, (b) any entity established in an EEA Member Country which is a parent of an institution described in clause (a) of this definition, or (c) any financial institution established in an EEA Member Country which is a Subsidiary of an institution described in clauses (a) or (b) of this definition and is subject to consolidated supervision with its parent.

"EEA Member Country" means any of the member states of the European Union, the United Kingdom, Iceland, Liechtenstein, and Norway.

"EEA Resolution Authority" means any public administrative authority or any person entrusted with public administrative authority of any EEA Member Country (including any delegee) having responsibility for the resolution of any EEA Financial Institution.

"Effective Date" has the meaning set forth in the preamble hereto.

"EMA" means the European Medicines Agency or any successor agency or authority thereto.

"Equity Interests" means, with respect to any Person, all of the shares of capital stock of (or other ownership or profit interests in) such Person, all of the warrants, options or other rights for the purchase or acquisition from such Person of shares of capital stock of (or other ownership or profit interests in) such Person, all of the securities convertible into or exchangeable for shares of capital stock of (or other ownership or profit interests in) such Person or warrants, rights or options for the purchase or acquisition from such Person of such shares (or such other interests), and all of the other ownership or profit interests in such Person (including partnership, member, membership or trust interests therein), whether voting or nonvoting, and whether or not such shares, warrants, options, rights or other interests are outstanding on any date of determination.

"ERISA" means the Employee Retirement Income Security Act of 1974 as amended.

"ERISA Affiliate" means any trade or business (whether or not incorporated) under common control with the Company within the meaning of Section 414(b) or (c) of the Internal Revenue Code (and Sections 414(m) and (o) of the Internal Revenue Code for purposes of provisions relating to Section 412 of the Internal Revenue Code).

"ERISA Event" means (a) a Reportable Event with respect to a Pension Plan, (b) the withdrawal of the Company or any ERISA Affiliate from a Pension Plan subject to Section 4063 of ERISA during a plan year in which such entity was a "substantial employer" as defined in Section 4001(a)(2) of ERISA or a cessation of operations that is treated as such a withdrawal under Section 4062(e) of ERISA, (c) a complete or partial withdrawal (within the meaning of Sections 4203 and 4205 of ERISA) by the Company or any ERISA Affiliate from a Multiemployer Plan, (d) the filing by the plan administrator of a notice of intent to terminate a Pension Plan or the treatment of a Pension Plan amendment as a termination under Sections 4041 of ERISA, (e) the institution by the PBGC of proceedings under Section 4042 of ERISA to terminate a Pension Plan, (f) the determination that any Multiemployer Plan is considered an at-risk plan or a plan in endangered or critical status within the meaning of Section 432 of the Internal Revenue Code or Section 305 of ERISA or is insolvent, within the meaning of Section 4245 of ERISA, or has been terminated, within the meaning of Section 4041A of ERISA, (g) the determination that any Pension Plan is in at-risk status within the meaning of Section 303 of ERISA, or (h) the imposition of any liability pursuant to Sections 4062(e) or 4069 of ERISA or by reason of the application of Section 4212(c) of ERISA upon the Company or any ERISA Affiliate.

"Event of Default" means any of the events set forth in Section 11.1.

"Event of Default Payment" means, as of any date of determination, the amount equal to the sum of (i) the Hard Cap less the aggregate of all of the payments of the Company in respect of the Revenue Interests (including any Under Performance Payment) made to the Investors prior to such date, plus (ii) any other Obligations due and payable by the Company Parties under this Agreement and the other Transaction Documents (if any).

"Excluded Liabilities and Obligations" has the meaning set forth in Section 2.2.

"Excluded Taxes" means (i) Taxes imposed on or measured by the Investor's net income, however denominated, franchise (and similar) Taxes imposed in lieu of net income Taxes, and branch profits Taxes (or any similar Taxes), in each case, imposed by any jurisdiction as a result of the Investor being organized in or having its principal office in such jurisdiction, or as a result of any other present or former connection between the Investor and such jurisdiction other than any connections arising from executing, delivering, being a party to, engaging in any transactions pursuant to, performing its obligations under, receiving payments under, or enforcing this Agreement, (ii) Taxes attributable to the failure of the Investor to deliver any documentation reasonably requested by the Company that the Investor is legally eligible to deliver, (iii) any U.S. federal withholding Taxes imposed on any payment by or on account of any obligation of any Company Party hereunder to an Investor pursuant to a Law in force at the time such Investor becomes a party hereto (or designates a new funding office), except to the extent that such Investor (or its assignor, if any) was entitled, immediately prior to the designation of a new funding office (or assignment), to receive Additional Amounts with respect to such withholding Tax pursuant to Section 6.22(c), and (iv) any withholding Taxes imposed under FATCA.

"FATCA" means Sections 1471 through 1474 of the Internal Revenue Code, as of the date of this Agreement (or any amended or successor version that is substantively comparable and not materially more onerous to comply with), any current or future regulations or official interpretations thereof, any agreements entered into pursuant to current Section 1471(b)(1) of the Internal Revenue Code (or any amended or successor version described above) and any fiscal or regulatory legislation, rules or official administrative guidance adopted pursuant to any intergovernmental agreement, treaty or convention among Governmental Authorities and that implement such Sections of the Internal Revenue Code.

"FCPA" has the meaning set forth in Section 4.24(b).

"FDA" means the U.S. Food and Drug Administration or any successor agency or authority thereto.

"Financial Statements" means the Audited Financial Statements and the Interim Financial Statements.

"Foreign Subsidiary" means any Subsidiary that is not a Domestic Subsidiary.

"French Subsidiary" means Rhythm Pharmaceuticals France SAS, a company organized under the laws of France.

"Fundamental Representations" means those representations and warranties of the Company set forth in Section 4.1 (Organization), Section 4.2 (No Conflicts), Section 4.2(a) (Authorization), Section 4.4 (Ownership), Section 4.8 (No Broker's Fees), Section 4.10 (Intellectual Property Matters) (except for Section 4.10(p)) , Section 4.13 (Bankruptcy), Section 4.21 (Perfection of Security Interests), Section 4.22 (Sufficiency of Collateral), Section 4.24 (Sanctions Concerns; Anti-Corruption Laws; PATRIOT Act) and Section 6.22 (Tax).

"GAAP" means generally accepted accounting principles in effect as the standard financial accounting guidelines in the United States from time to time (consistently applied and on a basis consistent with the accounting policies, practices, procedures, valuation methods and principles used in preparing the Financial Statements), and any successor thereto; provided that if a transition in such generally accepted accounting principles would substantively change the recognition of revenue with respect to Net Revenues (defined as of the Effective Date) and its calculation as set forth in this Agreement, then the Parties shall mutually agree to amendments to this Agreement in order to cause the amount of Revenue Interests as determined after giving effect to such transition in generally accepted accounting principles to be substantially the same as the amount of Revenue Interests as determined under generally accepted accounting principles in effect as the standard financial accounting guidelines in the United States as of the Effective Date.

"German Subsidiary" means Rhythm Pharmaceuticals Germany GmbH, a company organized under the laws of Germany.

"Governmental Authority" means the government of the United States, any other nation or any political subdivision thereof, whether state, local or otherwise, and any agency, authority (including supranational authority), commission, instrumentality, regulatory body, court, central bank or other Person exercising executive, legislative, judicial, taxing, regulatory or administrative powers or functions of or pertaining to government, including each Patent Office, the FDA, the EMA, the MHRA and any other government authority in any jurisdiction.

"Grantors" means the Company and the Guarantors.

"Guarantors" means (i) subject to Section 6.23 of this Agreement, the German Subsidiary, (ii) subject to Section 6.23 of this Agreement, the French Subsidiary and (iii) any other Subsidiary of the Company that executes and delivers a Joinder Agreement pursuant to Section 6.1 once such Subsidiary has recognized revenue from the sale or distribution of Imcivree.

"Guaranty" means a customary guaranty attached to the Security Agreement, to be executed in favor of the Investor Representative, for the benefit of the Investors, by the Company and each of the Guarantors, as amended or modified from time to time in accordance with the terms hereof.

"Hard Cap" means the percentage based Investment Amounts, as set forth in the chart below:

Received by:	Specified Percentage for Hard Cap
[***] 2028	185%
[***]	200%
[***]	225%
[***] 2032	250%

"Imcivree" means the compound described on Schedule 1 and any pharmaceutical or biological composition containing setmelanotide, including any modifications or improvements thereto and any other product that directly competes with or replaces Imcivree that may be developed or marketed by the Company or any of its Subsidiaries, including any products or product candidates that are being developed by the Company or any of its Subsidiaries as of the date of this Agreement.

"Imcivree Patent Rights" means the Owned Imcivree Patent Rights and the Licensed Imcivree Patent Rights.

"Included Product" means Imcivree and any other product that may be developed or marketed by any Company Party. For clarity, references in this Agreement to "an" Included Product or to "the" Included Product(s) refer to any Included Product(s).

"Included Product Payment Amount" means, for each Calendar Quarter, an amount equal to the Applicable Tiered Percentage multiplied by the Quarterly Net Revenues for such Calendar Quarter. For clarity, the Applicable Tiered Percentage used to calculate the Included Product Payment Amount for a given Calendar Quarter will be based on the aggregate Net Revenues billed or invoiced in such Calendar Quarter and all prior Calendar Quarters in the applicable Calendar Year. The Included Product Payment Amount for each Quarterly Payment Date shall be determined in a manner consistent with the example of such calculation set forth in Exhibit C.

"Indebtedness" of any Person means (a) any obligation of such Person for borrowed money, (b) any obligation of such Person evidenced by a bond, debenture, note or other similar instrument, (c) any obligation of such Person to pay the deferred purchase price of property or services (except (i) trade accounts payable that arise in the ordinary course of business, (ii) payroll liabilities and deferred compensation, and (iii) any purchase price adjustment, royalty, earnout, milestone payments, contingent payment or deferred payment of a similar nature incurred in connection with any license, lease, contract research and clinic trial arrangements or acquisition), (d) any obligation of such Person as lessee under a capital lease (under GAAP as in effect on the date hereof), (e) any obligation of such Person to purchase securities or other property that arises out of or in connection with the sale of the same or substantially similar securities or property, (f) any non-contingent obligation of such Person to reimburse any other Person in respect of amounts paid under a letter of credit or other Guaranty issued by such other Person, (g) any Indebtedness of others secured by a Lien on any asset of such Person, and (h) any Indebtedness of others

guaranteed by such Person; provided that intercompany loans among the Company and its Affiliates shall not constitute Indebtedness. For the avoidance of doubt no Permitted Warrant Transaction shall constitute Indebtedness.

"Indemnified Taxes" means all Taxes imposed on or with respect to any payment made by or on account of any obligation of any Company Party under this Agreement, other than Excluded Taxes.

"Initial Closing" has the meaning set forth in Section 8.1(a).

"Initial Closing Date" has the meaning set forth in Section 8.1(a).

"Initial Investment Amount" has the meaning set forth in Section 2.1(a).

"Instruction to Payors" has the meaning set forth in Section 3.2(a).

"Intellectual Property" means all intellectual property, including but not limited to all proprietary information, Trade Secrets, Know-How, utility models; Confidential Information; inventions (whether patentable or unpatentable and whether or not reduced to practice or claimed in a pending patent application) and improvements thereto, Patents, registered or unregistered Trademarks, trade names and service marks (including all goodwill associated therewith), registered and unregistered Copyrights and all applications thereof.

"Interim Financial Statements" means the unaudited, condensed and consolidated balance sheets of the Company and its Subsidiaries for the 3 month period ended March 31, 2022, and the related condensed and consolidated statements of operation and comprehensive Loss, stockholders' equity and cash flows for such period of the Company and its Subsidiaries, including the notes thereto.

"Internal Revenue Code" means the United States Internal Revenue Code of 1986, as amended.

"Investment Amount" means the aggregate of the Initial Investment Amount and, if funded pursuant to Section 2.1(b), the Second Investment Amount and, if funded pursuant to Section 2.1(c), the Third Investment Amount.

"Investor" or "Investors" means the Persons identified as an "Investor" on the signature pages hereto and their successors and assigns.

"Investor Account" means such account as designated by the Investor Representative to the Company in writing from time to time.

"Investor Indemnification Obligations" has the meaning set forth in Section 10.2.

"Investor Indemnified Party" has the meaning set forth in Section 10.1.

"Investor Representative" has the meaning set forth in the preamble.

"Involuntary Disposition" means any loss of, damage to or destruction of, or any condemnation or other taking for public use of, any property of any Party or any of its Subsidiaries.

"Ipsen License Agreement" means that certain License Agreement dated February 26, 2010, by and between the Company and Ipsen Pharma S.A.S., a French corporation, as may be amended, supplemented, restated or otherwise modified from time to time.

"IRS" means the United States Internal Revenue Service.

"Joinder Agreement" means a joinder agreement substantially in the form of Exhibit D executed and delivered by each Subsidiary in accordance with the provisions of Section 6.1.

"Know-How" means all non-public information, results and data of any type whatsoever, in any tangible or intangible form (and whether or not patentable), including databases, practices, methods, techniques, specifications, formulations, formulae, knowledge, skill, experience, data and results (including pharmacological, medicinal chemistry, biological, chemical, biochemical, toxicological and clinical study data and results), analytical and quality control data, stability data, studies and procedures, and manufacturing process and development information, results and data.

"Knowledge" means, with respect to the Company, (a) for purposes of ARTICLE IV, the knowledge, after due inquiry, as of the date of this Agreement, of any of the officers of the Company identified on Schedule 1.1-1, and (b) for all other purposes of this Agreement, the knowledge, after due inquiry, as of a specified time, of any of the officers of the Company identified on Schedule 1.1-1 or any successor to any such officer holding the same or substantially similar officer position at such time.

"Laws" means, collectively, all international, foreign, federal, state and local statutes, treaties, rules, guidelines, regulations, ordinances, codes and administrative or judicial precedents or authorities, including the interpretation or administration thereof by any Governmental Authority charged with the enforcement, interpretation or administration thereof, in each case, having the force of law.

"Legal Maturity Date" means the date that is the 12 year anniversary of the Initial Closing Date.

"License Agreement" means any Contract pursuant to which a Third Party to whom the Company or any Affiliate of the Company grants a license or sublicense (or any Third Party to whom such Third Party grants a license or sublicense) to develop, have developed, make, have made, seek Regulatory Approvals for, distribute, use, have used, import, sell, offer to sell, have sold or otherwise Commercialize such Included Product under the applicable Contract.

"Licensee" means, with respect to any Included Product, a Third Party to whom the Company or any Affiliate of the Company has granted a license or sublicense (or any Third Party to whom such Third Party has granted a license or sublicense) to develop, have developed, make, have made, seek Regulatory Approvals for, distribute, use, have used, import, sell, offer to sell,

have sold or otherwise Commercialize such Included Product under the applicable License Agreement.

"Licensed Imcivree Patent Rights" means all Patent Rights that relate to Imcivree and are licensed or sublicensed to the Company or any of its Subsidiaries.

"Lien" means any security interest, mortgage, pledge, hypothecation, assignment, deposit arrangement, encumbrance, lien (statutory or otherwise), charge against or interest in property or other priority or preferential arrangement of any kind or nature whatsoever, in each case to secure payment of a debt or performance of an obligation, including any conditional sale or any sale with recourse.

"Lockbox Account" means one Deposit Account per Company or Guarantor, as applicable, established and maintained at any Depositary Bank solely for the purpose of receiving remittance of proceeds of accounts and royalty receivables of the Company arising from sales of Included Products or Other Royalty Payments and disbursement thereof as provided herein, and any successor Lockbox Account entered into in accordance with Section 3.2(d).

"Loss" means any loss, assessment, award, cause of action, claim, charge, Tax, cost, expense (including reasonable expenses of investigation and reasonable attorneys' fees), fine, judgment, liability, obligation or penalty; provided, however that Loss shall not include any lost profits or revenue or consequential, punitive, special or incidental damages except (a) the amount of any Revenue Interests that are not received by Investor Representative (on behalf of the Investors) due to failure by any Third Party to make payment thereof (other than resulting from any matter described in Section 10.1, Section 10.2, Section 10.3 or Section 10.4) and (b) any lost profits or revenue or consequential, punitive, special or incidental damages awarded or payable by an Investor to a Third Party in connection with a claim or action for which the Company is required to indemnify the Investors pursuant to Section 10.1.

"Major European Markets" means the countries set forth on Schedule 1.1-4.

"Marketing Authorization" means, with respect to an Included Product, the Regulatory Approval required by Applicable Law to sell such Included Product in a country or region, including, to the extent required by Applicable Law for the sale of such Included Product, all pricing approvals and government reimbursement approvals.

"Massachusetts Securities Corporation" means any Subsidiary that is classified as a "security corporation" under Massachusetts General Law c. 63, § 38B and that meets the requirements of that section for the year in question.

"Material Adverse Effect" means (a) a material adverse change in, or a material adverse effect upon, the business, assets, properties, liabilities or condition (financial or otherwise) of the Company and its Subsidiaries taken as a whole, (b) a material impairment of the rights and remedies of the Investors under any Transaction Document to which it is a party or a material impairment in the perfection or priority of the Investors' security interests in the Collateral, (c) an impairment of the ability of the Company Parties (taken as a whole) to perform their respective obligations under the Transaction Documents that could reasonably be expected to have a material

adverse effect on the business, assets, properties, liabilities or condition (financial or otherwise) of the Company and its Subsidiaries taken as a whole, (d) a material adverse effect upon the legality, validity, binding effect or enforceability against any Company Party of any Transaction Document, when taken as a whole, to which it is a party, or (e) an adverse effect (other than a *de minimis* effect) on the timing, amount or duration of payments due in respect of Net Revenues in accordance with the Transaction Documents or the right of the Investors to receive payments due in respect of Net Revenues that was as a result of any action or inaction by the Company or any of its Subsidiaries.

"Material Contract Counterparty" means a counterparty to any Material Contract.

"Material Contracts" means (i) the Ipsen License Agreement, (ii) the Camurus License Agreement, (iii) the Rarestone License Agreement and (iv) any License Agreement entered into by the Company or any of its Subsidiaries for the Commercialization of Imcivree anywhere in the world.

"MHRA" means the United Kingdom's Medicines and Healthcare products Regulatory Authority.

"Minimum Multiple" means the multiples of the then-current Investment Amount as set forth in Column A of the chart in Section 3.1(b).

"Minimum Return Date" means the date on which the Investors have received aggregate payments on account of the Revenue Interest equal to 120% of the Investment Amount.

"Multiemployer Plan" means any "employee benefit plan" (as defined in Section 3(3) of ERISA) that is a "multiemployer plan" as defined in Section 4001(a)(3) of ERISA, to which the Company or any ERISA Affiliate makes or is obligated to make contributions, or during the preceding 5 plan years, has made or been obligated to make contributions.

"Net Revenues" means the Net Sales, Other Royalty Payments and any other payments made in lieu of the sale of any Included Product (to the extent such payments are not included in the Net Sales or Other Royalty Payments) recognized as revenue by the Company and its Subsidiaries in accordance with GAAP.

"Net Sales" means, with respect to the Included Product, the gross amount recognized as revenue by the Company and its Subsidiaries in accordance with GAAP in respect of sales or other Dispositions of the Included Product by the Company, its Affiliates or (with respect to the U.S. and the EEA) Licensees (or any permitted assignee or transferee hereunder) (but not including sales to an Affiliate or Licensee unless the Affiliate or Licensee is the ultimate end user of the Included Product; provided that for purposes of this Net Sales definition, a Third Party distributor to which the Company has sold Included Product for no less than wholesale value shall be considered an "end user", and sales by such distributor to any Third Parties shall not be included in Net Sales), less the following deductions to the extent included in the gross amount recognized as revenue by the Company and its Subsidiaries in accordance with GAAP: (a) rebates, credits or allowances actually granted for damaged or defective products, returns or rejections of Included Products or recalls, or for retroactive price reductions and billing errors; (b) normal and

customary trade, cash, quantity and other customary discounts, allowances and credits (including chargebacks) given to Third Parties in the ordinary course of business; (c) excise Taxes, sales Taxes, duties, VAT Taxes and other Taxes to the extent imposed upon and paid with respect to the sales price, and a pro rata portion of pharmaceutical excise Taxes imposed on sales of pharmaceutical products as a whole and not specific to Included Products (such as those imposed by the U.S. Patient Protection and Affordable Care Act of 2010, Pub. L. No. 111-148, as amended) (and excluding in each case national or local Taxes based on income); (d) freight, postage, shipping and shipping insurance expense and other transportation charges directly related to the distribution of the Included Product; (e) distribution services agreement fees and other similar amounts allowed or paid to Third Party distributors, including specialty distributors of the Included Product, (f) rebates made with respect to sales paid for by any Governmental Authority (including, without limitation, Medicaid and Medicare), their agencies and purchasers and reimbursers, managed health care organizations, or to trade customers; (g) the portion of administrative fees paid during the relevant time period to group purchasing organizations or pharmaceutical benefit managers relating to the Included Product; (h) any invoiced amounts that are not collected by the Company, its Affiliates or Licensees, including bad debts; and (i) any customary or similar payments to the foregoing (a) – (h) that apply to the sale or Disposition of pharmaceutical products.

"New Drug Application" means a new drug application submitted to the FDA under 21 U.S.C. § 355(b) and all amendments or supplements thereto.

"Obligations" means all liabilities, obligations, covenants and duties of any the Company Parties arising under this Agreement or any other Transaction Document with respect to the payment of the Revenue Interest (including any Under Performance Payment) up to the Hard Cap, any Special Termination Amount and the obligations of the Company to pay any interest accrued on any unpaid Revenue Interests or unpaid portion of the Event of Default Payment and reimburse or indemnify the Investors for any Losses incurred by the Investors in connection with the enforcement of its rights under this Agreement.

"OFAC" means the Office of Foreign Assets Control of the United States Department of the Treasury.

"Orange Book" means the FDA publication "Approved Drug Products with Therapeutic Equivalence Evaluations," as may be amended from time to time.

"Organization Documents" means, (a) with respect to any corporation, the certificate or articles of incorporation and the bylaws (or equivalent or comparable constitutive documents with respect to any non-U.S. jurisdiction), (b) with respect to any limited liability company, the certificate or articles of formation or organization and operating agreement, and (c) with respect to any partnership, joint venture, trust or other form of business entity, the partnership, joint venture or other applicable agreement of formation or organization and any agreement, instrument, filing or notice with respect thereto filed in connection with its formation or organization with the applicable Governmental Authority in the jurisdiction of its formation or organization and, if applicable, any certificate or articles of formation or organization of such entity.

"Other Royalty Payments" means, without duplication, any partnership distributions, royalty payments, upfront payments, milestone payments or similar payments or any other amounts payable by the Licensees to the Company or its Affiliates under or in respect of the applicable License Agreement or any other amounts or proceeds arising from the applicable License Agreement other than: (a) payments by the Licensees for payment or reimbursement of expenses, including patent prosecution, defense, enforcement or maintenance expenses in respect of any Intellectual Property; (b) the fair market value of payments received by Company from a Licensee for any debt and/or equity securities or instruments issued by Company, or payments for an acquisition of all or substantially all of its assets that include the assignment of this Agreement; (c) funds received from a Licensee as a reimbursement of expenses for bona fide research and development of Included Products (including payments for full-time employees, clinical development and manufacturing expenses); (d) currently unrecognized revenue from any cash payments received on or before the Initial Closing Date under lease agreements in effect as of the Initial Closing Date; and (e) royalty payments payable by any Licensee to the Company or any of its Affiliates with respect to Net Sales by any such Licensee in the U.S. or the Major European Markets (to the extent that end user sales by such Licensees would be recognized as Net Sales hereunder if such sales had been made by the Company or any of its Subsidiaries).

"Owned Imcivree Patent Rights" means Patent Rights relating to Imcivree which are owned by the Company or its Subsidiaries.

"Patent License" means any agreement, whether written or oral, providing for the grant of any right under any Patent.

"Patent Office" means the applicable patent office, including the United States Patent and Trademark Office and any comparable foreign patent office, for any Patents.

"Patent Rights" means all letters patent and patent applications in the United States and all other countries (and all letters patent that issue therefrom or from an application claiming priority therefrom) and all patent term extensions, supplementary protection certificates, reissues, reexaminations, extensions, renewals, divisions and continuations (including continuations-in-part and continuing prosecution applications) thereof, for the full term thereof, together with the right to claim the priority thereto and the right to sue for past infringement of any of the foregoing.

"Payment Term" means the time period commencing on the Initial Closing Date and expiring on the date upon which the Investor Representative has received in full (i) cash payments in respect of the Revenue Interests totaling, in the aggregate, the Hard Cap and (ii) any other Obligations payable by the Company Parties under this Agreement and the other Transaction Documents.

"Pension Plan" means any "employee pension benefit plan" (as defined in Section 3(2) of ERISA), other than a Multiemployer Plan, that is maintained or is contributed to by the Company and any ERISA Affiliate and is either covered by Title IV of ERISA or is subject to minimum funding standards under Section 412 of the Internal Revenue Code.

"Permits" means licenses, certificates, accreditations, Regulatory Approvals, other authorizations, registrations, permits, consents, clearances and approvals required in connection

with the conduct of the Company's or any Subsidiary's business or to comply with any Applicable Laws, and those issued by state governments for the conduct of the Company's or any Subsidiary's business.

"Permitted Bond Hedge Transaction" means any call or capped call option (or substantively equivalent derivative transaction) relating to the Company's common stock (or other securities or property following a merger event or other change of the common stock of the Company) purchased by the Company in connection with the issuance of any Permitted Convertible Notes; provided that the purchase price for such Permitted Bond Hedge Transaction, less the proceeds received by the Company from the sale of any related Permitted Warrant Transaction, does not exceed the net proceeds received by borrower from the issuance of such Permitted Convertible Notes in connection with such Permitted Bond Hedge Transaction.

"Permitted Convertible Notes" means unsecured Indebtedness of the Company to be issued in the form of notes that are convertible into a number (subject to customary anti-dilution adjustments, "make whole" increases and other customary changes thereto) of shares of common stock of the Company (or other securities or property following a merger event or other change of the common stock of the Company), cash or any combination thereof (with the amount of such cash or such combination determined by reference to the market price of such common stock or other securities); provided that: (i) such convertible notes shall not be guaranteed by any Subsidiary of the Company that is a Guarantor or any Subsidiary the Equity Interests of which are pledged to the Investors, (ii) the aggregate of the principal amounts of such convertible notes shall not exceed [***]% of the market capitalization of the Company (determined at the time of signing of the definitive agreement for the purchase or sale of such convertible notes) and (iii) such convertible notes shall not have a maturity date earlier than the 7th anniversary of the Initial Closing Date.

"Permitted Convertible Notes Creditors" means the lenders or holders of Permitted Convertible Notes.

"Permitted Debt" means any of the following Indebtedness of the Company and its Subsidiaries (which, for purposes of determining whether such Indebtedness exceeds any maximum amount provided in the applicable clause below, shall be calculated on a consolidated basis with respect to the Company and its Subsidiaries):

(a) the Indebtedness of the Company and its Subsidiaries in respect of any Permitted Debt Facility;

(b) Indebtedness under the Transaction Documents;

(c) unsecured Indebtedness to trade creditors incurred in the ordinary course of business;

(d) Guarantees of the Company and its Subsidiaries in respect of Indebtedness and other obligations of the Company and any Subsidiary otherwise expressly permitted hereunder;

(e) Indebtedness incurred by the Company or its Subsidiaries consisting of (i) the financing of the payment of insurance premiums (ii) take or pay obligations contained in supply agreements, in each case, in the ordinary course of business or consistent with past practice, (iii) deferred compensation or equity based compensation to current or former officers, directors, consultants, advisors or employees thereof, in each case in the ordinary course of business and (iv) customer deposits and advance payments received in the ordinary course of business or consistent with past practice from customers for goods or services purchased in the ordinary course of business or consistent with past practice;

(f) Indebtedness owed to any Person providing worker's compensation, health, disability or other employee benefits or property, casualty or liability insurance to the Company or any Subsidiary incurred in connection with such Person providing such benefits or insurance pursuant to customary reimbursement or indemnification obligations to such Person;

(g) Indebtedness in respect of performance, indemnity, bid, stay, customs, appeal, replevin and surety bonds, performance and completion guarantees and other similar bonds or guarantees, trade Contracts, government Contracts and leases, in each case, incurred in the ordinary course of business but excluding Guaranties with respect to any obligations for borrowed money;

(h) Indebtedness arising from (i) the honoring by a bank or other financial institution of a check, draft, or similar instrument drawn against insufficient funds in the ordinary course of business or other cash management services in the ordinary course of business provided that such Indebtedness is extinguished within five (5) Business Days of notification to the Company of its incurrence and (ii) Treasury Management Arrangements;

(i) (i) Indebtedness of the Company or any Subsidiary of the Company supported by a letter of credit issued pursuant to any Permitted Debt Facility in an amount not in excess of the stated amount of such letter of credit, and (ii) letters of credit, bankers' acceptances, guarantees or other similar instruments or obligations issued or relating to liabilities or obligations incurred in the ordinary course of business; provided, that, the aggregate outstanding amount of such letters of credit issued under clause (ii) above shall not exceed $[***] at any time outstanding;

(j) judgments, decrees, attachments or awards (to the extent that they would be deemed Indebtedness) that do not constitute an Event of Default;

(k) Indebtedness in the form of (i) guarantees of loans and advances to officers, directors, consultants, managers and employees, in an aggregate amount not to exceed $[***] at any one time outstanding, and (ii) reimbursements owed to officers, directors, managers, consultants and employees of the Company or any Subsidiary for business expenses of the Company or any Subsidiary;

(l) Indebtedness consisting of obligations to make payments to current or former officers, directors and employees of the Company or any of its Subsidiaries, their respective estates, spouses or former spouses with respect to the cancellation, purchase or redemption of Equity Interests of the Company or any of its Subsidiaries to the extent such cancellation, purchase or redemption is permitted under Section 7.7;

(m) the incurrence by the Company or any Subsidiary of Indebtedness arising from agreements providing for indemnification, holdback, earnout, adjustment of purchase price, working capital adjustments or similar obligations, or guarantees or letters of credit, surety bonds or performance bonds securing any obligations of the Company or any Subsidiary pursuant to such agreements, in any case incurred in connection with the disposition or acquisition of any business or assets of the Company or any Subsidiary or Equity Interests of a Subsidiary that is not prohibited under this Agreement;

(n) Indebtedness consisting of capitalized lease obligations and purchase money Indebtedness, in each case incurred to finance the acquisition, repair, improvement or construction of fixed or capital assets of such person, provided that the principal amount of such Indebtedness does not exceed the lower of the cost or fair market value of the property so acquired or built or of such repairs or improvements financed with such Indebtedness (each measured at the time of such acquisition, repair, improvement or construction is made); provided, that, (i) the total of all such Indebtedness for all such Persons taken together shall not exceed an aggregate principal amount of $[***] at any one time outstanding, (ii) such Indebtedness when incurred shall not exceed the purchase price of (or the repair, improvement or constructions costs for) the asset(s) financed and (iii) no such Indebtedness shall be refinanced, renewed or extended for a principal amount in excess of the principal balance outstanding thereon at the time of such refinancing, renewal or extension;

(o) Indebtedness in respect of hedging agreements; provided, that, such obligations are (or were) entered into by such Person in the ordinary course of business for the purpose of directly mitigating risks associated with liabilities, commitments, investments, assets, or property held or reasonably anticipated by such Person, or changes in the value of securities issued by such Person, and not for purposes of speculation or taking a "market view";

(p) other unsecured Indebtedness not otherwise permitted hereunder, provided that under no circumstances shall the aggregate outstanding principal amount of such Indebtedness permitted shall not exceed $[***];

(q) secured or unsecured revolving line(s) or credit (secured only by accounts receivable and inventory and assets which are unrelated to Imcivree) in an amount not to exceed $[***];

(r) to the extent constituting Indebtedness, the grant of any indefeasible right of use or similar arrangements, including put rights granted in connection therewith;

(s) Indebtedness incurred to refinance the Permitted Debt set forth in any of clauses (a) through (e); provided that the type and amount of such refinancing Indebtedness is permitted under such clause;

(t) Indebtedness secured by Liens of any of the types described under clauses (c), (d) and (f) of the definition of Permitted Liens, but only to the extent of the Indebtedness related thereto; and

(u) Acquired Debt provided that prior to the Minimum Return Date, the aggregate outstanding amount of all of the Acquired Debt shall not exceed $[***] at any one time outstanding;

(v) the Indebtedness set forth on Schedule 4.15.

"Permitted Debt Creditors" means the lenders or noteholders, and any administrative agent, collateral agent, security agent or similar agent under any Permitted Debt Facility.

"Permitted Debt Facility" means an unsecured credit facility provided under the Permitted Convertible Notes.

"Permitted Debt Facility Documents" means the documents relating to the Permitted Convertible Notes.

"Permitted Licensee" means a Third Party counterparty to a Permitted License.

"Permitted Licenses" means, collectively, (a) licenses of over-the-counter software that is commercially available to the public, (b) non-exclusive and exclusive licenses for the use of the Intellectual Property of the Company or any of its Subsidiaries entered into in the ordinary course of business, including nonexclusive license entered into in the ordinary course of the Company's business in the development, manufacture and/or Commercialization of Imcivree or the distribution of Imcivree in the United States, (c) licenses of Imcivree outside the United States and the Major European Markets provided, that, with respect to each such license described in clause (b) or (c), (i) no Special Termination Event, Default or Event of Default has occurred or is continuing at the time of entry into such license, (ii) the license constitutes an arms-length transaction, the terms of which, on their face, do not provide for a sale or assignment from the Company or its Affiliates to a Third Party of any Intellectual Property that, at the time of execution of such license, comprises a portion of the Collateral or the assets of the Pledged Subsidiaries relating to Imcivree, and do not restrict the ability of the Company or any of its Subsidiaries, as applicable, to pledge, grant a Lien on or assign or otherwise transfer such Intellectual Property (in each case other than customary non-assignment provisions that restrict the assignability of the license but do not otherwise restrict the ability of the Company or any Subsidiary (as applicable) to pledge, grant a Lien on or assign any such Intellectual Property) and (iii) in the case of any exclusive license to Commercialize Imcivree outside the United States and the Major European Markets, (A) the Company delivers to the Investor Representative a copy of the final executed exclusive license promptly upon consummation thereof, subject to reasonable redaction to comply with obligations of confidentiality, and (B) may be exclusive in respects other than geographical area and may be exclusive as to geographical area only as to geographical areas outside of the United States and the Major European Markets and (iv) all Other Royalty Payments that are payable to the Company or any of its Subsidiaries thereunder are paid or promptly transferred to a Lockbox Account; (d) any license granted to any Third Party for the manufacture of any Included Product or otherwise granted to a vendor or service provider in order to provide services for the benefit of the Company or its Affiliates; and (e) any sponsored research or similar agreement providing for the development of an Included Product that does not grant Commercialization rights to such Included Product. It is understood and agreed that, notwithstanding anything to the contrary

set forth in this definition, in no event shall a "Permitted License" include any exclusive license to Commercialize Imcivree (or any Intellectual Property associated therewith) in the United States or the Major European Markets (or, in each case, any state or other political subdivision thereof), and a "Permitted License" may include a nonexclusive license to a Third Party in the ordinary course of the Company's business in the import, export, manufacture, make, use, sale, offer for sale, promotion or distribution of such Included Products so long as such nonexclusive license does not grant to any Third Party the right to sell, offer for sale, market or promote such Included Product on a royalty payment basis, profit sharing basis or any other similar payment structure.

"Permitted Liens" means:

(a) Liens created in favor of the Investor Representative, for the benefit of the Investors, pursuant to the Transaction Documents;

(b) Liens incurred by the Investors;

(c) Liens in respect of property of the Company imposed by Applicable Law which were incurred in the ordinary course of business and do not secure Indebtedness, such as carriers', warehousemen's, distributors', wholesalers', materialmen's and mechanics' Liens and other similar Liens arising in the ordinary course of business and secure payment obligations (i) not then due, (ii) if due, not yet overdue by more than 30 days, (iii) that if overdue by more than 30 days, are being contested in good faith by appropriate proceedings for which adequate reserves have been established in accordance with GAAP or (iv) with respect to which the failure to make payment would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect;

(d) Liens incurred in the ordinary course of business in connection with worker's compensation, unemployment insurance or other forms of governmental insurance or benefits, insurance, surety bonds, or other obligations of a like nature or to secure the performance of letters of credit, banker's acceptances, bids, tenders, statutory obligations, leases and Contracts (other than for borrowed money) entered into in the ordinary course of business, other than any Lien imposed by ERISA which has resulted or would result in liability, together with any other Lien imposed by ERISA, in an aggregate amount in excess of $[***];

(e) Liens for Taxes, assessments and governmental charges that are not delinquent or remain payable without penalty or that are being contested in good faith and with due diligence by appropriate proceedings and for which adequate reserves have been established in accordance with GAAP;

(f) banker's Liens for collection or rights of set off or similar rights and remedies as to Deposit Accounts or other funds maintained with depositary institutions; provided that such Deposit Accounts or funds are not established or deposited for the purpose of providing collateral for any Indebtedness and are not subject to restrictions on access by the Company in excess of those required by applicable banking regulations;

(g) Liens on assets that do not constitute (i) Collateral or (ii) the assets of the Pledged Subsidiaries relating to Imcivree;

(h) Liens in favor of the Company or any Subsidiary;

(i) Liens on property or Equity Interests of another Person existing at the time of acquisition or such other Person becoming a Subsidiary of the Company; provided that such Liens were in existence prior to the contemplation of such acquisition, merger, amalgamation or consolidation and do not extend to any assets other than those of the Person that becomes a Subsidiary of the Company and provided, further that such Liens were granted to secure repayment of Acquired Debt;

(j) Liens on Equity Interests of Subsidiaries that are not (i) Guarantors or (ii) Pledged Subsidiaries;

(k) Liens existing on the date of this Agreement and set forth on Schedule 1.1-2;

(l) Liens securing Indebtedness permitted to be incurred under clause (p) of the definition of "Permitted Debt" covering only the assets acquired with or financed by such Indebtedness; provided that individual financings provided by one lender may be cross collateralized to other financings provided by such lender or its Affiliates;

(m) customary Liens incurred in the ordinary course of business to secure obligations in respect of payment processing services, business credit card programs, and netting services, overdrafts and related liabilities arising from treasury, depositary and cash management services;

(n) Liens on insurance policies, premiums and proceeds thereof, or other deposits, to secure insurance premium financings with respect to unearned premiums and other liabilities to insurance carriers;

(o) Liens on specific items of inventory or other goods (and the proceeds thereof) of the Company securing such Person's obligations in respect of bankers' acceptances issued or created for the account of such Person to facilitate the purchase, shipment or storage of such inventory or other goods;

(p) Liens arising out of conditional sale, title retention, consignment or similar arrangements for the sale of goods entered into in the ordinary course of business;

(q) Liens in favor of customs and revenue authorities arising as a matter of law to secure payment of customs duties in connection with the importation of goods in the ordinary course of business;

(r) any interest or title of a lessor or licensor under any lease, sublease, license or sublicense entered into by the Company or any Subsidiary entered into in the ordinary course of its business;

(s) Liens on cash collateral securing hedging agreements entered into for bona fide hedging purposes in the ordinary course of business and not for speculative purposes; and

(t) Liens securing or arising out of judgments, decrees, orders, awards or notices of lis pendens and associated rights related to litigation with respect to which such Person shall then be proceeding with an appeal or other proceedings for review, or in respect of which the period within which such appeal or proceedings may be initiated shall not have expired, and Liens on litigation proceeds securing obligations to pay expenses incurred in connection with such litigation and Liens arising from judgments, decrees, attachments or awards that do not constitute an Event of Default;

(u) Liens in favor of collecting or payor banks having a right of Set-off, revocation, refund or chargeback with respect to money or instruments of the Company or any Subsidiary on deposit with or in possession of such bank;

(v) Liens on equipment or inventory of the Company or any Subsidiary granted in the ordinary course of business to the Company's or such Subsidiary's supplier at which such equipment or inventory is located;

(w) Liens arising from precautionary Uniform Commercial Code financing statements regarding operating leases or consignments and other precautionary UCC financing statements or similar filings;

(x) Liens on any assets held by a trustee (i) under any indenture or other debt instrument where the proceeds of the securities issued thereunder are held in escrow pursuant to customary escrow arrangements pending the release thereof, and (ii) under any indenture pursuant to customary discharge, redemption or defeasance provisions;

(y) Liens of (i) a collection bank arising under Section 4-210 of the Uniform Commercial Code (or any analogous statutory provision of applicable foreign Law) on items in the course of collection and which arise from general banking conditions, (ii) attaching to commodity trading accounts or other commodities brokerage accounts incurred in the ordinary course of business and (iii) in favor of a banking or other financial institution arising as a matter of law or under customary general terms and conditions encumbering deposits or other funds maintained with a financial institution (including the right of setoff) and that are within the general parameters customary in the banking industry or arising pursuant to such banking institutions general terms and conditions;

(z) survey exceptions, encumbrances, ground leases, easements (including reciprocal easement agreements), survey exceptions or reservations of, or rights of others for, licenses, rights of way, sewers, electric lines, telegraph and telephone lines and other similar purposes, or zoning, building codes or other restrictions (including minor defects or irregularities in title and similar encumbrances) as to the use of real property or Liens incidental to the conduct of the business of such Person or to the ownership of its properties that do not in the aggregate materially adversely affect the value of said properties or materially impair their use in the operation of the business of such Person; and

(aa) Liens on deposits or other amounts held in escrow to secure payments (contingent or otherwise) payable by the Company with respect to (i) the settlement, satisfaction, compromise or resolution or judgments, litigation, arbitration or other Disputes and (ii) any

commercial Contracts for manufacturing, production and other service arrangements entered into in the ordinary course of business.

"Permitted Warrant Transaction" means any call option, warrant or right to purchase (or substantively equivalent derivative transaction) relating to the Company's common stock (or other securities or property following a merger event or other change of the common stock of the Company) and/or cash (in an amount determined by reference to the price of such common stock) sold by the Company substantially concurrently with any purchase by the Company of a related Permitted Bond Hedge Transaction.

"Person" means any natural person, firm, corporation, limited liability company, partnership, joint venture, association, joint-stock company, trust, unincorporated organization, Governmental Authority or any other legal entity, including public bodies, whether acting in an individual, fiduciary or other capacity.

"Personal Information" has the meaning set forth in Section 4.25(b).

"Plan" means any "employee benefit plan" within the meaning of Section 3(3) of ERISA (including a Pension Plan) that is maintained for employees of the Company or, in the case of any Pension Plan, any ERISA Affiliate or to which the Company or, in the case of any Pension Plan, any ERISA Affiliate is required to contribute on behalf of any of its employees.

"Pledged Subsidiaries" has the meaning set forth in Section 6.1.

"Product Plan" means the key manufacturing, marketing, sale and product development and research plans with respect to Imcivree set forth on Schedule 1.1-3.

"Proprietary Databases" means any material non-public proprietary database or information repository.

"Proprietary Software" means any proprietary software (other than any software that is generally commercially available, off-the-shelf and/or open source) including, without limitation, the object code and source code forms of such software and all associated documentation.

"Purpose" has the meaning set forth in Section 9.1.

"Quarterly Net Revenues" means, with respect to any Calendar Quarter, the aggregate amount of Net Revenues for that Calendar Quarter.

"Quarterly Payment Date" means, with respect to a Calendar Quarter, the date that is 45 days following the end of each Calendar Quarter after the Initial Closing Date (provided if any such date is not a Business Day, the Quarterly Payment Date shall be the next succeeding Business Day, and provided, further, that for such Calendar Quarter ending December 31, the Quarterly Payment Date shall mean the date that is 90 days following the end of each such Calendar Quarter).

"RareStone License Agreement" means that certain Exclusive License Agreement, dated December 3, 2021, by and between the Company and RareStone Group Ltd., a limited company registered in Grand Cayman.

"Recipient" has the meaning set forth in Section 9.1.

"Reference Date" means the reference dates set forth in the Column B of the chart in Section 3.1(b).

"Regulatory Agency" means a Governmental Authority with responsibility for the approval of the marketing and sale of pharmaceuticals or other regulation of pharmaceuticals in any jurisdiction.

"Regulatory Approvals" means, collectively, all approvals, registrations, certificates, authorizations, Permits and supplements thereto pursuant to which the Included Product may be marketed, sold and distributed in a country or region, issued by the appropriate Regulatory Agency.

"Regulatory Milestone Event" means the receipt by the Company of Marketing Authorization in the EEA for Imcivree for use in certain patients with Bardet-Biedl Syndrome on or prior to June 30, 2023.

"Reportable Event" means any of the events set forth in Section 4043(c) of ERISA, other than events for which the thirty-day notice period has been waived.

"Responsible Officer" means the chief executive officer, president, chief financial officer, chief operating officer, general counsel or treasurer of a Company Party and, solely for purposes of the delivery of certificates pursuant to this Agreement, the secretary or any officer appointed by the Board of Directors of a Company Party. Any document delivered hereunder that is signed by a Responsible Officer of a Company Party shall be conclusively presumed to have been authorized by all necessary corporate, partnership and/or other action on the part of such Company Party and such Responsible Officer shall be conclusively presumed to have acted on behalf of such Company Party.

"Restricted Payment" means (a) any dividend or other distribution, direct or indirect, on account of any shares (or equivalent) of any class of Equity Interests of the Company or any of its Subsidiaries, now or hereafter outstanding, (b) any redemption, retirement, sinking fund or similar payment, purchase or other acquisition for value, direct or indirect, of (i) any shares (or equivalent) of any class of Equity Interests of the Company or any of its Subsidiaries, now or hereafter outstanding or (ii) any call option on any shares (or equivalent) of any class of Equity Interests of the Company or any of its Subsidiaries (irrespective of whether such call option can be cash, net share or physically settled), (c) any payment made to retire, or to obtain the surrender of, any outstanding warrants, options or other rights to acquire shares of any class of Equity Interests of the Company or any of its Subsidiaries, now or hereafter outstanding and (d) any payment made in cash to the holders of Permitted Debt under the Permitted Debt Facility Documents in excess of the original principal (or notional) amount thereof, interest thereon and any fees due thereunder.

"Revenue Interests" means all of the Company's rights, title and interest in and to, free and clear of any and all Liens, that portion of the Annual Net Revenues of the Company in an amount equal to the Included Product Payment Amount for each Calendar Quarter during the Payment Term.

"Safety Notices" means any recalls, field notifications, market withdrawals, warnings, "dear doctor" letters, investigator notices, safety alerts or other notices of action issued or instigated by the Company, any Subsidiary or any Governmental Authority relating to an alleged lack of safety or regulatory compliance of the Included Products.

"Sales Milestone Event" means that Net Sales of Imcivree between July 1, 2022 and September 30, 2023 shall have been equal to or greater than $[***].

"Sanction(s)" means any sanction administered or enforced by the United States government (including, without limitation, OFAC), the United Nations Security Council, the European Union, Her Majesty's Treasury ("HMT") or other relevant sanctions authority.

"SEC" means the Securities and Exchange Commission or any successor agency or authority thereto.

"Second Closing" has the meaning set forth in Section 8.1(b).

"Second Closing Date" has the meaning set forth in Section 8.1(b).

"Second Investment Amount" has the meaning set forth in Section 2.1(b).

"Securities Account" means a "securities account" (as defined in Article 8 of the UCC) or other account to or for the credit or account of any Party to which a financial asset is or may be credited in accordance with an agreement under which the Person maintaining the account undertakes to treat the Person for whom the account is maintained as entitled to exercise the rights that comprise the financial asset.

"Security Agreement" means a security agreement dated as of the Initial Closing Date executed in favor of the Investor Representative, for the benefit of the Investors, by the Company and each of the Guarantors, as amended or modified from time to time in accordance with the terms hereof.

"Set-off" means any set-off, off-set, reduction or similar deduction.

"Special Maturity Payment Amount" means, as of the Legal Maturity Date, the sum of (A) the Investment Amount minus the aggregate of all of the payments received by the Investor Representative in respect of the Revenue Interests (including the Under Performance Payments) and (B) the amount that the Investors would need to receive to yield an internal rate of return on the Investment Amount equal to [***] determined after taking into account all of the amounts received by the Investor Representative prior to such date of payment under the Transaction Documents (other than any payments made as a reimbursement of expenses (including legal fees) incurred by the Investors and any indemnification amounts paid as reimbursement to any Investor Indemnified Party to extent such amounts were previously or contemporaneously paid to a Third

Party in connection with any Third Party Claim) and the time at which such payments were received.

"Special Termination Amount" means as of any date of payment, the lesser of (a)(i) the sum of the Hard Cap less the aggregate of all of the payments of the Company in respect of the Revenue Interests (including any Under Performance Payment) made to the Investors prior to such date, plus (ii) any other Obligations payable by the Company Parties under this Agreement and the other Transaction Documents (if any) or (b)(i) the Investment Amount minus the aggregate of all of the payments received by the Investors in respect of the Revenue Interests (including any Under Performance Payment) and (ii) the amount that the Investors would need to receive to achieve a *per annum* rate of return on the Investment Amount equal to [***]% determined after taking into account all of the amounts received by the Investors prior to such date of payment under the Transaction Documents (other than any payments made as a reimbursement of expenses (including legal fees) incurred by the Investors and any indemnification amounts paid as reimbursement to any Investor Indemnified Party to extent such amounts were previously or contemporaneously paid to a Third Party in connection with any Third Party Claim) and the time at which such payments were received.

"Special Termination Event" means any of the following events:

(i) Material Adverse Effect. There occurs any circumstance or circumstances that could reasonably be expected, either individually or in the aggregate, to have a Material Adverse Effect;

(ii) Representations and Warranties. Any representation, warranty, certification or statement of fact made or deemed made by or on behalf of the Company or any other Company Party in Section 4.4 (Ownership), Section 4.7 (Solvency), Section 4.10 (Intellectual Property Matters), Section 4.12 (Material Contracts), Section 4.13 (Bankruptcy), Section 4.16 (Financial Statements; No Material Adverse Effect), Section 4.17 (No Default; No Special Termination Event), Section 4.21 (Perfection of Security Interests in the Collateral) or, Section 4.26 (Compliance of Included Products) of this Agreement shall be materially incorrect or materially misleading when made or deemed made and, if susceptible to cure, such inaccuracy continues for 90 days after the earlier of the date on which (A) a Responsible Officer of any Company Party has knowledge of such inaccuracy or (B) written notice thereof shall have been given to the Company by the Investor Representative (it being understood and agreed that the representations and warranties set forth in Section 4.7 and Section 4.13, are not susceptible to cure and shall not be subject to a cure period);

(iii) Specified Covenants. Any Company Party fails to perform or observe any term, covenant or agreement contained in Section 6.8(b) or Section 6.8(c) and such failure continues for 60 days after the earlier of the date on which (A) a Responsible Officer of any Company Party has knowledge of such Default or (B) written notice thereof shall have been given to the Company by the Investor Representative; or

(iv) Imcivree. There occurs any revocation, withdrawal, suspension or cancellation of any Regulatory Approval in the United States or, following the Second Closing in the EEA, of Imcivree which results in the Company or its Subsidiaries being prevented from

marketing or selling Imcivree in the United States or, following the Second Closing in the EEA, and such revocation, withdrawal, suspension or cancellation continues for [***] days or more.

"Subsidiary" means with respect to any Person (a) any entity as to which such Person directly or indirectly owns outstanding voting securities with power to vote 50% or more of the outstanding Voting Stock of such entity or (b) any entity as to which 50% or more of its outstanding Voting Stock are directly or indirectly owned, controlled or held by such Person with power to vote such securities. As of the Effective Date, the Subsidiaries of the Company are set forth on Schedule 4.20.

"Tax" or "Taxes" means any U.S. federal, state, local or non-U.S. tax, levy, impost, duty, assessment or withholding or other similar fee, deduction or charge, including all excise, sales, use, value added, transfer, stamp, documentary, filing, recordation and other fees imposed by any taxing authority (and interest, fines, penalties and additions related thereto).

"Third Closing Date" has the meaning set forth in Section 8.1(c).

"Third Investment Amount" has the meaning set forth in Section 2.1(c).

"Third Party" means any Person other than (a) the Company, (b) each of the Investors or (c) an Affiliate of either the Company or any of the Investors (as applicable).

"Third Party Claim" means any claim, action, suit or proceeding by a Third Party, excluding any lender, officer, directors, employee or agent or other representative of a Party, including any investigation by any Governmental Authority.

"Trade Secrets" means any data or information that is not commonly known by or available to the public, and which (a) derives economic value, actual or potential, from not being generally known to and not being readily ascertainable by proper means by other Persons who can obtain economic value from its disclosure or use and (b) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

"Trademark License" means any agreement, written or oral, providing for the grant of any right to use any Trademark.

"Trademarks" means all statutory and common-law trademarks, trade names, corporate names, company names, business names, fictitious business names, trade styles, service marks, logos and other source or business identifiers, and the goodwill associated therewith, now existing or hereafter adopted or acquired, all registrations and recordings thereof, and all applications to register in connection therewith, under the Laws of the United States, any state thereof or any other country or any political subdivision thereof, or otherwise, for the full term and all renewals thereof.

"Transaction Documents" means this Agreement, the Security Agreement, the Guaranty, the Deposit Agreement and any Joinder Agreement.

"Treasury Management Arrangement" means any agreement or other arrangement governing the provision of treasury or cash management services, including Deposit Accounts,

netting services, overdraft, credit or debit card, funds transfer, automated clearinghouse, zero balance accounts, returned check concentration, controlled disbursement, lockbox, account reconciliation and reporting, direct debit, cash concentration, trade finance services and other cash management services.

"U.S." or "United States" means the United States of America, its 50 states, each territory and possession thereof and the District of Columbia.

"UCC" means the Uniform Commercial Code as in effect from time to time in New York; provided, that, if, with respect to any financing statement or by reason of any provisions of Applicable Law, the perfection or the effect of perfection or non-perfection of the back-up security interest or any portion thereof granted pursuant to the Security Agreement is governed by the Uniform Commercial Code as in effect in a jurisdiction of the United States other than New York, then "UCC" means the Uniform Commercial Code as in effect from time to time in such other jurisdiction for purposes of the provisions of this Agreement and any financing statement relating to such perfection or effect of perfection or non-perfection.

"Under Performance Payments" has the meaning set forth in Section 3.1(b).

"Unused Amounts" has the meaning set forth in Section 7.7(k).

"Voting Stock" means, with respect to any Person, Equity Interests issued by such Person the holders of which are ordinarily, in the absence of contingencies, entitled to vote for the election of directors (or persons performing similar functions) of such Person, even though the right so to vote has been suspended by the happening of such a contingency.

"Website Agreements" means all agreements between the Company and/or any Subsidiary and any other Person pursuant to which such Person provides any services relating to the hosting, design, operation, management or maintenance of any Website, including without limitation, all agreements with any Person providing website hosting, database management or maintenance or disaster recovery services to the Company and/or any Subsidiary and all agreements with any domain name registrar, as all such agreements may be amended, supplemented or otherwise modified from time to time.

"Websites" means all websites operated, managed or controlled through a Domain Name, whether on an exclusive basis or a nonexclusive basis, including, without limitation, all content, elements, data, information, materials, hypertext markup language (HTML), software and code, works of authorship, textual works, visual works, aural works, audiovisual works and functionality embodied in, published or available through each such website.

"Work" means any work or subject matter that is subject to protection pursuant to Title 17 of the United States Code.

Section 1.2 Rules of Construction. Unless the context otherwise requires, in this Agreement:

(a) An accounting term not otherwise defined has the meaning assigned to it in accordance with GAAP.

(b) Words of the masculine, feminine or neuter gender shall mean and include the correlative words of other genders.

(c) The definitions of terms shall apply equally to the singular and plural forms of the terms defined.

(d) The terms “include”, “including” and similar terms shall be construed as if followed by the phrase “without limitation”.

(e) Unless otherwise specified, references to an agreement or other document include references to such agreement or document as from time to time amended, restated, reformed, supplemented or otherwise modified in accordance with the terms thereof (subject to any restrictions on such amendments, restatements, reformations, supplements or modifications set forth herein or in any of the other Transaction Documents) and include any annexes, exhibits and schedules attached thereto.

(f) References to any Applicable Law shall include such Applicable Law as then in effect.

(g) References to any Person shall be construed to include such Person’s successors and permitted assigns (subject to any restrictions on assignment, transfer or delegation set forth herein or in any of the other Transaction Documents), and any reference to a Person in a particular capacity excludes such Person in other capacities.

(h) The word “will” shall be construed to have the same meaning and effect as the word “shall”.

(i) The words “hereof”, “herein”, “hereunder” and similar terms when used in this Agreement shall refer to this Agreement as a whole and not to any particular provision hereof, and Article, Section and Exhibit references herein are references to Articles and Sections of, and Exhibits to, this Agreement unless otherwise specified.

(j) In the computation of a period of time from a specified date to a later specified date, the word “from” means “from and including” and each of the words “to” and “until” means “to but excluding”.

(k) Where any payment is to be made, any funds are to be applied or any calculation is to be made under this Agreement on a day that is not a Business Day, unless this Agreement otherwise provides, such payment shall be made, such funds shall be applied and such calculation shall be made on the succeeding Business Day, and payments shall be adjusted accordingly.

(l) Unless otherwise specified, references to an agreement or other document include references to such agreement or document as from time to time amended, restated, reformed, supplemented or otherwise modified in accordance with the terms thereof (subject to any restrictions on such amendments, restatements, reformations, supplements or modifications set forth herein or in any of the other Transaction Documents) and include any annexes, exhibits and schedules attached thereto.

ARTICLE II
REVENUE INTEREST FINANCING

Section 2.1 Investment Amount. Subject to the terms and conditions set forth herein, the Investors shall pay (or cause to be paid) to the Company, or the Company's designee, the following:

(a) On the Initial Closing Date, subject to the satisfaction of the conditions set forth in Section 8.4(a), the sum of thirty-seven million five hundred thousand Dollars ($37,500,000) (the "Initial Investment Amount"), in immediately available funds by wire transfer to an account designated in writing by the Company to the Investor Representative prior to such funding;

(b) on the Second Closing Date, subject to the satisfaction of the conditions set forth in Section 8.2 and the performance of the obligations set forth in Section 8.4(b), the sum of thirty-seven million five hundred thousand Dollars ($37,500,000) (the "Second Investment Amount"), in immediately available funds by wire transfer to an account designated in writing by the Company to the Investor Representative prior to the Second Closing Date; and

(c) on the Third Closing Date, subject to the satisfaction of the conditions set forth in Section 8.3 and the performance of the obligations set forth in Section 8.4(c), the sum of twenty-five million Dollars ($25,000,000) (the "Third Investment Amount"), in immediately available funds by wire transfer to an account designated in writing by the Company to the Investor Representative prior to the Third Closing Date. Following the Third Closing Date (should the Third Closing Date occur), the term "Investment Amount" shall thereafter be deemed amended to include the funds paid on the Third Closing Date (*i.e.*, an aggregate of one hundred million Dollars ($100,000,000)).

(d) In connection with the funding of the Initial Investment Amount on the Initial Closing Date, the Investors shall have the right to, at its option, fund the amount due under Section 2.1(a), on a net basis less the reimbursement owed by the Company pursuant to Section 8.4(a)(vi).

Section 2.2 No Assumed Obligations. Notwithstanding any provision in this Agreement or any other writing to the contrary, the Investors are not assuming any liability or obligation of the Company or any of the Company's Affiliates of whatever nature, whether presently in existence or arising or asserted hereafter. All such liabilities and obligations shall be retained by and remain liabilities and obligations of the Company or the Company's Affiliates, as the case may be (the "Excluded Liabilities and Obligations").

Section 2.3 Excluded Assets. The Investors do not, pursuant to any of the Transaction Documents, purchase, acquire or accept any assets or contract rights of the Company or any Company Party, or any other assets of the Company or any Company Party, other than its rights with respect to the Revenue Interests and, to the extent provided in the Transaction Documents, the Collateral. The Company has sole authority and responsibility for the research, development and Commercialization of Included Products.

ARTICLE III
PAYMENTS ON ACCOUNT OF THE REVENUE INTEREST FINANCING

Section 3.1 Payments on Account of the Revenue Interest Financing.

(a) In consideration of the Investors paying the Investment Amount hereunder, the Company shall pay the Revenue Interests to the Investor Representative as follows: On each Quarterly Payment Date, the Company shall pay the Revenue Interests to the Investor Representative for such Quarterly Payment Date until the earlier of (i) the date on which the Investor Representative has received payments equal to the Hard Cap or (ii) the Legal Maturity Date. If (A) the Investor Representative has not received payments equal to the Hard Cap by the Legal Maturity Date (after giving effect to any payments made on the Legal Maturity Date) and (B) no Special Termination Event, Default or Event of Default has occurred or is continuing, the Company shall pay the Special Maturity Payment Amount on the Legal Maturity Date. The Company shall have the right, at any time and from time to time, to make voluntary prepayments to the Investor Representative, and such payments shall be credited against the Hard Cap and the Under Performance Payments set forth in Section 3.1(b). This Agreement shall be in full force and effect for the duration of the Payment Term.

(b) If the Investor Representative has not received the applicable Minimum Multiple of the Investment Amount set forth below by the corresponding Reference Date set forth below, the Company shall, within 30 days of the applicable Reference Date, make a cash payment to the Investor Representative sufficient to gross the Investor Representative up to such minimum amount (each, an "Under Performance Payment").

A. Minimum Multiple	B. Reference Date
0.60x	March 31, 2027
1.20x	March 31, 2029

(c) Upon the occurrence of a Change of Control, the Company shall promptly pay to the Investor Representative the Change of Control Payment, whereupon this Agreement shall terminate on the date such payment is received by the Investor Representative.

(d) If a Special Termination Event has occurred and is continuing, the Investor Representative may, in its sole discretion, terminate this Agreement and notify the Company of its election to terminate this Agreement. In consideration for such termination, the Company shall pay the Special Termination Amount and any other unpaid Obligations to the Investor Representative within, in the case of clause (i) of the definition of Special Termination Event, [***] days, and, in the case of clause (ii) of the definition of Special Termination Event, [***] days, in each case, following receipt of such notice of the election to terminate this Agreement. The remedy set forth in this Section 3.1(d) shall be the Investors' and the Investor Representative's sole and exclusive remedy in the event of a Special Termination Event; provided, however, that to the extent the Special Termination Amount is not paid as aforesaid in full within such applicable period, for the avoidance of doubt, the failure to make such payment shall constitute an Event of Default.

(e) Once the Investor Representative has received (i) aggregate payments under Section 3.1(a) and Section 3.1(b) equal to the Hard Cap or (ii) the amounts due pursuant to Section 3.1(c), Section 3.1(d), or Section 11.1, in either case, along with all of the other Obligations owed by the Company Parties under this Agreement and the other Transaction Documents, (i) the Company shall have no further obligations to the Investors with respect to the Revenue Interests, and Investor Representative will not be entitled to any additional payments in respect of Revenue Interests and (ii) each of the Transaction Documents shall terminate immediately and automatically. Immediately upon termination of this Agreement pursuant to Section 3.1(a), Section 3.1(b), Section 3.1(c), Section 3.1(d) or Section 11.1 (A) all Liens on the Collateral granted to the Investor Representative pursuant to this Agreement and the other Transaction Documents shall immediately and automatically be released, without the delivery of any instrument or performance of any act by any Person, (B) the Company (or its designee) shall be permitted, and is hereby authorized to terminate any financing statement which has been filed pursuant to the Transaction Documents, and (C) the Investors and the Investor Representative shall execute and deliver to, or at the direction of, the Company, at the Company's sole cost and expense, all other releases and other documents as the Company shall reasonably request to evidence any such release.

(f) All Revenue Interests and any other Obligations required to be paid but not paid to the Investor Representative on each Quarterly Payment Date shall bear interest at a rate of [***] per month from the due date until paid in full or, if less, the maximum interest rate permitted by Applicable Law. In addition, in the event that an Event of Default has occurred, and for so long as it is occurring, interest shall accrue on the amount of the Event of Default Payment that remains unpaid at a rate of [***] per month from the date on which Company receives notice from the Investor Representative of such Event of Default until the Event of Default Payment is paid in full or, if less, the maximum interest rate permitted by Applicable Law. Any such overdue payment shall, when made, be accompanied by, and credited first to, all interest so accrued.

(g) The Company shall deposit all amounts payable by the Company to the Investor Representative under this Agreement into the Investor Account, unless otherwise instructed by the Investor Representative.

(h) For all purposes of this Section 3.1, the amount of payments deemed received by the Investors shall (i) include any additional amounts payable to the Investors pursuant to Section 6.22(c) ("Additional Amounts") and (ii) be computed net of any applicable Tax withholding (including any Tax withholding in respect of any Additional Amounts), other than any withholding in respect of Excluded Taxes.

Section 3.2 Lockbox Account; Collection Account; Collection Account Management.

(a) On or prior to the date that is sixty days following the Initial Closing Date, the Company shall enter into a Deposit Agreement with the Depositary Bank with respect to the Lockbox Accounts. The Company shall deliver instructions to all Licensees and account debtors (the "Instruction to Payors"), in each case, solely with respect to any proceeds arising from sales of Included Products by the Company or its Subsidiaries and any Other Royalty Payments relating to Included Products (which instruction shall be in form and substance reasonably satisfactory to

the Investor Representative and identify each Investor as having a right to a receive a portion of such amounts, and a copy of which shall be delivered to the Investor Representative promptly following delivery to such Licensee or account debtor) to remit such proceeds and Other Royalty Payments to the Lockbox Accounts, to the extent the Instruction to Payors was not sent to such Licensee and account debtors on or prior to the Initial Closing Date. To the extent any proceeds arising from sales of Included Products or any Other Royalty Payments related to Included Products are paid directly to the Company, the Company shall remit to the Lockbox Account for U.S. payors all such amounts within five Business Days of such receipt of any such funds. The Company shall instruct non-U.S. payors in individual non-U.S. countries to pay into specified Deposit Accounts listed on Schedule 3.2 (as may be updated from time to time), and shall enter into sweep agreements from each such non-U.S. country Deposit Account to a non-U.S. Lockbox Account. To the extent any proceeds arising from sales of Included Products or any Other Royalty Payments related to Included Products are paid directly to the Company's non-U.S. Subsidiaries, the Company shall cause such payments to be remitted to a non-U.S. Lockbox Account for non-U.S. payors within ten Business Days of such receipt of any such funds.

(b) On or prior to the date that is sixty days following the Initial Closing Date, the Company shall establish with the Depositary Bank the Collection Account and enter into a Deposit Agreement with the Depositary Bank with respect to the Collection Account. The Company shall cause all of the funds on deposit in the Lockbox Accounts to be transferred to the Collection Account on a daily basis. With respect to any amounts that are deposited into the Collection Account on any day, so long as no Default or Event of Default has occurred and is continuing, (A) a minimum of [***] of such amounts shall remain in the Collection Account until the Quarterly Payment Date immediately following the date of such deposit and may not be transferred to a Company Account, except as otherwise permitted by this Section 3.2(b), and (B) any remaining amounts may be disbursed to a Company Account from time to time at the direction of the Company; provided that if the aggregate funds to be retained in the Collection Account pursuant to clause (A) exceeds [***] on any date, such amount in excess of [***] may be disbursed to a Company Account at the direction of the Company on or after such date. The Company shall provide the Depositary Bank notice no more frequently than daily of such amount to be disbursed to a Company Account pursuant to this Section 3.2(b). During the Payment Term, on each Quarterly Payment Date, the Company shall instruct the Depositary Bank to disburse to the Investor Account an amount equal to the lesser of (x) the funds on deposit in the Collection Account and (y) the Revenue Interests for such Quarterly Payment Date. If the amount to be disbursed to the Investor Account on any Quarterly Payment Date pursuant to the preceding sentence is less than the Revenue Interests to which the Investors are entitled for the relevant Calendar Quarter, the Company shall pay the amount of such shortfall to the Investor Representative on such Quarterly Payment Date. If the amount of funds on deposit in the Collection Account on any Quarterly Payment Date exceeds the Revenue Interests for such Quarterly Payment Date, such excess amount may be transferred to a Company Account at the direction of the Company.

(c) If a Default or an Event of Default has occurred and is continuing, the Investor Representative shall have the right to exercise all of its rights and remedies under ARTICLE XI, the Security Agreement and the Deposit Agreement, including, without limitation, directing the Depositary Bank to transfer all of the funds in the Collection Account to the Investor

Representative until all of the Obligations owed by the Company under this Agreement and other Transaction Documents have been paid in full.

(d) During the Payment Term, the Company shall have no right to terminate the Lockbox Accounts or the Collection Account without the Investor Representative's prior written consent; provided that, without the Investor Representative's consent to the change of location of such accounts (provided such location is in the United States), the Company shall have the right from time to time to establish a replacement Lockbox Accounts or Collection Account with a replacement Depositary Bank, provided, that such replacement Depositary Bank shall have entered into a Deposit Agreement with respect to such replacement accounts effective no later than the date of replacement. For purposes of this Agreement, any reference to the "Lockbox Account", "Collection Account", "Depositary Bank" or "Deposit Agreement" shall refer to such replacement Collection Account, Depositary Bank or Deposit Agreement, as the context requires.

Section 3.3 Mode of Payment/Currency Exchange. All payments made by a Party hereunder shall be made by deposit of U.S. Dollars by wire transfer in immediately available funds into the applicable account. With respect to sales outside the U.S., for the purpose of calculating Net Revenues for the purposes of determining the Revenue Interests payable under Section 3.1, Net Revenues shall be calculated, if pursuant to a License Agreement, in the currency set forth therein, or otherwise in the currency of sale, and then such amounts shall be converted into U.S. Dollars at the monthly rate of exchange utilized by the Company, in accordance with GAAP, fairly applied and as employed on a consistent basis throughout the Company's operations. Should the Company change its foreign currency translation methodology, the new methodology will be disclosed in writing to the Investor Representative prior to its implementation. For clarity, to the extent that the Company receives a payment from a Third Party in U.S. Dollars on which Revenue Interests are payable to Investor Representative under Section 3.1, the foregoing currency exchange rates shall not apply to such amount, and in particular the Company will have no obligation to re-calculate any currency conversion that was employed in connection with such Third Party payment.

Section 3.4 Included Product Payment Reports and Record Retention. On or prior to each Quarterly Payment Date, the Company shall deliver to the Investor Representative (i) a written report of the amount of gross sales of the Included Product in each country during the applicable Calendar Quarter, an itemized calculation of Net Sales and Other Royalty Payments on a country-by-country basis and a calculation of the amount of the Revenue Interests due under Section 3.1(a) in respect of the applicable Calendar Quarter, showing the Applicable Tiered Percentage applied thereto and a calculation of the Under Performance Payment (if any) pursuant to Section 3.1(b) and (ii) copies of the most recent quarterly statements for each Deposit Account, Securities Account and other bank account or Securities Account of the Company and each other Grantor and (iii) a Compliance Certificate relating to each of the items described in clauses (i) and (ii) of this sentence. For three years after each sale of the Included Product made by the Company or any of its Affiliates, the Company shall keep (and shall ensure that its Affiliates shall keep) complete and accurate records of such sale in sufficient detail to confirm the accuracy of the applicable Revenue Interests paid pursuant to Section 3.1(a). The Company shall use commercially reasonable efforts to include, in each Contract of the Company for the distribution, marketing or selling of Included Products entered into on or after the Initial Closing Date, obligations reasonably appropriate to ensure that the counterparty to such Contract shall furnish

to the Company all information necessary for the Company to comply with this Section 3.4 and calculate the Revenue Interests that are payable as set forth in this Agreement.

Section 3.5 Audits.

(a) Upon the written request of the Investor Representative, and not more than once in each Calendar Year (so long as no Default or Event of Default has occurred and is continuing) the Company shall permit an independent certified public accounting firm of national prominence selected by the Investor Representative, and reasonably acceptable to the Company, to have access to and to review, during normal business hours and upon not less than thirty days' prior written notice, the relevant documents and records of the Company and its Subsidiaries as may reasonably be necessary to verify the accuracy and timeliness of the reports and payments (including calculation and payment of any Revenue Interest) made by the Company under this Agreement. Such review may cover the records for sales or other Dispositions of the Included Products, Net Revenues, Other Royalty Payments and the aggregate amount of deposits into the Lockbox Accounts and the Collection Account in any Calendar Year ending no earlier than the first day of the previous Calendar Year. The accounting firm shall be permitted to prepare and disclose to the Investor Representative a written report stating only whether Revenue Interests paid to the Investor Representative hereunder and the reports provided by the Company relating to such Revenue Interests required hereunder are correct or incorrect and the specific details concerning any discrepancies. Notwithstanding the foregoing, after the occurrence and during the continuance of a Special Termination Event, Default or Event of Default, the Investor Representative shall have the right, as often, at such times and with such prior notice, as the Investor Representative shall determine, in its reasonable discretion, to have an independent certified public accounting firm of national prominence selected by the Investor Representative review the relevant documents and records of the Company and its Subsidiaries.

(b) If such accounting firm reasonably concludes that any Revenue Interests were owed and were not paid when due during such period pursuant to the provisions of this Agreement, the Company shall pay any late or unpaid Revenue Interests within [***] days after the date the Investor Representative delivers to the Company a notice including the accounting firm's written report and requesting such payment. If the amount of the underpayment (exclusive of interest accrued thereon pursuant to Section 3.1(a)) is greater than the lesser of (i) [***]% of the total amount actually owed for the period audited or (ii) $[***], then the Company shall in addition (i) reimburse the Investor Representative for all reasonable costs and fees of the accounting firm related to such audit and (ii) pay interest accrued on such amount of the underpayment at a rate of [***]% per month from the initial due date until paid in full or, if less, the maximum interest rate permitted by Applicable Law. In the event of overpayment, any amount of such overpayment shall be fully creditable against Revenue Interests payable for the immediately succeeding Calendar Quarter(s). If the overpayment is not fully applied prior to the final quarterly Revenue Interest payment due hereunder, the Investors shall promptly refund an amount equal to any such remaining overpayment. The Investor Representative shall (i) treat all information that it receives under this Section 3.5 or under any License Agreement of the Company in accordance with the provisions of ARTICLE IX and (ii) cause its accounting firm to enter into a reasonably acceptable confidentiality agreement with the Company obligating such firm to retain all such information in confidence pursuant to such confidentiality agreement, in each case except to the extent necessary for the Investor Representative to enforce its rights under this Agreement.

ARTICLE IV
REPRESENTATIONS AND WARRANTIES OF THE COMPANY

Except as set forth in the disclosure schedules attached hereto (the "Disclosure Schedules"), the Company hereby represents and warrants to the Investor Representative as of the Effective Date and as of the date of each Closing as follows:

Section 4.1 Organization. The Company is a corporation duly organized, validly existing and in good standing under the Laws of Delaware and has all powers and authority, and all licenses, Permits, franchises, authorizations, consents and approvals of all Governmental Authorities, required to own its property and conduct its business as now conducted. The Company is duly qualified to transact business and is in good standing in every jurisdiction in which such qualification or good standing is required by Applicable Law (except where the failure to be so qualified or in good standing would not reasonably be expected to result in a Material Adverse Effect).

Section 4.2 No Conflicts.

(a) None of the execution and delivery by the Company of any of the Transaction Documents to which the Company is party, the performance by the Company of the obligations contemplated hereby or thereby or the consummation of the transactions contemplated hereby or thereby will: (i) contravene, conflict with, result in a breach, violation, cancellation or termination of, constitute a Default (with or without notice or lapse of time, or both) under, require prepayment under, give any Person the right to exercise any remedy (including termination, cancellation or acceleration) or obtain any additional rights under, or accelerate the maturity or performance of or payment under, in any respect, (A) any Applicable Law or any judgment, order, writ, decree, Permit or license of any Governmental Authority to which the Company or any of its Subsidiaries or any of their respective assets or properties may be subject or bound, (B) any term or provision of any contract, agreement, indenture, lease, license, deed, commitment, obligation or instrument to which the Company or any of its Subsidiaries is a party or by which the Company or any of its Subsidiaries or any of their respective assets or properties is bound or committed (other than a Material Contract), (C) any Material Contract or (D) any term or provision of any of the organizational documents of the Company or any of its Subsidiaries, except in the case of clause (A) or (B) where any such event would not reasonably be expected to result in a Material Adverse Effect; or (ii) except as provided in any of the Transaction Documents to which it is party, result in or require the creation or imposition of any Lien on the Collateral or any assets of any Pledged Subsidiary that is not a Guarantor relating to Imcivree (in each case other than Permitted Liens).

(b) The Company has not granted, nor does there exist, any Lien on the Transaction Documents or the Collateral (other than Permitted Liens).

Section 4.3 Authorization. The Company has all powers and authority to execute and deliver, and perform its obligations under, the Transaction Documents to which it is party and to consummate the transactions contemplated hereby and thereby. The execution and delivery of each of the Transaction Documents to which the Company is party and the performance by the Company of its obligations hereunder and thereunder have been duly

authorized by the Company. Each of the Transaction Documents to which the Company is party has been duly executed and delivered by the Company. Each of the Transaction Documents to which the Company is party constitutes the legal, valid and binding obligation of the Company, enforceable against the Company in accordance with its respective terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium or similar Applicable Laws affecting creditors' rights generally, general equitable principles and principles of public policy.

Section 4.4 Ownership. The Grantors are the exclusive owners of the entire right, title (legal and equitable) and interest in, to and under the Collateral, free and clear of all Liens, other than Permitted Liens, and the Pledged Subsidiaries that are not Grantors own their respective assets relating to Imcivree, free and clear of all Liens, other than Permitted Liens. The Revenue Interests sold, assigned, transferred, conveyed and granted to the Investor on the Closing Date and the other Collateral have not been pledged, sold, assigned, transferred, conveyed or granted by the Company to any other Person. The Company has full right to sell, assign, transfer, convey and grant the Revenue Interests to the Investors. Upon the sale, assignment, transfer, conveyance and granting by the Company of the Revenue Interests to the Investor Representative, the Investor shall acquire good and marketable title to the Revenue Interests free and clear of all Liens, other than Permitted Liens, and shall be the exclusive owner of the Revenue Interests. The Company has not caused, and to the Knowledge of the Company no other Person has caused, the claims and rights of Investor created by any Transaction Document in and to the Revenue Interests, the Collateral and the assets of the Pledged Subsidiaries that are not Grantors relating to Products, in each case, to be subordinated to any creditor or any other Person.

Section 4.5 Governmental and Third Party Authorizations. The execution and delivery by the Company of the Transaction Documents to which the Company is party, the performance by the Company of its obligations hereunder and thereunder and the consummation of any of the transactions contemplated hereunder and thereunder (including the sale, assignment, transfer, conveyance and granting of the Revenue Interests to the Investor) do not require any consent, approval, license, order, authorization or declaration from, notice to, action or registration by or filing with any Governmental Authority or any other Person, except for applicable filings under U.S. securities laws, the filing of UCC financing statements and those previously obtained or made or to be obtained or made on the Closing Date.

Section 4.6 No Litigation. There is no action, suit, arbitration proceeding, claim, citation, summons, subpoena, investigation or other proceeding (whether civil, criminal, administrative, regulatory, investigative or informal, and including by or before a Governmental Authority) pending or, to the Knowledge of the Company, threatened by or against the Company or any of its Subsidiaries, at law or in equity, that (i) if adversely determined, could reasonably be expected to result in a liability to the Company in excess of $[***], or (ii) challenges or seeks to prevent or delay the consummation of any of the transactions contemplated by any of the Transaction Documents to which the Company is party.

Section 4.7 Solvency. The Company has determined that, and by virtue of its entering into the transactions contemplated by the Transaction Documents to which the Company is party and its authorization, execution and delivery of the Transaction Documents to which the Company is party, the Company's incurrence of any liability hereunder or thereunder or contemplated hereby or thereby is in its own best interests. Upon consummation of the

transactions contemplated by the Transaction Documents and the application of the proceeds therefrom, (a) the fair saleable value of the Company's assets will be greater than the sum of its debts, liabilities and other obligations, including known contingent liabilities, (b) the present fair saleable value of the Company's assets will be greater than the amount that would be required to pay its probable liabilities on its existing debts, liabilities and other obligations, including known contingent liabilities, as they become absolute and matured, (c) the Company will be able to realize upon its assets and pay its debts, liabilities and other obligations, including known contingent obligations, as they mature, (d) the Company will not have unreasonably small capital with which to engage in its business and will not be unable to pay its debts as they mature, (e) the Company has not incurred, will not incur and does not have any present plans or intentions to incur debts or other obligations or liabilities beyond its ability to pay such debts or other obligations or liabilities as they become absolute and matured, (f) the Company will not have become subject to any Bankruptcy Event and (g) the Company will not have been rendered insolvent within the meaning of any Applicable Law. No step has been taken or is intended by the Company or, to its Knowledge, any other Person to make the Company subject to a Bankruptcy Event.

Section 4.8 No Brokers' Fees. Except as set forth on Schedule 4.8, the Company has not taken any action that would entitle any person or entity to any commission or broker's fee in connection with the transactions contemplated by this Agreement.

Section 4.9 Compliance with Laws. None of the Company nor any of its Subsidiaries (a) has during the last three years violated or is in violation of, or, to the Knowledge of the Company, is under investigation by a Governmental Authority with respect to or has been threatened by a Governmental Authority to be charged with or been given notice of any violation of, any Applicable Law or any Permits or (b) is subject to any judgment, order, writ, decree, injunction, stipulation, consent order, Permit or license granted, issued or entered by any Governmental Authority, in each case, that could reasonably be expected to result in a liability to the Company in excess of $[***].

Section 4.10 Intellectual Property Matters.

(a) Schedule 4.10(a) sets forth an accurate and complete list of sets forth a complete and accurate list of Patent Rights, including the complete and accurate list of the Owned Imcivree Patent Rights, and the exclusively in-licensed Licensed Imcivree Patent Rights. For each Patent set forth on Schedule 4.10(a) the Company has indicated: (i) the application number (if any); (ii) the patent or registration number, if any; (iii) the country or other jurisdiction where the Patent Right was issued, registered, or filed; (iv) the scheduled expiration date of any issued Patent Right, including a notation if such scheduled expiration date includes a term extension or supplementary protection certificate; and (v) the registered owner thereof.

(b) Except as disclosed on Schedule 4.10(b), the Company is the sole and exclusive owner of the entire right, title and interest in each of the Owned Imcivree Patent Rights. The Owned Imcivree Patent Rights are not subject to any encumbrance, Lien or claim of ownership by any Third Party, and to the Knowledge of the Company, there are no facts that would preclude the Company from having unencumbered title to such Patent Rights. No Company Party has

received any notice of any claim by any Third Party challenging the ownership of the rights of the Company in and to the Owned Imcivree Patent Rights.

(c) To the Knowledge of the Company, each Person who has or has had any rights in or to the Owned Imcivree Patent Rights, and to the Knowledge of the Company, with respect to the exclusively in-licensed Licensed Imcivree Patent Rights, including each inventor named on such Patent Rights, has executed a Contract assigning their entire right, title and interest in and to such Patent Rights and the inventions embodied, described and/or claimed therein, to the owner thereof, and each such Contract that relate to the Owned Imcivree Patent Rights, and to the Knowledge of the Company, with respect to the exclusively in-licensed Licensed Imcivree Patent Rights, has been duly recorded at the United States Patent and Trademark Office and each such Contract has been duly recorded at the United States Patent and Trademark Office as of the Closing Date.

(d) To the Knowledge of the Company, no issued Owned Imcivree Patent Right has lapsed, expired or otherwise been terminated and no Owned Imcivree Patent Right applications have lapsed, expired, been abandoned or otherwise been terminated, in each case, other than by operation of law.

(e) To the Knowledge of the Company, there are no unpaid maintenance fees, annuities or other like payments that are overdue with respect to the Owned Imcivree Patent Rights required to be paid as of the Closing Date, and to the Knowledge of the Company, with respect to the exclusively in-licensed Licensed Imcivree Patent Rights.

(f) To the Knowledge of the Company, the Company has a valid license to each of the in-licensed Licensed Imcivree Patent Rights, in each case pursuant to the terms of the applicable License Agreement.

(g) To the Knowledge of the Company, each of the Owned Imcivree Patent Rights, and to the Knowledge of the Company, with respect to the exclusively in-licensed Licensed Imcivree Patent Rights, correctly identifies each and every inventor of the claims thereof as determined in accordance with the Laws of the jurisdiction in which such Patent Right was issued or is pending. To the Knowledge of the Company, there is not any Person who is or claims to be an inventor of any of the Owned Imcivree Patent Rights or any exclusively in-licensed Licensed Imcivree Patent Rights, who is not a named inventor thereof. No Company Party has received any notice from any Person who is or claims to be an inventor of any of the Owned Imcivree Patent Rights who is not a named inventor thereof.

(h) To the Knowledge of the Company, each of Owned Imcivree Patent Rights and exclusively in-licensed Licensed Imcivree Patent Rights is valid, enforceable and subsisting. No Company Party has received any opinion of counsel that any of the Owned Imcivree Patent Rights or exclusively in-licensed Licensed Imcivree Patent Rights is invalid or unenforceable. No Company Party has received any notice of any claim by any Third Party challenging the validity or enforceability of any of the Owned Imcivree Patent Rights or exclusively in-licensed Licensed Imcivree Patent Rights.

(i) To the Knowledge of the Company, each individual associated with the filing and prosecution of the Owned Imcivree Patent Rights or exclusively in-licensed Licensed Imcivree Patent Rights for which Company controls has complied in all material respects with all applicable duties of candor and good faith in dealing with any Patent Office, including any duty to disclose to any Patent Office all information known by such individual to be material to patentability of each such Owned Imcivree Patent Right or exclusively in-licensed Licensed Imcivree Patent Rights, in those jurisdictions where such duties exist.

(j) There is at least one valid claim in each of the Imcivree Patent Rights listed in the Orange Book that would be infringed by the Company's or any Subsidiary's Commercialization of Imcivree but for the Company's and the Subsidiaries' rights in such Patent Rights.

(k) To the Knowledge of the Company, except for information disclosed to the applicable Patent Office during prosecution of the Owned Imcivree Patent Rights, there are no patents, published patent applications, articles, abstracts or other prior art deemed material to patentability of any of the inventions claimed in the issued Owned Imcivree Patent Rights, or that would otherwise reasonably be expected to materially adversely affect the validity or enforceability of any of the claims of the issued Owned Imcivree Patent Rights.

(l) There is no pending or, to the Knowledge of the Company, threatened opposition, interference, reexamination, injunction, claim, suit, action, citation, summons, subpoena, hearing, inquiry, investigation (by the International Trade Commission or otherwise), complaint, arbitration, mediation, demand, decree or other dispute, disagreement, proceeding, claim or inter partes review (in each case, other than standard patent prosecution before a Patent Office) (collectively, "Disputes") challenging the legality, validity, enforceability or ownership of any of the Patent Rights set forth on Schedule 4.10 as may be updated from time to time. To the Knowledge of the Company, there are no Disputes by or with any Third Party against the Company involving the Imcivree Patent Rights or any other Patent Rights related to an Included Product that are owned or controlled by Company. To the Knowledge of the Company the Patent Rights set forth on Schedule 4.10 are not subject to any outstanding injunction, judgment, order, decree, ruling, change, settlement or other Disposition of a Dispute.

(m) To the Knowledge of the Company, and except as separately disclosed to Investor Representative, there is no pending or threatened, and no event has occurred or circumstance exists that (with or without notice or lapse of time, or both) would result in or serve as a basis for any, action, suit or proceeding, or any investigation or claim, and the Company has not received any written notice of the foregoing, that claims that the manufacture, use, marketing, sale, offer for sale, importation or distribution of the Included Product as currently contemplated infringes on any Patent Rights or Intellectual Property rights of any other Person or constitutes misappropriation of any other Person's Trade Secrets.

(n) To the Knowledge of the Company, none of the conception, development and reduction to practice of the inventions claimed in the Owned Imcivree Patent Rights or exclusively in-licensed Licensed Imcivree Patent Rights for which Company controls has constituted or involved the misappropriation of Trade Secrets.

(o) No Company Party has filed any disclaimer, other than a terminal disclaimer, or made or permitted any other voluntary reduction in the scope of any Imcivree Patent Right.

(p) To the Knowledge of the Company, no Third Party Patent has been, or is, or will be, infringed by the Company's Commercialization of Imcivree. The Company has not received any notice of any claim by any Third Party asserting that the Company's Commercialization of any Included Product infringes such Third Party's patents. The Company has not received any written opinion of counsel regarding infringement or non-infringement of any Third Party Patent by the Company's Commercialization of any Included Product.

(q) To the Knowledge of the Company, there are no pending, published patent applications with claims reasonably likely to issue which are owned by any Third Party, which the Company does not have the right to use, which if issued with claims reasonably likely to issue, would limit or prohibit in any material respect the Company's Commercialization of any Imcivree.

(r) To the Knowledge of the Company, no Third Party is infringing any of the issued Owned Imcivree Patent Rights or exclusively in-licensed Licensed Imcivree Patent Rights. No Company Party has put any Third Party on notice of any infringement of the issued Patent Rights Owned Imcivree Patent Rights or exclusively in-licensed Licensed Imcivree Patent Rights.

(s) Schedule 4.10(r) lists Copyrights, Trademarks, Trade Secrets or net names material to Company Parties' Commercialization of any Included Product that are owned or exclusively in-licensed to Company.

(t) To the Knowledge of the Company, the Imcivree Patent Rights constitute all of the Patents owned or controlled by the Company or any of the Company's Affiliates necessary for the sale of the Imcivree in the U.S., the EEA, China, South Korea and Japan.

(u) The Company is the sole and exclusive owner of all the rights, title and interests to any and all inventions relating to Bardet-Biedl Syndrome disclosed in the Patent Rights identified by the Company's patent family reference number 7005.

Section 4.11 Margin Stock. The Company is not engaged in the business of extending credit for the purpose of buying or carrying margin stock, and no portion of the Investment Amount shall be used by the Company for a purpose that violates Regulation T, U or X promulgated by the Board of Governors of the Federal Reserve System from time to time.

Section 4.12 Material Contracts.

(a) Schedule 4.12(a) hereto contains a list of the Material Contracts as of the date hereof. As of the date hereof, the Company has provided a true and complete copy of each Material Contract to the Investor Representative.

(b) Except as separately disclosed in writing to Investor Representative, neither the Company nor, to the Knowledge of the Company, any Material Contract Counterparty is in breach or default of any Material Contract and no circumstances or grounds exist that would, upon the giving of notice, the passage of time or both, give rise (i) to a claim by the Company or any

Material Contract Counterparty of a breach or default of any Material Contract, or (ii) to a right of rescission, termination, revision, Set-off, by any Person, in, to or under any Material Contract. The Company has not received from, or delivered to, any Material Contract Counterparty, any written notice alleging a breach or default under any Material Contract, which breach or default has not been cured as of the Closing Date.

(c) Each Material Contract is a valid and binding obligation of the Company and, to the Knowledge of the Company, of the applicable Material Contract Counterparty, enforceable against each of the Company and, to the Knowledge of the Company, each applicable Material Contract Counterparty in accordance with its terms, except as may be limited by general principles of equity (regardless of whether considered in a proceeding at law or in equity) and by applicable bankruptcy, insolvency, moratorium and other similar laws of general application relating to or affecting creditors' rights generally. The Company has not received any notice from any Material Contract Counterparty or any other Person challenging the validity or enforceability of any Material Contract. Neither the Company, nor to the Knowledge of the Company, any other Person, has delivered or intends to deliver any written notice to the Company or a Material Contract Counterparty challenging the validity or enforceability of any Material Contract.

(d) There are no settlements, covenants not to sue, consents, judgements, orders or similar obligations which: (i) restrict the rights of the Company or any of its Subsidiaries from using any Intellectual Property relating to the research, development, manufacture, production, use, Commercialization, marketing, importing, storage, transport, offer for sale, distribution or sale of the Included Products (in order to accommodate any Third Party Intellectual Property or otherwise), or (ii) permit any Third Parties to use any Company Intellectual Property.

(e) Except for the Material Contracts, there are no other Contracts to which the Company or its Subsidiaries are a party that relate in any respect to Imcivree.

Section 4.13 Bankruptcy. Neither the Company nor, to the Knowledge of the Company, any Material Contract Counterparty is contemplating or planning to commence any case, proceeding or other action relating to such Material Contract Counterparty's bankruptcy, insolvency, liquidation or dissolution or reorganization.

Section 4.14 Office Locations; Names; Bank Accounts.

(a) The chief place of business, the chief executive office and each office where each Grantor keeps its records regarding the Collateral are, as of the date hereof, each located at 222 Berkeley Street, 12th Floor, Boston, Massachusetts 02116.

(b) No Company Party (or any predecessor by merger or otherwise) has, within the 5 year period preceding the date hereof, had a name that differs from its name as of the date hereof.

(c) Schedule 4.14(c) sets forth a list of all bank accounts maintained by the Company and its Subsidiaries as of the Closing Date.

Section 4.15 Permitted Debt. There is no Indebtedness incurred by the Company or any of its Subsidiaries other than the Permitted Debt. Schedule 4.15 hereto lists all of the

Permitted Debt Facility Documents as of the date hereof, and true, complete and correct copies of the Permitted Debt Facility Documents have been provided to the Investor Representative as of the date hereof. There is no material default or event of default (in each case, with or without notice or lapse of time, or both) under the Permitted Debt Facility Documents.

Section 4.16 Financial Statements; No Material Adverse Effect. (a) The Audited Financial Statements (i) were prepared in accordance with GAAP consistently applied throughout the period covered thereby, except as otherwise expressly noted therein, (ii) fairly present in all material respects the financial condition of the Company and its Subsidiaries as of the date thereof and their results of operations for the period covered thereby in accordance with GAAP consistently applied throughout the period covered thereby, except as otherwise expressly noted therein, and (iii) show all material Indebtedness and other liabilities, direct or contingent, of the Company and its Subsidiaries as of the date thereof, including material liabilities for Taxes, commitments and Indebtedness to the extent required by GAAP. (b) The Interim Financial Statements (i) were prepared in accordance with GAAP consistently applied throughout the period covered thereby, except as otherwise expressly noted therein, (ii) fairly present in all material respects the financial condition of the Company and its Subsidiaries as of the date thereof and their results of operations for the period covered thereby, and (iii) show all material Indebtedness and other liabilities, direct or contingent, of the Company and its Subsidiaries as of the date thereof, including material liabilities for Taxes, material commitments and Indebtedness to the extent required by GAAP, subject, in the case of clauses (i), (ii) and (iii) of this sentence, to the absence of footnotes and to normal year-end audit adjustments.

(c) From the date of the Audited Financial Statements to and including the Initial Closing Date, there has been no Disposition by any Company Party or any Subsidiary, or any Involuntary Disposition, of any material part of the business or property of any Company Party or any Subsidiary, and no purchase or other acquisition by any of them of any business or property (including any Equity Interests of any other Person) material to any Company Party or any Subsidiary, in each case, which is not reflected in the Financial Statements or in the notes thereto and has not otherwise been disclosed in writing to the Investor Representative on or prior to the Initial Closing Date.

(d) Since the date of the Audited Financial Statements, there has been no event or circumstance, either individually or in the aggregate, that has had or could reasonably be expected to result in a Material Adverse Effect.

Section 4.17 No Default; No Special Termination Event.

(a) Neither any Company Party nor any Subsidiary is in default (with or without notice or lapse of time, or both) under or with respect to any Contractual Obligation that could reasonably be expected to result in a Material Adverse Effect.

(b) No Special Termination Event, Default or Event of Default has occurred and is continuing.

Section 4.18 Insurance. The properties of the Company and each of its Subsidiaries are insured with financially sound and reputable insurance companies which are not Affiliates of such Persons, in such amounts, with such deductibles and covering such risks as are customarily carried by companies engaged in similar businesses and owning similar properties in localities where the Company or the applicable Subsidiary operates.

Section 4.19 ERISA Compliance.

(a) Except as would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect, (i) each Plan is in compliance with the applicable provisions of ERISA, the Internal Revenue Code and other federal or state Laws, and (ii) each Pension Plan that is intended to be a qualified plan under Section 401(a) of the Internal Revenue Code has received a favorable determination letter from the IRS to the effect that the form of such Plan is qualified under Section 401(a) of the Internal Revenue Code, an application for such a letter is currently being processed by the IRS or is entitled to rely on the opinion or advisory letter issued by the IRS to the sponsor of a preapproved plan document and, to the Knowledge of the Company, nothing has occurred that would prevent, or cause the loss of, such Tax-qualified status.

(b) There are no pending or, to the Knowledge of the Company, threatened claims, actions or lawsuits, or action by any Governmental Authority, with respect to any Plan that would reasonably be expected to result in a Material Adverse Effect. The Company has not engaged in any prohibited transaction or violation of the fiduciary responsibility rules with respect to any Plan, in any case, that would reasonably be expected to result in a Material Adverse Effect.

(c) Except as would not reasonably be expected to result in a Material Adverse Effect, (i) no ERISA Event has occurred with respect to any Pension Plan, (ii) the Company and each ERISA Affiliate has met all applicable requirements under the applicable pension funding rules in respect of each Pension Plan, and no waiver of the minimum funding standards under the applicable pension funding rules has been applied for or obtained, and (iii) neither the Company nor any ERISA Affiliate has incurred any liability to the PBGC other than for the payment of premiums due but not delinquent under Section 4007 of ERISA.

Section 4.20 Subsidiaries. Set forth on Schedule 4.20 is a complete and accurate list as of the date hereof of each Subsidiary of the Company, together with (a) such Subsidiary's jurisdiction of organization and (b) the percentage of the Equity Interests in such Subsidiary owned by the Company.

Section 4.21 Perfection of Security Interests in the Collateral. The Collateral Documents create valid security interests in, and Liens on, the Collateral purported to be covered thereby to the extent such security interests may be created pursuant to Article 9 of the UCC, which security interests and Liens will be, upon the timely and proper filings, deliveries, notations and other actions contemplated in the Collateral Documents perfected security interests and Liens (to the extent that such security interests and Liens can be perfected by such filings, deliveries, notations and other actions), prior to all other Liens other than Permitted Liens.

Section 4.22 Sufficiency of Collateral. The Collateral comprises all material rights and assets relating to Imcivree, now owned or hereafter acquired, that is owned or controlled by the Company.

Section 4.23 Disclosure. The Company has disclosed to the Investor all agreements, instruments and corporate or other restrictions to which it or any of its Subsidiaries is subject, and all other matters known to it, that, either individually or in the aggregate, could reasonably be expected to result in a Material Adverse Effect. No report, financial statement, certificate or other information furnished (whether written or oral) by or on behalf of any Company Party to the Investor Representative in connection with the transactions contemplated hereby and the negotiation of this Agreement or delivered hereunder or under any other Transaction Document (in each case, as modified or supplemented by other information so furnished) contains any material misstatement of fact or omits to state any fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, that, with respect to financial projections, estimates, budgets or other forward-looking information, the Company Parties represent only that such information was prepared in good faith based upon assumptions believed to be reasonable at the time such information was prepared (it being understood that such information is as to future events and is not to be viewed as facts, is subject to significant uncertainties and contingencies, many of which are beyond the control of the Company and its Subsidiaries, that no assurance can be given that any particular projection, estimate, budget or forecast will be realized and that actual results during the period or periods covered by any such projections, estimate, budgets or forecasts may differ significantly from the projected results and such differences may be material).

Section 4.24 Sanctions Concerns; Anti-Corruption Laws; PATRIOT Act.

(a) Sanctions Concerns. No Company nor any Subsidiary, nor, to the Knowledge of the Company, any director, officer, employee, agent, Affiliate or representative thereof, is an individual or entity that is, or is owned or controlled by, any individual or entity that is (i) currently the subject or target of any Sanctions, (ii) included on OFAC's List of Specially Designated Nationals, HMT's Consolidated List of Financial Sanctions Targets and the Investment Ban List, or any similar list enforced by any other relevant sanctions authority or (iii) located, organized or resident in a Designated Jurisdiction.

(b) Anti-Corruption Laws. Neither the Company nor, to the Knowledge of the Company, any of the Company's directors, officers, employees or agents have, directly or indirectly, made, offered, promised or authorized any payment or gift of any money or anything of value to or for the benefit of any "foreign official" (as such term is defined in the U.S. Foreign Corrupt Practices Act (the "FCPA")), foreign political party or official thereof or candidate for foreign political office for the purpose of (i) influencing any official act or decision of such official, party or candidate, (ii) inducing such official, party or candidate to use his, her or its influence to affect any act or decision of a foreign Governmental Authority or (iii) securing any improper advantage, in the case of (i), (ii) and (iii) above in order to assist the Company or any of its Affiliate in obtaining or retaining business for or with, or directing business to, any person. Neither the Company nor, to the Knowledge of the Company, any of its directors, officers, employees or agents have made or authorized any bribe, rebate, payoff, influence payment, kickback or other unlawful payment of funds or received or retained any funds in violation of any Law, rule or

regulation. The Company further represents that it has maintained, and has caused each of its Subsidiaries and Affiliates to maintain, systems of internal controls (including accounting systems, purchasing systems and billing systems) to ensure compliance with all Anti-Corruption Laws. The Company and its Subsidiaries have conducted their business in compliance with all Anti-Corruption Laws, and have instituted and maintained policies and procedures designed to promote and achieve compliance with such Laws.

(c) PATRIOT Act. To the extent applicable, the Company and each Subsidiary is in compliance, with (i) and (ii) the USA PATRIOT Act (Title III of Pub. L. 107-56 (signed into Law October 26, 2001)), as amended from time to time.

Section 4.25 Data Security; Data Privacy.

(a) The Company has not experienced any breach of security of unauthorized access by Third Parties of any Personal Information in its possession, custody, or control that could reasonably be expected to result in a Material Adverse Effect.

(b) In connection with its collection, storage, transfer (including, without limitation, any transfer across national borders) and/or use of any personally identifiable information from any individuals, including, without limitation, any customers, prospective customers employees and/or other Third Parties (collectively "Personal Information"), the Company is and for the past three years has been, to the Knowledge of the Company, in compliance in all material respects with all Applicable Laws in all relevant jurisdictions, including the General Data Protection Regulation, the Company's privacy policies and the requirements of any contracts or codes of conduct to which the Company is a party, except for any such non-compliance that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Effect. The Company has commercially reasonable physical, technical, organizational and administrative security measures and policies in place to protect all Personal Information collected by it from and against unauthorized access, use and/or disclosure. The Company is and for the past three years has been, to the Knowledge of the Company, in compliance in all material respects with all Laws relating to data loss, theft and breach of security notification obligations, except for any such non-compliance that, individually or in the aggregate, could reasonably be expected to result in a Material Adverse Effect.

Section 4.26 Compliance of Included Products.

(a)

(i) The Company and its Subsidiaries possess all material Permits, including Regulatory Approvals from the FDA, the EMA, the MHRA and other Governmental Authorities required for the conduct of their business as currently conducted, and all such Permits are in full force and effect;

(ii) The Company and its Subsidiaries have not received any written communication from any Governmental Authority alleging any failure of the Company or its Subsidiaries to materially comply with any Laws, including any terms or requirements of any Regulatory Approval and, to the Knowledge of the Company, there are no facts or circumstances

that are reasonably likely to give rise to any revocation, withdrawal, suspension, cancellation, material limitation, material termination or adverse modification of any Regulatory Approval;

(iii) To the Knowledge of the Company, none of the officers, directors, employees or, or to the Knowledge of the Company, Affiliates of the Company or any Subsidiary involved in any Drug Application, has been convicted of any crime or engaged in any conduct for which debarment is authorized by 21 U.S.C. Section 335a nor, to the Knowledge of the Company, are any debarment proceedings or investigations pending or threatened against the Company or any Subsidiary or any of their respective officers, employees or agents;

(iv) To the Knowledge of the Company, none of the officers, directors, employees or Affiliates of the Company or any Subsidiary or any of their agents or consultants has (A) made an untrue statement of material fact or fraudulent statement to any Regulatory Agency or failed to disclose a material fact required to be disclosed to a Regulatory Agency; or (B) committed an act, made a statement, or failed to make a statement that would reasonably be expected to provide a basis for the FDA to invoke its policy respecting "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities," set forth in 56 Fed. Regulation 46191 (September 10, 1991);

(v) All applications, notifications, submissions, information, claims, reports and statistics and other data and conclusions derived therefrom, utilized as the basis for or submitted in connection with any and all requests for Regulatory Approval from the FDA, the EMA, the MHRA or other Governmental Authority for Included Products, when submitted to the FDA, the EMA, the MHRA or other Governmental Authority were true, complete and correct in all material respects as of the date of submission or any necessary or required updates, changes, corrections or modifications to such applications, submissions, information and data have been submitted to the FDA, the EMA, the MHRA or other Governmental Authority;

(vi) All preclinical and clinical trials conducted by or on behalf of the Company and its Subsidiaries the results of which have been submitted to any Governmental Authority, including the FDA, the EMA, the MHRA and their counterparts worldwide, in connection with any request for a Regulatory Approval, are being or have been conducted in compliance in all material respects with all Applicable Laws;

(vii) All Included Products have since January 1, 2021 been manufactured, transported, stored and handled in all material respects in accordance with all Permits and Applicable Laws;

(viii) Neither the Company nor any Subsidiary has received any written notice from a Governmental Authority that such Governmental Authority, including without limitation the FDA, the EMA, the MHRA, the Office of the Inspector General of the United States Department of Health and Human Services or the United States Department of Justice has commenced or threatened to initiate any action against the Company or a Subsidiary, any action to enjoin the Company or a Subsidiary, its officers, directors, employees, agents and Affiliates from conducting its business at any facility owned or used by it or for any material civil penalty, injunction, seizure or criminal action that would reasonably be expected to result in a Material Adverse Effect;

(ix) Neither the Company nor any Subsidiary has received from the FDA, the EMA or the MHRA, at any time since January 1, 2021, a Warning Letter, Form FDA-483, "Untitled Letter," or similar written correspondence or notice alleging violations of Applicable Laws enforced by the FDA, the EMA, the MHRA or any comparable written correspondence from any other Governmental Authority, in each case, with regard to any Included Product or the manufacture, processing, packaging or holding thereof, the subject of which communication is unresolved and if determined adversely to the Company or such Subsidiary could reasonably be expected to result in a Material Adverse Effect; and

(x) Since January 1, 2021, (A) there have been no material Safety Notices, (B) to the Knowledge of the Company, there are no unresolved material product complaints with respect to Included Products, and (C) to the Knowledge of the Company, there are no facts that would result in (1) a material Safety Notice, (2) a material change in the labeling of any Included Products, or (3) a termination or suspension of marketing of any Included Products.

(b) All of the Included Products that exist as of the date hereof are listed on Schedule 4.26(b);

Section 4.27 Labor Matters. There are no existing or, to the Knowledge of the Company, threatened strikes, lockouts or other labor Disputes involving the Company or any Subsidiary that, individually or in the aggregate, would reasonably be expected to result in a Material Adverse Effect. Except as would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect, hours worked by and payments of compensation made by the Company and its Subsidiaries to their respective employees are not in violation of the Fair Labor Standards Act or any other Applicable Law, rule or regulation dealing with such matters.

Section 4.28 EEA Financial Institution. Neither the Company nor any of its Subsidiaries is an EEA Financial Institution.

Section 4.29 Taxes. The Company and each of its Subsidiaries has (A) filed all Tax returns and reports required by to have been filed by it (including in its capacity as a withholding agent), (B) paid all Taxes required to be paid by it (including in its capacity as a withholding agent), and (C) provided adequate accruals, charges and reserves in accordance with GAAP in their applicable financial statements in respect of all Taxes not yet due and payable, except, in each case, (i) any such Taxes that are being diligently contested in good faith by appropriate proceedings and for which adequate reserves have been provided in accordance with GAAP or (ii) any failure that would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect.

ARTICLE V
REPRESENTATIONS AND WARRANTIES OF THE INVESTOR

Each Investor hereby represents and warrants separately (and not jointly) to the Company as of the Effective Date and the date of each Closing as follows:

Section 5.1 Organization. Such entity is a Delaware limited partnership duly organized, validly existing and in good standing under the Laws of its state of formation and has all powers and authority, and all licenses, Permits, franchises, authorizations, consents and approvals of all Governmental Authorities, required to own its property and conduct its business as now conducted.

Section 5.2 No Conflicts. None of the execution and delivery by such entity of any of the Transaction Documents to which it is party, the performance by it of the obligations contemplated hereby or thereby or the consummation of the transactions contemplated hereby or thereby will contravene, conflict with, result in a breach, violation, cancellation or termination of, constitute a default (with or without notice or lapse of time, or both) under, require prepayment under, give any Person the right to exercise any remedy (including termination, cancellation or acceleration) or obtain any additional rights under, or accelerate the maturity or performance of or payment under, in any respect, (i) any Applicable Law or any judgment, order, writ, decree, Permit or license of any Governmental Authority to which such entity or any of its assets or properties may be subject or bound, (ii) any term or provision of any contract, agreement, indenture, lease, license, deed, commitment, obligation or instrument to which such entity is a party or by which such entity or any of its assets or properties is bound or committed or (iii) any term or provision of any of the organizational documents of such entity, except in the case of clause (i) where any such event would not result in a material adverse effect on the ability of such entity to consummate the transactions contemplated by the Transaction Documents.

Section 5.3 Authorization. Such entity has all powers and authority to execute and deliver, and perform its obligations under, the Transaction Documents to which it is party and to consummate the transactions contemplated hereby and thereby. The execution and delivery of each of the Transaction Documents to which such entity is party, and the performance by it of its obligations hereunder and thereunder, have been duly authorized by it. Each of the Transaction Documents to which such entity is party has been duly executed and delivered by it. Each of the Transaction Documents to which such entity is party constitutes the legal, valid and binding obligation of it, enforceable against it in accordance with its respective terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium or similar Applicable Laws affecting creditors' rights generally, general equitable principles and principles of public policy.

Section 5.4 Governmental and Third Party Authorizations. The execution and delivery by such entity of the Transaction Documents to which it is party, the performance by it of its obligations hereunder and thereunder and the consummation of any of the transactions contemplated hereunder and thereunder do not require any consent, approval, license, order, authorization or declaration from, notice to, action or registration by or filing with any Governmental Authority or any other Person.

Section 5.5 No Litigation. There is no action, suit, arbitration proceeding, claim, citation, summons, subpoena, investigation or other proceeding (whether civil, criminal, administrative, regulatory, investigative or informal and including by or before a Governmental Authority) pending or, to the knowledge of such entity, threatened by or against such entity, at law or in equity, that challenges or seeks to prevent or delay or which, if adversely determined, would prevent or delay the consummation of any of the transactions contemplated by any of the Transaction Documents to which it is party.

Section 5.6 No Brokers' Fees. Such entity has not taken any action that would entitle any person or entity to any commission or broker's fee in connection with the transactions contemplated by this Agreement.

Section 5.7 Funds Available. As of the date hereof, such entity has sufficient funds on hand to satisfy its obligations to pay the Investment Amount due and payable on the Initial Closing Date and has sufficient funds under commitment to it to satisfy its obligations to pay the Investment Amount due and payable on the Second Closing Date and Third Closing Date. Such entity acknowledges and agrees that its obligations under this Agreement are not contingent on obtaining financing.

Section 5.8 Access to Information. Such entity acknowledges that it has (a) reviewed such documents and information relating to the Revenue Interests, the Collateral and the Included Products and (b) had the opportunity to ask such questions of, and to receive answers from, representatives of the Company, in each case, as it deemed necessary to make an informed decision to purchase, acquire and accept the Revenue Interests in accordance with the terms of this Agreement. Such entity has such knowledge, sophistication and experience in financial and business matters that it is capable of evaluating the risks and merits of purchasing, acquiring and accepting the Revenue Interests in accordance with the terms of this Agreement.

Section 5.9 Tax Status. Such entity is a Unites States person as such term is defined in Section 7701(a)(30) of the Internal Revenue Code.

ARTICLE VI
AFFIRMATIVE COVENANTS

The Parties hereto covenant and agree as follows:

Section 6.1 Collateral Matters; Guarantors.

(a) On or prior to the Initial Closing Date, each of the Company and the Guarantors shall enter into the Security Agreement, pursuant to which the Company and the Guarantors shall grant to the Investor Representative, a continuing security interest of first priority in all of their respective right, title and interest in, to and under the Collateral, whether now or hereafter existing, and any and all "proceeds" thereof (as such term is defined in the UCC), in each case, for the benefit of the Investors as security for the prompt and complete payment and performance of the Obligations. Pursuant to the Security Agreement, the Company shall pledge (x) all of its Equity Interests in the Guarantors and (y) to the extent that any Subsidiary organized as a Massachusetts Securities Corporation owns any portion of the assets listed in the definition of "Collateral", all of its Equity Interests in such Subsidiary organized as a Massachusetts Securities Corporation (such Subsidiaries referred to in clauses (x) and (y), the "Pledged Subsidiaries"), in each case, to the Investor Representative for the benefit of the Investor to secure the Obligations. In addition, each Guarantor shall enter into the Guaranty, pursuant to which each Guarantor shall guarantee the prompt performance of the Obligations. The Company shall cause any Subsidiary that may acquire or own any portion of the Collateral after the Initial Closing Date to enter into a Joinder Agreement to become a party to the Guaranty as Guarantor and to the Security Agreement as Grantor once such Subsidiary has recognized revenue from the sale or distribution of Imcivree.

(b) The Company authorizes and consents to the Investor Representative filing, including with the Secretary of State of the State of Delaware, one or more UCC financing statements (and continuation statements with respect to such financing statements when applicable) or other instruments and notices, in such manner and in such jurisdictions, as in the Investor Representative's determination may be necessary or appropriate to evidence the purchase, acquisition and acceptance by the Investors of the Revenue Interests hereunder and to perfect and maintain the perfection of each of the Investor's ownership in the Revenue Interests and the security interest in the Revenue Interests granted by each Grantor to the Investors pursuant to the Security Agreement; provided that the Investor Representative will provide the Company with a reasonable opportunity to review any such financing statements (or similar documents) prior to filing and the Collateral identified in any such financing shall be limited to a legally sufficient description of the "Collateral" as defined herein and proceeds and products thereof. For greater certainty, the Investor Representative will not file this Agreement in connection with the filing of any such financing statements (or similar documents) but may file a summary or memorandum of this Agreement if required under Applicable Laws providing for such filing. For sake of clarification, the foregoing statements in this Section 6.1 shall not bind either Party regarding the reporting of the transactions contemplated hereby for GAAP or SEC reporting purposes.

Section 6.2 Update Meetings. During the Payment Term, but subject to ARTICLE IX, the Investor Representative shall be entitled to a quarterly update call or meeting (at the Investor Representative's election, in person, via teleconference or videoconference or at a location reasonably designated by the Company) to discuss (i) the reports delivered by thee Company pursuant to Section 3.4, (ii) certain topics or documents listed on Schedule 6.2, (iii) the progress of sales and product development and marketing efforts made by the Company pursuant to the Product Plan, (iv) the status and the historical and potential performance of Imcivree, (v) any material regulatory or Patent developments and/or (vi) such other matters that the Investor Representative deems appropriate. Any information disclosed by either Party during such update meetings or calls or provided to the Investor Representative pursuant to its request shall be considered "Confidential Information" of the disclosing Party subject to the terms of ARTICLE IX. Notwithstanding the foregoing, after the occurrence and during the continuance of a Special Termination Event, Default or an Event of Default, the Investor Representative shall have the right, as often, at such times and with such prior notice as the Investor Representative shall determine in its reasonable discretion, to have such update meetings at the Company's headquarters or inspect any records and operations of the Company and its Affiliates.

Section 6.3 Notices.

(a) To the extent permitted by Applicable Law, promptly after receipt by the Company of notice of any action, suit, claim, demand, Dispute, investigation, arbitration or other legal proceeding (commenced or threatened) involving or related to Imcivree or any Pledged Subsidiary which owns any assets (including Intellectual Property) related to Imcivree, the transactions contemplated by any Transaction Document, or to the Revenue Interests, the Company shall, subject to any confidentiality obligations to any Third Party, (i) inform the Investor Representative in writing of the receipt of such notice and the substance thereof and (ii) if such notice is in writing, furnish the Investor Representative with a copy of such notice and any related materials with respect thereto reasonably requested by the Investor Representative, and if

such notice is not in writing, furnish to the Investor Representative a written summary describing in reasonable detail the substance thereof.

(b) To the extent permitted by Applicable Law, promptly following receipt by the Company of any written notice, claim or demand challenging the legality, validity, enforceability or ownership of any of the Intellectual Property included in the Collateral or owned by any Pledged Subsidiary and relating to Imcivree or pursuant to which any Third Party commences or threatens any action, suit or other proceeding against the Company and relating to Imcivree or any Pledged Subsidiary which owns any assets (including Intellectual Property) related to Imcivree, the Company shall, subject to any confidentiality obligation to any Third Party, (i) inform the Investor Representative in writing of such receipt and (ii) furnish the Investor Representative with a copy of such notice, claim or demand, or if such notice is not in writing, furnish to the Investor Representative a written summary describing in reasonable detail the contents thereof.

(c) The Company shall promptly (and in any event within fifteen Business Days) provide Investor Representative with copies of any material information, reports and notices if the contents of such information, report or notice could, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect.

(d) The Company shall provide the Investor Representative with prompt written notice after the Company has Knowledge of any of the following: (i) the occurrence of a Bankruptcy Event in respect of the Company or any Material Contract Counterparty to any Material Contract; (ii) any material breach or Default (in each case, with or without notice or lapse of time, or both) by the Company of or under any covenant, agreement or other provision of any Transaction Document; (iii) any representation or warranty made by the Company in any of the Transaction Documents or in any certificate delivered to the Investor pursuant to this Agreement shall prove to be untrue, inaccurate or incomplete in any material respect on the date as of which made; or (iv) any change, effect, event, occurrence, state of facts, development or condition with respect to the assets of the Company and its Subsidiaries, taken as a whole, that could reasonably be expected to result in a Material Adverse Effect.

(e) The Company shall promptly notify the Investor Representative of the occurrence of a Change of Control.

(f) The Company shall notify the Investor Representative in writing not less than 5 Business Days prior to any change in, or amendment or alteration of, any Company Party's (i) legal name, (ii) form of legal entity or (iii) jurisdiction of organization,

(g) The Company shall notify the Investor Representative of any ERISA Event promptly (and in any event, within ten Business Days) following the Company becoming aware of such ERISA Event.

(h) The Company shall notify the Investor Representative of the occurrence of any material default or event of default (in each case, with or without notice or lapse of time, or both) related to any Permitted Debt Facility promptly following the Company becoming aware of

such default or event of default (and in any event, within five Business Days or within one Business Day if any Indebtedness under such Permitted Debt Facility has been accelerated).

(i) The Company shall promptly (and in any event, within ten days) notify the Investor Representative of (i) the termination of any Material Contract other than upon its scheduled termination date; (ii) the receipt by any Company Party or any of its Affiliates from a counterparty asserting a default by the Company or any of its Subsidiaries under any Material Contract where such alleged default, if accurate, would permit such counterparty to terminate such Material Contract; (iii) the entering into of any new Material Contract by a Company Party or any Affiliate; or (iv) any material amendment to an Material Contract.

(j) The Company shall promptly notify the Investor Representative of the occurrence of a Special Termination Event, Default or Event of Default.

(k) The Company shall promptly notify the Investor Representative of the occurrence of any event with respect to the assets of the Company or any Affiliates of the Company that could reasonably be expected to result in a Material Adverse Effect.

Each notice pursuant to clauses (a) through (k) of this Section 6.3 shall be accompanied by a statement of a Responsible Officer of the Company setting forth details of the occurrence referred to therein and stating what action the applicable Company Party has taken and proposes to take with respect thereto. Such statement shall set forth the actions the applicable Company Party has taken and proposes to take with respect thereto. Each notice pursuant to Section 6.3(g), Section 6.3(i) or Section 6.3(j) shall describe with particularity any and all provisions of this Agreement and any other Transaction Document that have been breached.

Section 6.4 Public Announcement.

(a) As soon as reasonably practicable following the date hereof, one or both of the Parties shall issue a mutually agreed to press release substantially in the applicable form attached hereto as Exhibit A. Except as required by Applicable Law (including disclosure requirements of the SEC, the Nasdaq Stock Market or any other stock exchange on which securities issued by a Party or its Affiliates are traded) or for statements that are materially consistent with all or any portion of a previously approved public disclosure, neither Party shall make any other public announcement concerning this Agreement or the subject matter hereof without the prior written consent of the other Party, which shall not be unreasonably withheld, conditioned or delayed.

(b) The Parties shall coordinate in advance with each other in connection with the filing of this Agreement (including proposed redaction of certain provisions of this Agreement) with the SEC, the Nasdaq Stock Market or any other stock exchange or Governmental Authority on which securities issued by a Party or its Affiliate are traded, and each Party shall use reasonable efforts to seek confidential treatment for the terms of this Agreement proposed to be redacted, if any; provided that each Party shall ultimately retain control over what information to disclose to the SEC, the Nasdaq Stock Market or any other stock exchange or Governmental Authority, as the case may be, and provided further that the Parties shall use their reasonable efforts to file redacted versions with any Governmental Authorities which are consistent with redacted versions

previously filed with any other Governmental Authorities. Other than such obligation, neither Party (nor its Affiliates) shall be obligated to consult with or obtain approval from the other Party with respect to any filings with the SEC, the Nasdaq Stock Market or any other stock exchange or Governmental Authority. For clarity, once a public announcement or other disclosure is made by a Party in accordance with this Section 6.4, then no further consent or compliance with this Section 6.4 shall be required for any substantially similar disclosure thereafter.

Section 6.5 Further Assurances.

(a) The Company shall promptly, upon the reasonable request of the Investor Representative, at the Company's sole cost and expense, (a) execute, acknowledge and deliver, or cause the execution, acknowledgment and delivery of, and thereafter register, file or record, or cause to be registered, filed or recorded, in an appropriate governmental office, any document or instrument supplemental to or confirmatory of the Transaction Documents or otherwise deemed by the Investor Representative reasonably necessary for the continued validity, perfection and priority of the Liens on the Collateral covered thereby subject to no other Liens except as permitted by the applicable Transaction Document, or obtain any consents or waivers as may be necessary in connection therewith; (b) deliver or cause to be delivered to the Investor Representative from time to time such other documentation, consents, authorizations, approvals and orders in form and substance reasonably satisfactory to the Investor Representative as the Investor Representative shall reasonably deem necessary to perfect or maintain the Liens on the Collateral pursuant to the Transaction Documents; and (c) upon the exercise by the Investors of any power, right, privilege or remedy pursuant to any Transaction Document which requires any consent, approval, registration, qualification or authorization of any Governmental Authority, execute and deliver all applications, certifications, instruments and other documents and papers that the Investor Representative may require. In addition, the Company shall promptly, at its sole cost and expense, execute and deliver to the Investor Representative such further instruments and documents, and take such further action as the Investor Representative may, at any time and from time to time, reasonably request in order to carry out the intent and purpose of this Agreement and the other Transaction Documents and to establish and protect the rights, interests and remedies created, or intended to be created, in favor of the Investors hereby and thereby.

(b) The Company and each of the Investors shall cooperate and provide assistance as reasonably requested by each of the Parties hereto, at the expense of the requesting Party (except as otherwise set forth herein), in connection with any litigation, arbitration, investigation or other proceeding (whether threatened, existing, initiated or contemplated prior to, on or after the date hereof) to which the requesting party, any of its Affiliates or controlling persons or any of their respective officers, directors, equityholders, controlling persons, managers, agents or employees is or may become a party or is or may become otherwise directly or indirectly affected or as to which any such Persons have a direct or indirect interest, in each case relating to any Transaction Document, the transactions contemplated herein or therein or the Revenue Interests, but in all cases excluding any litigation brought by the Company (for itself or on behalf of any Company Indemnified Party) against the Investors or brought by the Investor or Investor Representative (for itself or on behalf of any Investor Indemnified Party) against the Company.

(c) Each Party shall comply with all Applicable Laws with respect to the Transaction Documents and the Revenue Interests except where any non-compliance could not reasonably be expected to result in a Material Adverse Effect.

Section 6.6 Imcivree Patent Rights. The Company shall: (a) use commercially reasonable efforts to take any and all actions, and prepare, execute, deliver and file any and all agreements, documents and instruments, that are material or reasonably necessary to preserve diligently and maintain the Imcivree Patent Rights and the Company's rights under the Material Contracts related to Imcivree in the United States and the Major European Markets, including payment of maintenance fees or annuities, at the sole expense of the Company, (b) use commercially reasonable efforts to diligently defend (and enforce) the Imcivree Patent Rights related to Imcivree in such countries against infringement or interference by any other Person, and against any claims of invalidity or unenforceability (including by bringing any legal action for infringement or defending any counterclaim of invalidity or action of a Third Party for declaratory judgment of non-infringement or non-interference), (c) use commercially reasonable efforts to diligently defend against any material claim or action in such countries by any other Person that the manufacture, use, marketing, sale, offer for sale, importation or distribution of Imcivree as currently contemplated infringes on any Patent Rights or other Intellectual Property rights of any other Person or constitutes misappropriation of any other Person's Trade Secrets or other Intellectual Property rights, and (d) when available in respect of Imcivree and where applicable, use commercially reasonable efforts to obtain a patent listing in the Orange Book or apply for similar data exclusivity where available in other countries in which sales of Imcivree occur. The Company shall not exercise and enforce its applicable rights in any manner that would result in a breach of this Agreement.

Section 6.7 Existence. The Company shall (a) preserve and maintain its existence, (b) preserve and maintain its rights, franchises and privileges unless failure to do any of the foregoing would not reasonably be expected to result in a Material Adverse Effect, (c) qualify and remain qualified in good standing in each jurisdiction where the failure to preserve and maintain such qualifications could reasonably be expected to result in a Material Adverse Effect, including appointing and employing such agents or attorneys in each jurisdiction where it shall be necessary to take action under this Agreement, and (d) comply in all material respects with its organizational documents.

Section 6.8 Commercialization of Imcivree.

(a) The Company and its Pledged Subsidiaries (if any) shall use Commercially Reasonable and Diligent Efforts to prepare, execute, deliver and file any and all agreements, documents or instruments that are necessary or desirable to secure and maintain Marketing Authorization in the United States and the EEA for Imcivree. The Company shall not, without the prior consent of the Investor Representative, withdraw or abandon, or fail to take any action necessary to prevent the withdrawal or abandonment of, Marketing Authorization (i) in the United States, (ii) any Major European Market in which the Company has received Marketing Authorization or (iii) any other jurisdiction in which the Company has received Marketing Authorization; provided, however, that with respect to the jurisdictions referred to in clause (iii), the consent of the Investor Representative shall not be required if such withdrawal or abandonment is commercially reasonable (as determined by whether such can be achieved or prevented by a

company using Commercially Reasonable and Diligent Efforts). The Company shall use Commercially Reasonable and Diligent Efforts, itself or through one or more Subsidiaries or Permitted Licensees, to Commercialize Imcivree in the United States, the EEA and any other jurisdiction in which the Company has received Marketing Authorization in accordance with the Product Plan.

(b) The Company shall not enter into any Material Contract unless the Company (i) shall have used Commercially Reasonable and Diligent Efforts in selecting the applicable Material Contract Counterparty to such Material Contract and negotiating and agreeing to the terms of such Material Contract (or any amendment, modification, restatement, cancellation, supplement, termination or waiver of any of the material terms thereof) or (ii) shall have obtained the prior written consent of the Investors. In addition, if any existing Material Contract (other than the Rarestone License Agreement and any License Agreement outside the United States and the Major European Markets) terminates for any reason whatsoever and such Contract was, as of the time of termination, still a Material Contract, the Company shall use Commercially Reasonable and Diligent Efforts to enter into a replacement Material Contract. In the case of Material Contracts consisting of licenses or other arrangements under which the counterparty is to make payments to the Company in respect of such Commercialization, such counterparties shall be instructed to make all payments to the Lockbox Account for receipt and disbursement in accordance with the terms hereof.

(c) The Company shall, and shall cause its Subsidiaries to, comply with all material terms and conditions of and fulfill all material obligations under each Material Contract (including, without limitation, each License Agreement) to which any of them is party. Upon the occurrence of a material breach of any such Material Contract by the Company or any of its Subsidiaries, the Company shall use Commercially Reasonable and Diligent Efforts to cure (or cause its Subsidiary to cure) such material breach.

(d) Upon the occurrence of a material breach of any Material Contract by any other party thereto, the Company shall use Commercially Reasonable and Diligent Efforts to seek to enforce all of its (and cause its Affiliates to seek to enforce all of their) rights and remedies thereunder.

Section 6.9 Financial Statements.

(a) The Company shall deliver to the Investor Representative, in form and detail reasonably satisfactory to the Investor Representative as soon as available, and in any event within 90 days after the end of each fiscal year of the Company (or, if earlier, when required to be filed with the SEC), a consolidated balance sheet of the Company and its Subsidiaries as at the end of such fiscal year, and the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity and cash flows for such fiscal year, setting forth in each case in comparative form the figures for the previous fiscal year, all in reasonable detail and prepared in accordance with GAAP, audited and accompanied by a report and opinion of an independent certified public accountant of nationally recognized standing, which report and opinion shall be prepared in accordance with generally accepted auditing standards and shall not be subject to any qualification or exception as to the scope of such audit (except for a qualification or an exception to the extent related to the maturity or refinancing of borrowings under Permitted Debt or this

Agreement); provided, that to the extent the components of such financial statements relating to a prior fiscal period are separately audited by different independent public accounting firms, the audit report of any such accounting firm may contain a qualification or exception as to scope of such financial statements as they relate to such components; and

(b) The Company shall deliver to the Investor Representative, as soon as available, and in any event within 45 days after the end of each of the first three fiscal quarters of each fiscal year of the Company (or, if earlier, when required to be filed with the SEC), a consolidated balance sheet of the Company and its Subsidiaries as at the end of such fiscal quarter, and the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity and cash flows for such fiscal quarter and for the portion of the Company's fiscal year then ended, setting forth, in each case in comparative form, the figures for the corresponding fiscal quarter of the previous fiscal year and the corresponding portion of the previous fiscal year, all in reasonable detail.

Section 6.10 Certificates; Other Information. The Company shall (a) deliver to the Investor Representative, in form and detail reasonably satisfactory to the Investor Representative:

(i) concurrently with the delivery of the Financial Statements referred to in Section 6.9(a) and (b), a duly completed Compliance Certificate signed by the chief executive officer, chief financial officer, treasurer or controller of the Company, setting forth (i) the amount of gross sales of the Included Product in each country, (ii) the amount of Other Royalty Payments in each country, (iii) the amount of the Net Revenues and a calculation thereof, (iv) a calculation of the Included Product Payment Amount for each Quarterly Payment Date, showing the Applicable Tiered Percentage applied thereto and a calculation of Under Performance Payments (if applicable), in each case, for each fiscal quarter period covered by such Compliance Certificate;

(ii) as soon as practicable upon the reasonable request of the Investor Representative, copies of the most recent quarterly statements for each Deposit Account, Securities Account and other bank account or Securities Account of the Company and each other Grantor;

(iii) concurrently with the delivery of the Financial Statements referred to in Section 6.9(a) and Section 6.9(b), a certificate of a Responsible Officer of the Company listing (A) all applications by any Company Party, if any, for Copyrights, Patents or Trademarks made since the date of the prior certificate (or, in the case of the first such certificate, the Initial Closing Date), (B) all issuances of registrations or letters on existing applications by any Company Party for Copyrights, Patents and Trademarks received since the date of the prior certificate (or, in the case of the first such certificate, the Initial Closing Date), (C) all material Trademark Licenses, Copyright Licenses and Patent Licenses entered into by any Company Party since the date of the prior certificate (or, in the case of the first such certificate, the Initial Closing Date), (D) such supplements to Schedule 4.10 as are (i) necessary to add items solely for events occurring between the Initial Closing Date and the date of such certificate in order to cause such schedule to be true and complete in all material respects as of the date of such certificate (it being understood that such

supplements are not meant to cure inaccurate disclosure made as of the Initial Closing Date for purposes of the Investors' rights to indemnification hereunder) and (ii) reasonably acceptable to the Investor Representative.

Documents required to be delivered pursuant to Section 6.9(a) or Section 6.9(b) may be delivered electronically and if so delivered, shall be deemed to have been delivered on the date (i) on which the Company posts such documents, or provides a link thereto on the Company's Website, or (ii) on which such documents are posted on the Company's behalf on an internet or intranet Website, if any, to which the Investor Representative has access (whether a commercial, third-party Website or whether sponsored by the Investor); provided, that the Company shall notify the Investor Representative (by electronic mail) of the posting of any such documents and provide to the Investor Representative by electronic mail electronic versions (*i.e.*, soft copies) of such documents. The Investor Representative shall have no obligation to request the delivery of or to maintain paper copies of the documents referred to above, and in any event shall have no responsibility to monitor compliance by the Company with any such request for delivery by the Investor or the Investor Representative, and the Investor or the Investor Representative shall be solely responsible for requesting delivery to it or maintaining its copies of such documents.

Section 6.11 Payment of Obligations. Each Company Party shall pay and discharge all of their respective obligations and liabilities (a) prior to the date on which penalties attach thereto, all federal and state and other Taxes imposed upon it or its properties or assets, unless the same are being contested in good faith by appropriate proceedings diligently conducted and adequate reserves in accordance with GAAP are being maintained by the Company Party, (b) as the same shall become due and payable, all lawful claims which, if unpaid, would by Law become a Lien (other than a Permitted Lien) upon any Collateral, and (c) prior to the date on which such Indebtedness shall become delinquent or in default, all material Indebtedness, but subject to any subordination provisions contained in any instrument or agreement evidencing such Indebtedness.

Section 6.12 Maintenance of Properties. Each of the Company and its Subsidiaries shall maintain, preserve and protect all of its material properties and equipment necessary in the operation of its business in good working order and condition (ordinary wear and tear and casualty and condemnation events excepted) except where the failure to do so would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect, and shall make all necessary repairs thereto and renewals and replacements thereof, except where the failure to do so would not reasonably be expected to result in a Material Adverse Effect.

Section 6.13 Maintenance of Insurance.

(a) Except as would not reasonably be expected to result in a Material Adverse Effect, each of the Company and its Subsidiaries shall maintain with financially sound and reputable insurance companies that are not Affiliates of the Company, insurance with respect to its properties and business against Loss or damage of the kinds customarily insured against by Persons engaged in the same or similar business, of such types and in such amounts as are customarily carried under similar circumstances by such other Persons.

(b) Within 30 days of the Initial Closing Date, (i) the Company shall provide the Investor Representative a schedule of the insurance coverage of the Company and its Subsidiaries as is then in effect, outlined as to carrier, policy number, expiration date, type, amount and deductibles, and (ii) each of the Company and its Subsidiaries shall cause the Investor and its successors and/or assigns to be named as lender's loss payee or mortgagee as its interest may appear, and/or additional insured with respect to any such insurance providing liability coverage or coverage in respect of any tangible Collateral or assets of the Pledged Subsidiaries relating to Imcivree (if any).

Section 6.14 Books and Records. Each of the Company and its Subsidiaries shall maintain proper books of record and account, in which full, true and correct entries in conformity with GAAP consistently applied shall be made of all financial transactions and matters involving the assets and business of such Company Party or such Subsidiary, as the case may be. Each of the Company and its Subsidiaries shall maintain such books of record and account in material conformity with all applicable requirements of any Governmental Authority having regulatory jurisdiction over such Company Party or such Subsidiary, as the case may be.

Section 6.15 Use of Proceeds. The Company and its Subsidiaries, taken as a whole, shall use substantially all of the Investment Amount to support the development and Commercialization of Imcivree, including the commercial launch of Imcivree in accordance with the Product Plan. In no event, however, shall the Investment Amount be used to fund any activities of or business with any Person, or in any Designated Jurisdiction, that, at the time of such funding, is the subject of Sanctions, or in any other manner that will result in a violation by any Person (including any Person participating in the transaction, whether as Investor or otherwise) of Sanctions or otherwise in contravention of any Law or of any Transaction Document.

Section 6.16 ERISA Compliance. Each of the Company and its Subsidiaries shall do each of the following: (a) maintain each Plan in compliance with the applicable provisions of ERISA, the Internal Revenue Code and other federal or state Law, (b) cause each Pension Plan that is qualified under Section 401(a) of the Internal Revenue Code to maintain such qualification, and (c) make all contributions required to be made by the Company and its Subsidiaries to any Pension Plan subject to Section 412 or Section 430 of the Internal Revenue Code, in each case, except as would not reasonably be expected to result in a Material Adverse Effect.

Section 6.17 Compliance with Material Contracts. Each of the Company and its Subsidiaries shall comply in all respects with each Contractual Obligation of such Person, except as could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect.

Section 6.18 Compliance with Laws. The Company shall maintain, and shall cause its Subsidiaries to maintain, compliance in all material respects with all Applicable Laws (including any Law, rule or regulation with respect to the making or brokering of loans or financial accommodations), and shall, or cause its Subsidiaries to, obtain and maintain all required material Permits.

Section 6.19 Anti-Corruption Laws; Anti-Terrorism Laws.

(a) Neither the Company nor, to the Knowledge of the Company, any of its Subsidiaries, nor any of their respective directors, officers, employees or agents shall, directly or indirectly, engage in any activity which would constitute a violation of the FCPA make, offer, promise or authorize any payment or gift of any money or anything of value to or for the benefit of any "foreign official" (as such term is defined in the FCPA), foreign political party or official thereof or candidate for foreign political office for the purpose of (i) influencing any official act or decision of such official, party or candidate, (ii) inducing such official, party or candidate to use his, her or its influence to affect any act or decision of a foreign Governmental Authority or (iii) securing any improper advantage, in the case of (i), (ii) and (iii) above in order to assist the Company or any of its Affiliate in obtaining or retaining business for or with, or directing business to, any person.

(b) Neither the Company nor, to the Knowledge of the Company, any of its Subsidiaries shall, nor shall the Company or any of its Subsidiaries permit any Affiliate controlled by the Company to, directly or indirectly, knowingly enter into any documents, instruments, agreements or Contracts with any Sanctioned Person. Neither the Company nor any of its Subsidiaries shall, nor shall the Company or any of its Subsidiaries, permit any Affiliate controlled by the Company to, directly or indirectly, (i) conduct any business or engage in any transaction or dealing with any Sanctioned Person, including, without limitation, the making or receiving of any contribution of funds, goods or services to or for the benefit of any Sanctioned Person, (ii) deal in, or otherwise engage in any transaction relating to, any property or interests in property blocked pursuant to Executive Order No. 13224 or any similar executive order or other Anti-Terrorism Law, or (iii) engage in or conspire to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding, or attempts to violate, any of the prohibitions set forth in Executive Order No. 13224 or other Anti-Terrorism Law.

Section 6.20 Data Privacy. In connection with its collection, storage, transfer (including, without limitation, any transfer across national borders) and/or use of any Personal Information, the Company shall, and shall cause its Subsidiaries to, maintain compliance in all material respects with all Applicable Laws in all relevant jurisdictions, including the General Data Protection Regulation, the Company's and its Subsidiaries' privacy policies and the requirements of any contracts or codes of conduct to which the Company's or any of its Subsidiaries is a party, except for any such non-compliance that, individually or in the aggregate, could not reasonably be expected to result in a Material Adverse Effect. The Company shall maintain commercially reasonable physical, technical, organizational and administrative security measures and policies in place to protect all Personal Information collected by it from and against unauthorized access, use and/or disclosure. The Company shall, and shall cause its Subsidiaries to, maintain compliance in all material respects with all Applicable Laws relating to data loss, theft and breach of security notification obligations, except for any such non-compliance that, individually or in the aggregate, could not reasonably be expected to result in a Material Adverse Effect.

Section 6.21 Included Products. In connection with the development, testing, manufacture, marketing or sale of each and any Included Product by the Company or any Subsidiary, the Company or such Subsidiary shall comply in all material respects with all material Permits.

Section 6.22 Tax.

(a) The Parties (i) agree that for U.S. federal and applicable state and local income Tax purposes, the transactions contemplated by this Agreement are intended to constitute a debt instrument that is subject to U.S. Treasury Regulations under Section 1.1275-4(b) governing contingent payment debt instruments. Within 90 days after the date of this Agreement, the Company will prepare and deliver to the Investor Representative a determination of the comparable yield and a projected payment schedule under Section 1.1275-4(b) (the "Comparable Yield"). Unless the Investor Representative objects to the Comparable Yield within 15 days after receipt thereof, the Comparable Yield shall become final and binding on the Parties. If the Investor Representative objects to the Comparable Yield within 15 days of receipt, then the Parties shall cooperate in good faith to agree on a revised Comparable Yield within 20 days of the Investor's objection. The Parties intend that the provisions of the U.S. Treasury Regulation 1.1275-2(a)(1) would apply, subject to the exceptions in the U.S. Treasury Regulation 1.1275-2(a)(2), to treat any non-contingent payments on the debt instrument and the projected amount of any contingent payments as first, a payment of any accrued and any unpaid original issue discount at such time and second, a payment of principal (including for purposes of the rules applicable to "applicable high yield discount obligations"). The Parties agree not to take and to not cause or permit their Affiliates to take, any position that is inconsistent with the provisions of this Section 6.22(a) on any U.S. federal, state or local income Tax return or for any other U.S. federal, state or local income Tax purpose, unless required by Law or the good faith resolution of a Tax audit or other Tax proceeding.

(b) On or prior to the Initial Closing Date, each entity constituting collectively the Investors shall provide the Company with a duly completed and executed IRS Form W-9 certifying that such entity is a United States person, as such term is defined in Section 7701(a)(30) of the Internal Revenue Code, that is exempt from U.S. federal backup withholding with respect to all payments pursuant to this Agreement.

(c) Payments by or on account of any obligation of the Company under this Agreement shall be made without deduction or withholding for any Taxes, except as required by Applicable Law. If the Company is required by Law to deduct or withhold any Tax in respect of any amounts payable to an Investor pursuant to this agreement, (1) the Company shall make such deduction or withholding and timely pay such amount to the applicable Governmental Authority, (2) the Company shall provide such Investor with a receipt evidencing such payment or other evidence of such payment reasonably satisfactory to such Investor and (3) if the Tax deducted or withheld was an Indemnified Tax, the sum payable by the Company shall be increased so that after all required deductions and withholdings for Indemnified Taxes have been made (including deductions and withholdings applicable to additional sums payable under this Section 6.22(c)), such Investor receives an amount equal to the sum it would have received had no such deductions or withholdings been made. The Company will promptly notify an Investor if it becomes required to deduct or withhold any Tax in respect of any payment to such Investor pursuant to this Agreement.

(d) If the Investor determines, in its reasonable discretion exercised in good faith, that it has received a refund of any Taxes as to which it has received Additional Amounts pursuant to this Section 6.22, it shall pay to the Company an amount equal to such refund (but only to the extent of Additional Amounts paid under this Section 6.22 with respect to the Taxes giving rise to such refund), net of all out-of-pocket expenses (including Taxes) of the Investor and without

interest (other than any interest paid by the relevant Governmental Authority with respect to such refund). The Company, upon the request of the Investors, shall repay to the Investor the amount paid over pursuant to this Section 6.22(c) (plus any penalties, interest or other charges imposed by the relevant Governmental Authority) in the event that the Investor is required to repay such refund to such Governmental Authority. Notwithstanding anything to the contrary in this Section 6.22(c), in no event will the Investor be required to pay any amount to the Company pursuant to this Section 6.22(c) the payment of which would place the Investor in a less favorable net after-Tax position than the Investor would have been in if the Tax for which the Company paid Additional Amounts and giving rise to such refund had not been deducted, withheld or otherwise imposed and the Additional Amounts with respect to such Tax had never been paid. This paragraph shall not be construed to require the Investor to make available its Tax returns (or any other information relating to its Taxes that it deems confidential) to the Company or any other Person.

(e) Each Party's obligations under this Section 6.22 shall survive the termination of this Agreement, any assignment by an Investor and the repayment, satisfaction or discharge of all obligations under this Agreement.

Section 6.23 Post-Closing Obligations.

(a) Notwithstanding any provision herein or in any Transaction Documents, Company, within 60 days of the Closing Date (which may be extended by the Investor Representative at its reasonable discretion), shall cause the French Subsidiary to become a Guarantor and execute a Joinder Agreement pursuant to Section 6.1.

(b) Notwithstanding any provision herein or in any Transaction Documents, Company, within 60 days of the Closing Date (which may be extended by the Investor Representative at its reasonable discretion), shall cause the German Subsidiary to become a Guarantor and execute a Joinder Agreement pursuant to Section 6.1.

ARTICLE VII
NEGATIVE COVENANTS

During the Payment Term, no Company Party shall, nor shall it permit any Subsidiary to, directly or indirectly:

Section 7.1 Liens. Create, incur, assume or suffer to exist any Lien upon any Collateral or any assets of the Pledged Subsidiaries relating to Imcivree (if any), whether now owned or hereafter acquired, other than the Permitted Liens.

Section 7.2 Indebtedness. Create, incur, assume or suffer to exist any Indebtedness without the prior written consent of the Investor Representative, except Permitted Debt and Permitted Convertible Notes.

Section 7.3 Dispositions. Make any Disposition (other than, for the avoidance of doubt, Permitted Transfers) unless (a) the consideration paid in connection therewith shall be in an amount not less than the fair market value of the property Disposed of, (b) no Special Termination Event, Default or Event of Default shall have occurred and be continuing both

immediately prior to and immediately after giving effect to such Disposition, (c) such transaction does not involve the sale or other Disposition of a minority Equity Interest in any Subsidiary (other than to another Grantor), (d) such transaction does not involve a sale, transfer, license or other Disposition of Imcivree assets or rights included in the Collateral or owned by any Pledged Subsidiary relating to Imcivree (or any Intellectual Property Rights associated therewith) in the United States, the EEA or any state or political subdivision thereof and (e) prior to the Minimum Return Date, the aggregate net book value of all of the assets sold or otherwise Disposed of (including, for the avoidance of doubt, the assets sold or otherwise Disposed of in such Disposition) does not exceed $[***] in any fiscal year. For the avoidance of doubt, no early unwind, termination of any Permitted Bond Hedge Transaction shall constitute a Disposition.

Section 7.4 Change in Nature of Business. Engage in any material line of business other than the discovery, development, manufacture or Commercialization of biopharmaceutical products or other related or ancillary lines of business.

Section 7.5 Prepayment of Other Indebtedness. Prior to the Minimum Return Date, make (or give any notice with respect thereto) any voluntary or optional payment or prepayment or redemption, cash settlement or acquisition for value of (including without limitation, by way of depositing money or securities with the trustee with respect thereto before due for the purpose of paying when due), refund, refinance or exchange of any Indebtedness of the Company or any Subsidiary in excess of $[***] in any fiscal year (other than exchanging any such Indebtedness for capital stock (other than Disqualified Capital Stock) or the proceeds from the sale of capital stock (other than Disqualified Capital Stock)) or, with respect to the Indebtedness arising under the Transaction Documents, Permitted Debt and, in the case of the Permitted Convertible Notes, other than from using the proceeds from the sale of Permitted Convertible Notes or exchanging any such Indebtedness for Permitted Convertible Notes.

Notwithstanding the foregoing, and for the avoidance of doubt, this Section 7.5 shall not prohibit the conversion by holders of (including any cash payment upon conversion), or required payment of any principal (including upon redemption following satisfaction of a stock price condition) or premium on, or required payment of any interest with respect to, any Permitted Convertible Notes, in each case, in accordance with the terms of the indenture governing such Permitted Convertible Notes except to the extent both (a) the aggregate amount of cash payable upon conversion or payment of any Permitted Convertible Notes (excluding any required payment of interest with respect to such Permitted Convertible Notes and excluding any payment of cash in lieu of a fractional share due upon conversion thereof) exceeds the aggregate principal amount thereof and (b) such conversion or payment does not trigger or correspond to an exercise or early unwind or settlement of a corresponding portion of the Permitted Bond Hedge Transactions relating to such Permitted Convertible Notes (including, for the avoidance of doubt, the case where there is no Permitted Bond Hedge Transaction relating to such Permitted Convertible Notes), the payment of such excess cash shall not be permitted.

Notwithstanding the foregoing, the Company may repurchase, exchange or induce the conversion of Permitted Convertible Notes by delivery of shares of the Company's common stock and/or a different series of Permitted Convertible Note (any such series of Permitted Convertible Indebtedness, "Refinancing Convertible Notes") and/or by payment of cash in an amount that does not exceed the proceeds received by the Company from the substantially

concurrent issuance of shares of the Company's common stock and/or Refinancing Convertible Notes plus the net cash proceeds, if any, received by the Company pursuant to the related exercise or early unwind or termination of the related Permitted Bond Hedge Transactions and Permitted Warrant Transactions, if any.

Section 7.6 Organization Documents; Fiscal Year; Legal Name, State of Formation and Form of Entity; Certain Amendments.

(a) Amend, modify or change its Organization Documents in a manner materially adverse to the rights or remedies of the Investors under the Transaction Documents.

(b) Without providing ten days' prior notice to the Investor Representative, change its fiscal year.

(c) Without providing ten days' prior notice to the Investor Representative, change its name, state of organization or form of organization or its Federal Taxpayer Indemnification Number or its organizational identification number.

(d) Amend, modify or change any of the terms or provisions of any Permitted Debt Facility Document in a manner inconsistent with the terms of the Transaction Documents.

(e) Amend, modify or change the Product Plan without the prior written consent of the Investor Representative.

(f) Amend, modify or change in any material respect any of the terms or provisions of a Material Contract (other than the Rarestone License Agreement and any License Agreement outside the United States and the Major European Markets) in a manner materially adverse to the Investors.

Section 7.7 Restricted Payments. Declare or make, directly or indirectly, any Restricted Payment, or incur any obligation (contingent or otherwise) to do so, except that:

(a) each Subsidiary may make Restricted Payments to any other Company Party;

(b) each Company Party may make Restricted Payments to any Company Party;

(c) each Subsidiary may make Restricted Payments to the holders of its Equity Interests on a *pro rata* basis;

(d) each Subsidiary that is not a Company Party may make Restricted Payments to any other Subsidiary;

(e) the Company and each Subsidiary may declare and make dividend payments or other distributions payable solely in the Equity Interests (other than Disqualified Capital Stock) of the Company or Subsidiary, as applicable;

(f) the Company may make scheduled payments to the Permitted Debt Creditors so long as (i) no Default or Event of Default (in each case, with or without notice or lapse of time, or both) exits under the Permitted Debt Facility Documents and (ii) such payments are made in accordance with the terms of the Permitted Debt Facility Documents;

(g) the Company may make Restricted Payments to the Permitted Convertible Notes Creditors;

(h) the Company may make any Restricted Payment in exchange for, or out of the net cash proceeds of a contribution to the common equity of the Company or a substantially concurrent sale (other than to a Subsidiary of the Company) of, Equity Interests (other than Disqualified Capital Stock) of the Company;

(i) the Company and its Subsidiaries may repurchase Equity Interests (i) deemed to occur upon the exercise of options, warrants or other convertible securities to the extent that such Equity Interests represent all or a portion of the exercise price thereof or (ii) deemed to occur upon the withholding of a portion of Equity Interests granted or awarded to any current or former officer, director, manager, employee or consultant (or permitted transferees, assigns, estates, trusts or heirs of any of the foregoing) to pay for Taxes payable by such Person in connection with such grant or award (or the vesting thereof);

(j) the Company and its Subsidiaries may make payments of cash in lieu of fractional Equity Interests pursuant to the exchange or conversion of any exchangeable or convertible securities;

(k) the Company and its Subsidiaries may repurchase, redeem or otherwise acquire or retire for value any Equity Interests of the Company or any of the Company's Subsidiaries held by any current or former employee, director, manager, consultant or director (or permitted transferees, assigns, estates, trusts or heirs of any of the foregoing) of the Company or any of the Company's Subsidiaries pursuant to the terms of any employee equity subscription agreement, stock option agreement or similar agreement; provided that the aggregate price paid under this clause (j) in any Calendar Year, commencing with the Calendar Year ended December 31, 2022, will not exceed $[***] (with unused amounts in any such Calendar Year being referred to as "Unused Amounts"); provided, further, that such amount may be increased by an amount not to exceed:

(A) the net cash proceeds from the sale of Equity Interests (other than Disqualified Capital Stock) of the Company to any current or former employee, director, manager, consultant or director of the Company or any of its Subsidiaries that occurs after the date of this Agreement; and

(B) the cash proceeds of life insurance policies received by the Company or the Subsidiaries after the date of this Agreement; and

(C) the aggregate Unused Amounts (which aggregate amount will be reduced to the extent used after the date of this Agreement to repurchase, redeem

or otherwise acquire or retire for value any Equity Interests pursuant to this clause (j)); and

(l) the Company and its Subsidiaries make may payments or distributions to dissenting stockholders pursuant to Applicable Law in connection with any merger, amalgamation or consolidation with, or other acquisition of, another Person;

(m) to the extent constituting Restricted Payments, the Company and its Subsidiaries may make payments of contingent liabilities in respect of any adjustment of purchase price, earn outs, deferred compensation and similar obligations of the Company and its Subsidiaries; and

(n) prior to the Minimum Return Date, the Company and its Subsidiaries may make any other Restricted Payments in an aggregate amount not to exceed $[***].

Notwithstanding the foregoing, and for the avoidance of doubt, (i) the conversion by holders of (including any cash payment upon conversion), or required payment of any principal or premium on, or required payment of any interest with respect to, any Permitted Convertible Notes, in each case, in accordance with the terms of the indenture governing such Permitted Convertible Notes, shall not constitute a Restricted Payment; provided that, to the extent both (a) the aggregate amount of cash payable upon conversion or payment of any Permitted Convertible Notes (excluding any required payment of interest with respect to such Permitted Convertible Notes and excluding any payment of cash in lieu of a fractional share due upon conversion thereof) exceeds the aggregate principal amount thereof and (b) such conversion or payment does not trigger or correspond to an exercise or early unwind or settlement of a corresponding portion of the Permitted Bond Hedge Transactions relating to such Permitted Convertible Notes (including, for the avoidance of doubt, the case where there is no Permitted Bond Hedge Transaction relating to such Permitted Convertible Notes), the payment of such excess cash shall constitute a Restricted Payment notwithstanding this clause (i); and (ii) any required payment with respect to, or required early unwind or settlement of, any Permitted Bond Hedge Transaction or Permitted Warrant Transaction, in each case, in accordance with the terms of the agreement governing such Permitted Bond Hedge Transaction or Permitted Warrant Transaction shall not constitute a Restricted Payment; provided that, to the extent cash is required to be paid under a Permitted Warrant Transaction as a result of the election of "cash settlement" (or substantially equivalent term) as the "settlement method" (or substantially equivalent term) thereunder by the Company (or its Affiliate) (including in connection with the exercise and/or early unwind or settlement thereof), the payment of such cash shall constitute a Restricted Payment notwithstanding this clause (ii).

Notwithstanding the foregoing, the Company may repurchase, exchange or induce the conversion of Permitted Convertible Notes by delivery of shares of the Company's common stock and/or Refinancing Convertible Notes and/or by payment of cash in an amount that does not exceed the proceeds received by the Company from the substantially concurrent issuance of shares of the Company's common stock and/or Refinancing Convertible Notes plus the net cash proceeds, if any, received by the Company pursuant to the related exercise or early unwind or termination of the related Permitted Bond Hedge Transactions and Permitted Warrant Transactions, if any.

Section 7.8 Burdensome Actions.

(a) The Company and its Subsidiaries shall not enter into any Contract, or grant any right to any other Person, in any case that would conflict with the Transaction Documents or serve or operate to limit or circumscribe any of the Investor's rights under the Transaction Documents (or the Investor's ability to exercise any such rights) or create, incur, assume or suffer to exist any Lien upon any Collateral or any assets of any Pledged Subsidiary relating to Imcivree (other than Permitted Liens), or agree to do or suffer to exist any of the foregoing. Without limiting the generality of the foregoing, the Company shall not enter into, or permit to exist, any Contractual Obligation that encumbers or restricts the ability of any Company Party (other than Permitted Liens) to (i) pledge its property pursuant to the Transaction Documents or (ii) perform any of its obligations under the Transaction Documents or any Material Contract in any material respect. Notwithstanding anything to the contrary in this Agreement, the Company shall not take any action or abstain from taking any action, directly or indirectly, which action or abstinence would have the effect of altering the terms and conditions of this Agreement or the other Transaction Documents (or any ancillary documents thereto) in a manner that could reasonably be expected to result in a Material Adverse Effect.

(b) The Company and its Subsidiaries shall not enter into any Contract, grant any right to any other Person with respect to Imcivree or amend or waive any requirements under any agreement with respect to Imcivree that could reasonably be expected to result in a Material Adverse Effect.

Section 7.9 Affiliates. The Company shall not (a) permit any Affiliate that is not a Subsidiary to own any portion of the Collateral (or assets owned by any Pledged Subsidiary relating to Imcivree (if any)) or (b) permit any Affiliate that is not a Subsidiary to own any assets that generate Net Revenues.

ARTICLE VIII
THE CLOSINGS

Section 8.1 Closing. Subject to the terms of this Agreement, the closings of the transactions contemplated hereby (each, a "Closing") shall take place on:

(a) for the initial Closing (the "Initial Closing"), on the date that is 15 Business Days following the date hereof (the "Initial Closing Date") following the satisfaction of the conditions set forth in Section 8.4(a) or such other time and place as the parties hereto mutually agree;

(b) for the second Closing (the "Second Closing"), subject to the satisfaction of the conditions set forth in Section 8.2, on the 15th Business Day (the "Second Closing Date") following the satisfaction of the conditions set forth in Section 8.2 and Section 8.4(b) or such other time and place as the parties hereto mutually agree; and

(c) for the third Closing (the "Third Closing"), subject to the satisfaction of the conditions set forth in Section 8.3, on the 45th day (the "Third Closing Date") following the satisfaction of the conditions set forth in Section 8.3 and Section 8.4(c) or such other time and place as the parties hereto mutually agree.

Section 8.2 Conditions to Second Closing. The obligations of each of the Investors relating to the Second Closing shall be conditional upon (i) no Bankruptcy Event with respect to the Company or any of its Subsidiaries or no Special Termination Event or Event of Default having occurred and be continuing (and the Investor Representative's receipt of the certification from a Responsible Officer to that effect), and (ii) the occurrence of the Regulatory Milestone Event. The Company shall notify the Investor Representative within ten Business Days after the occurrence of the Regulatory Milestone Event.

Section 8.3 Conditions to Third Closing. The obligations of each of the Investors relating to the Third Closing shall be conditional upon (i) no Bankruptcy Event with respect to the Company or any of its Subsidiaries or no Special Termination Event or Event of Default having occurred and be continuing (and the Investor Representative's receipt of the certification from a Responsible Officer to that effect) and (ii) the occurrence of the Sales Milestone Event. The Company shall notify the Investor Representative within ten Business Days after the occurrence of the Sales Milestone Event.

Section 8.4 Closing Deliverables of the Company.

(a) At the Initial Closing, the Company shall deliver or cause to be delivered to the Investor Representative the following:

(i) Transaction Documents. Receipt by the Investor Representative of executed counterparts (including by electronic means) of this Agreement and the Security Agreement, executed by the parties thereto (in a manner reasonably acceptable to the Investor Representative), in each case in form and substance satisfactory to the Investor Representative.

(ii) Organization Documents, Resolutions, Etc. Receipt by the Investor Representative of the following (to the extent not previously provided to the Investor Representative), each of which shall be originals, facsimiles or electronic copies, in form and substance reasonably satisfactory to the Investor Representative and its legal counsel:

(A) copies of the certificate of incorporation of each Grantor certified to be true and complete as of a recent date by the appropriate Governmental Authority of the state or other jurisdiction of its incorporation or organization, where applicable, and the other Organization Documents, in each case certified by a secretary or assistant secretary (or, if such entity does not have a secretary or assistant secretary, a Responsible Officer) of such Grantor to be true and correct as of the Initial Closing Date;

(B) such certificates of resolutions or other action, incumbency certificates and/or other certificates of Responsible Officers of each Grantor as the Investor Representative may reasonably require evidencing the identity, authority and capacity of each Responsible Officer thereof authorized to act as a Responsible Officer in connection with this Agreement and the other Transaction Documents to which such Grantor is a party; and

(C) such documents and certifications as the Investor Representative may reasonably require to evidence that each Grantor is duly organized or formed, and is validly existing, in good standing and qualified to engage in business in its state of organization or formation.

(iii) Opinions of Counsel. Receipt by the Investor Representative of a written legal opinion of Latham & Watkins, LLP, addressed to the Investor Representative, dated the Initial Closing Date and in form and substance previously agreed between the Company and the Investor Representative.

(iv) Perfection and Priority of Liens. Receipt by the Investor Representative of the following:

(A) searches of UCC filings in the jurisdictions where a filing would need to be made in order to perfect the Investor's security interest in the Collateral, copies of the financing statements on file in such jurisdictions and evidence that no Liens exist on the Collateral other than Permitted Liens;

(B) UCC financing statements for each appropriate jurisdiction as is necessary, in the Investor's reasonable discretion, to perfect the Investor's security interest in the Collateral;

(C) all certificates evidencing any certificated Equity Interests pledged to the Investor (if any), together with duly executed in blank and undated stock powers attached thereto; and

(D) searches of ownership of, and Liens on, the Imcivree Patent Rights of each Grantor in the appropriate U.S. governmental offices.

(v) Responsible Officer's Certificate. Receipt by the Investor Representative of a certificate of a Responsible Officer of the Company certifying that (i) the representations and warranties set forth in ARTICLE IV (other than the Fundamental Representations) are true and correct in all material respects on and as of the Initial Closing Date (or, if made as of a specific date, as of such date); provided, that to the extent that any such representation or warranty is qualified by the term "material" or "Material Adverse Effect" such representation or warranty (as so written, including the term "material" or "Material Adverse Effect") shall have been true and correct in all respects as of the date hereof and shall be true and correct in all respects as of the Initial Closing Date or such other date, as applicable and (ii) that the Fundamental Representations are true and correct in all respects on and as of the Initial Closing Date (or, if made as of a specific date, as of such date).

(vi) Attorney Costs; Due Diligence Expenses. The Company shall have paid all reasonable and documented fees, charges and disbursements of counsel to the Investor and all reasonable and documented due diligence expenses of the Investors, in each case, incurred prior to or at the Initial Closing Date in accordance with Schedule 8.3(a)(vi); provided that the condition set forth in this clause (vi) will be satisfied by the transfer by

the Investor of an amount equal to the Initial Investment Amount minus the amount owed by the Company under this clause (vi).

(vii) Other. Such other documents, instruments, reports, statements and information as may be reasonably requested by the Investor Representative.

(b) At the Second Closing (should the Second Closing occur), the Company shall deliver or cause to be delivered to the Investor Representative the following:

(i) A certificate of a Responsible Officer of the Company (the statements made in which shall be true and correct on and as of the applicable Closing Date): (A) attaching copies, certified by such officer as true and complete, of (x) the organizational documents of the Company and (y) confirming that resolutions of the governing body of the Company authorizing and approving the execution, delivery and performance by the Company of the Transaction Documents and the transactions contemplated herein and therein remain in full force and effect; and (B) attaching a copy, certified by such officer as true and complete, of a good standing certificate of the appropriate Governmental Authority of the Company's jurisdiction of organization, stating that the Company is in good standing under the Applicable Laws of such jurisdiction;

(ii) A certificate of a Responsible Officer of the Company certifying that (A) the Regulatory Milestone Event has occurred, and (B) no Bankruptcy Event with respect to the Company or any of its Subsidiaries and no Special Termination Event, Default or Event of Default has occurred and is continuing; and

(iii) A certificate of a Responsible Officer of the Company certifying that (A) the representations and warranties set forth in ARTICLE IV (other than the Fundamental Representations) are true and correct in all material respects on and as of the Second Closing Date (or, if made as of a specific date, as of such date); provided, that to the extent that any such representation or warranty is qualified by the term "material" or "Material Adverse Effect" such representation or warranty (as so written, including the term "material" or "Material Adverse Effect") shall have been true and correct in all respects as of the date hereof and shall be true and correct in all respects as of the Second Closing Date or such other date, as applicable, (B) that the Fundamental Representations are true and correct in all respects on and as of the Second Closing Date (or, if made as of a specific date, as of such date), subject to any additions that the Company may make to Schedule 4.10(a) as of the Second Closing Date and (C) that the Company has complied in all material respects with its covenants, agreements and other obligations under this Agreement and the other Transaction Documents.

(iv) Receipt by the Investor Representative of executed counterparts (including by electronic means) of updated Disclosure Schedules, executed by the parties thereto (in a manner reasonably acceptable to the Investor Representative), in each case in form and substance satisfactory to the Investor Representative.

(c) At the Third Closing (should the Third Closing occur), the Company shall deliver or cause to be delivered to the Investor Representative the following:

(i) A certificate of a Responsible Officer of the Company (the statements made in which shall be true and correct on and as of the applicable Closing Date): (A) attaching copies, certified by such officer as true and complete, of (x) the organizational documents of the Company and (y) confirming that resolutions of the governing body of the Company authorizing and approving the execution, delivery and performance by the Company of the Transaction Documents and the transactions contemplated herein and therein remain in full force and effect; and (B) attaching a copy, certified by such officer as true and complete, of a good standing certificate of the appropriate Governmental Authority of the Company's jurisdiction of organization, stating that the Company is in good standing under the Applicable Laws of such jurisdiction; and

(ii) A certificate of a Responsible Officer of the Company certifying that (A) the Sales Milestone Event has occurred, and (B) no Bankruptcy Event with respect to the Company or any of its Subsidiaries and no Special Termination Event, Default or Event of Default has occurred and is continuing.

ARTICLE IX
CONFIDENTIALITY

Section 9.1 Confidentiality; Permitted Use. During the Payment Term and for a period of 3 years thereafter, each Party shall maintain in strict confidence all Confidential Information and materials disclosed or provided to it by the other Party, except as approved in writing in advance by the disclosing Party, and shall not use or reproduce the disclosing Party's Confidential Information for any purpose other than as required to carry out its obligations and exercise its rights pursuant to this Agreement (the "Purpose"). The Party receiving such Confidential Information (the "Recipient") agrees to institute measures to protect the Confidential Information in a manner consistent with the measures it uses to protect its own most sensitive proprietary and Confidential Information, which must not be less than a reasonable standard of care. Notwithstanding the foregoing, the Recipient may permit access to the disclosing Party's Confidential Information to those of its employees or authorized representatives having a need to know such information for the Purpose and who have signed confidentiality agreements or are otherwise bound by confidentiality obligations at least as restrictive as those contained herein. Each Party shall be responsible for the breach of this Agreement by its employees or authorized representatives. Each Party shall immediately notify the other Party upon discovery of any loss or unauthorized disclosure of the other Party's Confidential Information.

Section 9.2 Exceptions. The obligations of confidentiality and non-use set forth in Section 9.1 shall not apply to any portion of Confidential Information that the Recipient or its Affiliates can demonstrate was: (a) known to the general public at the time of its disclosure to the Recipient or its Affiliates, or thereafter became generally known to the general public, other than as a result of actions or omissions of the Recipient, its Affiliates, or anyone to whom the Recipient or its Affiliates disclosed such portion; (b) known by the Recipient or its Affiliates, prior to the date of disclosure by the disclosing Party; (c) disclosed to the Recipient or its Affiliates on an unrestricted basis from a source unrelated to the disclosing Party and not known by the Recipient or its Affiliates to be under a duty of confidentiality to the disclosing Party; (d) independently developed by the Recipient or its Affiliates by personnel that did not use the

Confidential Information of the disclosing Party in connection with such development or (e) disclosed pursuant to Applicable Law (including disclosure requirements of the SEC, the Nasdaq Stock Market or any other stock exchange on which securities issued by a Party or its Affiliates are traded).

Section 9.3 Permitted Disclosures. The obligations of confidentiality and non-use set forth in Section 9.1 shall not apply to the extent that the receiving Party or its Affiliates:

(a) is required to disclose Confidential Information pursuant to: (i) an order of a court of competent jurisdiction; (ii) Applicable Laws (including disclosure requirements of the SEC, the Nasdaq Stock Market or any other stock exchange on which securities issued by a Party or its Affiliates are traded); (iii) regulations or rules of a securities exchange; (iv) requirement of a Governmental Authority for purposes related to development or Commercialization of an Included Product, or (v) the exercise by each Party of its rights granted to it under this Agreement or its retained rights or as required to perfect Investor's rights under the Transaction Documents; or

(b) discloses such Confidential Information solely on a "need to know basis" to Affiliates, potential or actual: acquirers, merger partners, Material Contract Counterparties, permitted assignees, collaborators (including Material Contract Counterparties), subcontractors, investment bankers, limited partners, lenders, or other financial partners, and their respective directors, employees, contractors and agents, or

(c) provides a copy of this Agreement or any of the other Transaction Documents to the extent requested by an authorized representative of a U.S. or foreign Tax authority,

(d) discloses Confidential Information in response to a routine audit or examination by, or a blanket document request from, a Governmental Authority; provided that (A) such Third Party or person or entity in clause (b) agrees to confidentiality and non-use obligations with respect thereto at least as stringent as those specified for in this ARTICLE IX; and (B) in the case of clauses (a)(i) through (iv) and clause (c), to the extent permitted by Applicable Law, the Recipient shall provide prior written notice thereof to the disclosing Party and provide the opportunity for the disclosing Party to review and comment on such required disclosure and request confidential treatment thereof or a protective order therefor; and provided, further that the Recipient will use reasonable efforts to secure confidential treatment of such information and the Confidential Information disclosed shall be limited to that information which is legally required to be disclosed.

Notwithstanding anything set forth in this Agreement, prior to any foreclosure on the Collateral, the Investors and the Investor Representative shall not file any patent application based upon or using the Confidential Information of the Company provided hereunder.

For the avoidance of doubt, nothing herein shall prohibit or limit the Company or any Subsidiary from making any disclosures it reasonably deems appropriate in connection with Applicable Laws, including rules of the SEC, the Nasdaq Stock Market or any other stock exchange on which securities issued by a the Company or its Affiliates are traded.

Section 9.4 Return of Confidential Information. Each Party shall return or destroy, at the other Party's instruction, all Confidential Information of the other Party in its possession upon termination or expiration of this Agreement; provided, however, that each Party shall be entitled to retain one (1) copy of such Confidential Information of the other Party for legal archival purposes and/or as may be required by Applicable Law and neither Party shall be required to return, delete or destroy Confidential Information or any electronic files or any information prepared by such Party that have been backed-up or archived in the ordinary course of business consistent with past practice.

ARTICLE X
INDEMNIFICATION

Section 10.1 Indemnification by the Company. The Company agrees to indemnify and hold each of the Investors and their respective Affiliates and any and all of their respective partners, directors, managers, members, officers, employees, agents and controlling persons (each, a "Investor Indemnified Party") harmless from and against, and will pay to each Investor Indemnified Party the amount of, any and all Losses awarded against or incurred or suffered by such Investor Indemnified Party arising out of (a) any breach of any representation, warranty or certification made by the Company in any of the Transaction Documents or certificates given by the Company to the Investor Representative in writing pursuant to this Agreement or any other Transaction Document, (b) any breach of or default under any covenant or agreement by the Company to the Investor Representative pursuant to any Transaction Document, (c) any Excluded Liabilities and Obligations and (d) any fees, expenses, costs, liabilities or other amounts incurred or owed by the Company to any brokers, financial advisors or comparable other Persons retained or employed by it in connection with the transactions contemplated by this Agreement (collectively, the "Company Indemnification Obligations"); provided, however, that the foregoing shall exclude any indemnification to any Investor Indemnified Party (i) that results from the bad faith or willful misconduct of such Investor Indemnified Party, (ii) to the extent resulting from acts or omissions of the Company based upon the written instructions from any Investor Indemnified Party or (iii) for any matter to the extent of, and in respect of, which any Company Indemnified Party would be entitled to indemnification under Section 10.2.

Section 10.2 Indemnification by the Investors. The Investors jointly and severally agree to indemnify and hold each of the Company, its Affiliates and any and all of their respective partners, directors, managers, members, officers, employees, agents and controlling Persons (each, a "Company Indemnified Party") harmless from and against, and will pay to each Company Indemnified Party the amount of, any and all Losses awarded against or incurred or suffered by such Company Indemnified Party arising out of (a) any breach of any representation, warranty or certification made by the Investors in any of the Transaction Documents or certificates given by the Investors in writing pursuant hereto or thereto, (b) any breach of or default under any covenant or agreement by the Investors pursuant to any Transaction Document and (c) any fees, expenses, costs, liabilities or other amounts incurred or owed by the Investors to any brokers, financial advisors or comparable other Persons retained or employed by it in connection with the transactions contemplated by this Agreement (collectively, the "Investor Indemnification Obligations"); provided, however, that the foregoing shall exclude any

indemnification to any Company Indemnified Party (i) that results from the bad faith or willful misconduct of such Company Indemnified Party, (ii) to the extent resulting from acts or omissions of the Investors based upon the written instructions from any Company Indemnified Party or (iii) for any matter to the extent of, and in respect of, which any Investor Indemnified Party would be entitled to indemnification under Section 10.1.

Section 10.3 Procedures. If any Third Party Claim shall be brought or alleged against an indemnified party in respect of which indemnity is to be sought against an indemnifying party pursuant to Section 10.1 or Section 10.2, the indemnified party shall, promptly after receipt of notice of the commencement of any such Third Party Claim, notify the indemnifying party in writing of the commencement thereof, enclosing a copy of all papers served, if any; provided, that the omission to so notify such indemnifying party will not relieve the indemnifying party from any liability that it may have to any indemnified party under Section 10.1 or Section 10.2 unless, and only to the extent that, the indemnifying party is actually prejudiced by such omission. In the event that any Third Party Claim is brought against an indemnified party and it notifies the indemnifying party of the commencement thereof in accordance with this Section 10.3, the indemnifying party will be entitled, at the indemnifying party's sole cost and expense, to participate therein. In any such Third Party Claim, an indemnified party shall have the right to retain its own counsel, but the reasonable fees and expenses of such counsel shall be at the sole cost and expense of such indemnified party unless (a) the indemnifying party and the indemnified party shall have mutually agreed to the retention of such counsel, (b) the indemnifying party has failed within a reasonable time to retain counsel reasonably satisfactory to such indemnified party or (c) the named parties to any such Third Party Claim (including any impleaded parties) include both the indemnifying party and the indemnified party and representation of both parties by the same counsel would be inappropriate due to actual or potential conflicts of interests between them based on the advice of counsel to the indemnifying party. It is agreed that the indemnifying party shall not, in connection with any Third Party Claim or related proceedings in the same jurisdiction, be liable for the reasonable fees and expenses of more than one separate law firm (in addition to local counsel where necessary) for all such indemnified parties. The indemnifying party shall not be liable for any settlement of any Third Party Claim effected without its written consent, but, if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party from and against any Loss by reason of such settlement or judgment. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement, compromise or discharge of any pending or threatened Third Party Claim in respect of which any indemnified party is or would have been a party and indemnity would have been sought hereunder by such indemnified party, unless such settlement, compromise or discharge, as the case may be, (i) includes an unconditional written release of such indemnified party, in form and substance reasonably satisfactory to the indemnified party, from all liability on claims that are the subject matter of such claim or proceeding, (ii) does not include any statement as to an admission of fault, culpability or failure to act by or on behalf of any indemnified party and (iii) does not impose any continuing material obligation or restrictions on such indemnified party.

Section 10.4 Other Claims. A claim by an indemnified party under this ARTICLE X for any matter not involving a Third Party Claim and in respect of which such indemnified party seeks indemnification hereunder may be made by delivering, in good faith, a written notice of demand to the indemnifying party, which notice shall contain (a) a description

and the amount of any Losses incurred or suffered by the indemnified party (and the method of computation of such Losses), (b) a statement that the indemnified party is entitled to indemnification under this ARTICLE X for such Losses and a reasonable explanation of the basis therefor, and (c) a demand for payment in the amount of such Losses. For all purposes of this Section 10.4, the Company shall be entitled to deliver such notice of demand to the Investor Representative on behalf of the Company Indemnified Parties, and the Investor Representative shall be entitled to deliver such notice of demand to the Company on behalf of the Investor Indemnified Parties. Within 30 days after receipt by the indemnifying party of any such notice, the indemnifying party may deliver to the indemnified party that delivered the notice a written response in which the indemnifying party (a) agrees that the indemnified party is entitled to the full amount of the Losses claimed in the notice from the indemnified party; (b) agrees that the indemnified party is entitled to part, but not all, of the amount of the Losses claimed in the notice from the indemnified party; or (c) indicates that the indemnifying party disputes the entire amount of the Losses claimed in the notice from the indemnified party. If the indemnified party does not receive such a response from the indemnifying party within such thirty (30)-day period, then the indemnifying party shall be conclusively deemed to have agreed that the indemnified party is entitled to the full amount. If the indemnifying party and the indemnified party are unable to resolve any Dispute relating to any amount of the Losses claimed in the notice from the indemnified party within 30 days after the delivery of the response to such notice from the indemnifying party, then the parties shall be entitled to resort to any legal remedy available to such party to resolve such Dispute that is provided for in this Agreement, subject to all the terms, conditions and limitations of this Agreement.

Section 10.5 Exclusive Remedies. The indemnification afforded by this ARTICLE X shall be the sole and exclusive remedy for any and all Losses awarded against or incurred or suffered by the Investor Indemnified Parties against the Company in connection with the Company Indemnification Obligations and the Company Indemnified Parties against the Investors in connection with the Investor Indemnification Obligations under Section 10.1 or Section 10.2, as applicable, in each case other than any Company Indemnification Obligations or Investor Indemnification Obligations, as applicable, resulting from (a) the gross negligence, the bad faith or willful misconduct of the other Party or (b) acts or omissions based upon the written instructions from the other Party; provided that nothing in this Section 10.5 shall alter or affect the rights of the either Party to specific performance by the other Party under the Transaction Documents or the rights of the Investors to exercise remedies under the Transaction Documents after an Event of Default or other rights of creditors under the UCC or any other Applicable Law.

Section 10.6 Certain Limitations. The indemnification afforded by this ARTICLE X shall be subject to the following limitations:

(a) With respect to indemnification by the Company pursuant to Section 10.1(a), the Company's maximum liability for any Loss suffered by an Investor Indemnified Party (other than any Loss resulting from a Third Party Claim) shall not exceed an amount (the "Company Indemnification Cap") equal to (1) the Hard Cap and the amount of all of the other Obligations owed by the Company Parties to the Investors under this Agreement and the other Transaction Documents (other than the indemnification amounts payable under Section 10.1(a)) as of the date of determination, *minus* (2) the aggregate amount of all of the payments collected or received by the Investor Representative (and any direct or indirect transferee of the Investor

Representative to whom any interest in the Revenue Interests is transferred) hereunder as of such date of determination (other than (i) any payments collected or received as a reimbursement of expenses incurred by any Investor Indemnified Party (including attorney's fees) and (ii) any indemnification payments collected or received pursuant to Section 10.1(a)), *minus* (3) the aggregate amount collected or received by the Investor Representative (and any direct or indirect transferee of the Investor Representative to whom any interest in the Revenue Interests is transferred) pursuant to the exercise of its rights under Section 10.1(a) (without duplication of any amounts collected or received pursuant to clause (2)) prior to such date of determination to the extent such amount was not collected or received in connection with a Third Party Claim. Notwithstanding the foregoing, the Company Indemnification Cap shall not apply to any Loss suffered by any Investor Indemnified Party in connection with a Third Party Claim.

(b) With respect to indemnification by the Investors pursuant to Section 10.2, the Investor's maximum liability shall not exceed an amount equal to the excess (if any) of (A) the aggregate amount of all of the payments collected or received by the Investors from the Company prior to the date of determination (excluding any amounts collected or received as a reimbursement of expenses incurred by the Investors or any indemnification amounts collected or received in connection with a Third Party Claim) over (B) the Investment Amount.

ARTICLE XI
EVENTS OF DEFAULT AND REMEDIES

Section 11.1 Events of Default. Any of the events set forth below shall constitute an Event of Default.

(a) Non-Payment. The Company or any Guarantor (if any) fails to pay any amounts to the Investor Representative when and as required to be paid herein, including, without limitation, the Company's failure to (i) pay the Revenue Interests on any Quarterly Payment Date and such failure continues for more than five Business Days (unless such failure was as a result of accounting errors made by the Company in good faith without gross negligence in calculating the Quarterly Net Revenues and the Included Product Payment Amount for such Quarterly Payment Date) or pay any late or unpaid Revenue Interests and any interest accrued thereto and reimburse the Investor Representative for audit expenses pursuant to Section 3.5(b), (ii) pay the Under Performance Payments pursuant to Section 3.1(b), (iii) pay the Change of Control Payment pursuant to Section 3.1(c); (iv) pay the Special Termination Amount pursuant to Section 3.1(d); or (v) pay any other amounts (not contested by the Company in good faith) within ten Business Days of the date upon which the Company is notified in writing by the Investor Representative that such amounts are due and payable hereunder; or

(b) Specific Covenants. Any Company Party fails to perform or observe any term, covenant or agreement contained in Section 6.6 (Intellectual Property), Section 6.7 (Existence), Section 6.8(a) (Commercialization of Imcivree), Section 6.9(a) (Financial Statements), Section 6.19 (Anti-Corruption Laws; Anti-Terrorism Laws) and ARTICLE VII (Negative Covenants) provided that in the case of any such Default is susceptible to cure and can be cured within ten Business Days after the earlier of the date on which (i) a Responsible Officer of any Company Party has Knowledge of such failure or (ii) written notice thereof shall have been

given to the Company by the Investor Representative, the Company shall have such ten Business Day period to cure such Default; or

(c) Other Defaults. Any Company Party fails to perform or observe any other covenant or agreement (not specified in Section 11.1(a) and Section 11.1(b)) and contained in any Transaction Document on its part to be performed or observed, and

(i) such failure continues for 30 days after the earlier of the date on which (A) a Responsible Officer of any Company Party has Knowledge of such Default or (B) written notice thereof shall have been given to the Company by the Investor Representative; and

(ii) such failure (without giving effect to any qualifications as to "materiality" "Material Adverse Effect" or any words of similar meaning) could reasonably be expected to have a Material Adverse Effect.

(d) Insolvency Proceedings, Etc. The Company or any Company Party institutes or consents to the institution of any proceeding under any Debtor Relief Law, or makes an assignment for the benefit of creditors; or applies for or consents to the appointment of any receiver, trustee, custodian, conservator, liquidator, rehabilitator or similar officer for it or for all or any material part of its property; or any receiver, trustee, custodian, conservator, liquidator, rehabilitator or similar officer is appointed without the application or consent of such Person and the appointment continues undischarged or unstayed for 60 days; or any proceeding under any Debtor Relief Law relating to any such Person or to all or any material part of its property is instituted without the consent of such Person and continues undismissed or unstayed for 60 days, or an order for relief is entered in any such proceeding; or

(e) Inability to Pay Debts; Attachment. Any writ or warrant of attachment or execution or similar process is issued or levied against all or any material part of the property of any such Person and is not released, vacated or fully bonded within 30 days after its issue or levy; or

(f) Judgments. There is entered against the Company or any Company Party one or more final judgments or orders for the payment of money in an aggregate amount exceeding $[***] (to the extent not covered by independent third-party insurance as to which the insurer does not dispute coverage) or any one or more non-monetary final judgments that could reasonably be expected to result in a Material Adverse Effect and, in either case, (i) enforcement proceedings are commenced by any creditor upon such judgment or order or (ii) there is a period of 90 consecutive days during which a stay of enforcement of such judgment, by reason of a pending appeal or otherwise, is not in effect; or

(g) Indebtedness. Any Company Party (i) fails to pay when due beyond any grace period provided with respect thereto (whether by scheduled maturity, required prepayment, acceleration, demand or otherwise) any Indebtedness (other than the Obligations hereunder) in excess of $[***] (or its foreign currency equivalent) or (ii) fails to perform or observe any covenant or agreement to be performed or observed by it contained in any Permitted Debt Facility Documents or any documents relating to Indebtedness or more and, as a result of such failure, any

other party to that agreement or instrument has accelerated the maturity of any Indebtedness thereunder; or

(h) ERISA. (i) An ERISA Event occurs with respect to a Pension Plan or Multiemployer Plan which has resulted or would result in liability of any Company Party under Title IV of ERISA to the Pension Plan, Multiemployer Plan or the PBGC in an aggregate amount in excess of $[***], or (ii) the Company or any ERISA Affiliate fails to pay when due, after the expiration of any applicable grace period, any installment payment with respect to its withdrawal liability under Section 4201 of ERISA under a Multiemployer Plan that has resulted or would result in liability of any Company Party in an aggregate amount in excess of $[***] or

(i) Invalidity of Transaction Documents. Any Transaction Document, at any time after its execution and delivery and for any reason other than as expressly permitted hereunder or thereunder or satisfaction in full of all Obligations, ceases to be in full force and effect; or any Company Party or any other Person contests in any manner the validity or enforceability of any Transaction Document; or any Company Party denies that it has any or further liability or obligation under any Transaction Document, or purports to revoke, terminate or rescind any Transaction Document; or

(j) Security Interest. Any security interest purported to be created by the Security Agreement shall cease to be in full force and effect, or shall cease to give the rights, powers and privileges purported to be created and granted hereunder or thereunder (including a perfected first priority security interest in and Lien on substantially all of the Collateral (except for Permitted Liens and as otherwise expressly provided herein and therein)) in favor of the Investors pursuant hereto or thereto (other than as a result of the failure by any Investor to take any action required to maintain the perfection of such security interests), or shall be asserted by the Company not to be a valid, perfected, first priority (except as otherwise expressly provided in this Agreement or such Security Agreement) security interest in the Collateral.

Section 11.2 Remedies Upon Event of Default. If any Event of Default occurs and is continuing, the Company shall promptly following written notice from the Investor Representative pay the Event of Default Payment to the Investor Representative. In addition, the Investor Representative may exercise on behalf of itself and the Investors all rights and remedies available to it and the Investors under the Transaction Documents and Applicable Law; provided, however, that upon the occurrence of an actual or deemed entry of an order for relief with respect to the Company under the Bankruptcy Code of the United States or under any other Debtor Relief Law, the obligation of each of the Investors to pay or advance any funds shall automatically terminate, and the Event of Default Payment shall automatically become due and payable, in each case without further act of the Investors.

ARTICLE XII
MISCELLANEOUS

Section 12.1 Survival. All representations, warranties and covenants made herein and in any other Transaction Document or any certificate delivered pursuant to this Agreement shall survive the execution and delivery of this Agreement and the Closing. The rights hereunder to indemnification and payment of Losses under ARTICLE X or to seek specific

performance under Section 12.2 based on such representations, warranties and covenants shall not be affected by any investigation conducted with respect to, or any knowledge acquired (or capable of being acquired) at any time (whether before or after the execution and delivery of this Agreement or the Closing) in respect of the accuracy or inaccuracy of or compliance with, any such representation, warranty or covenant.

Section 12.2 Specific Performance. Each of the Parties hereto acknowledges that the other Party hereto may not have adequate remedy at law if the other Party fails to perform any of its obligations under any of the Transaction Documents. In such event, each of the Parties hereto agrees that the other Party hereto shall have the right, in addition to any other rights it may have (whether at law or in equity), to seek specific performance of this Agreement without the necessity of posting a bond or proving the inadequacy of monetary damages as a remedy and to seek injunctive relief against any breach or threatened breach of the Transaction Documents. The Parties further agree not to assert that a remedy of specific performance is unenforceable, invalid, contrary to Applicable Law or inequitable for any reason.

Section 12.3 Notices. All notices, consents, waivers and other communications hereunder shall be in writing and shall be effective (a) upon receipt when sent through the mails, registered or certified mail, return receipt requested, postage prepaid, with such receipt to be effective the date of delivery indicated on the return receipt, (b) upon receipt when sent by an overnight courier (costs prepaid and receipt requested), (c) on the date personally delivered to an authorized officer of the party to which sent or (d) on the date transmitted by electronic transmission with a confirmation of receipt, in all cases, with a copy emailed to the recipient at the applicable address, addressed to the recipient as follows:

if to the Company, to:

Rhythm Pharmaceuticals, Inc.
222 Berkeley St., 12th Floor
Boston, MA 02116
Attention: Jim Flaherty, Hunter C. Smith
Email: [***]

with a copy to (which shall not constitute notice):

Latham & Watkins LLP
505 Montgomery Street
Suite 2000
San Francisco, CA 94111
Attention: Haim Zaltzman
Email: [***]

if to the Investors, to:

HealthCare Royalty Management, LLC
on behalf of each entity constituting the Investor
300 Atlantic Street, Suite 600
Stamford, CT 06901
Attention: Clarke B. Futch
Managing Partner
Email: [***]

with a copy (which shall not constitute notice) to:

HealthCare Royalty Management, LLC
on behalf of each entity constituting the Investor
300 Atlantic Street, Suite 600
Stamford, CT 06901
Attention: John A. Urquhart
Email: [***]

with a copy (which shall not constitute notice) to:

HealthCare Royalty Management, LLC
on behalf of each entity constituting the Investor
300 Atlantic Street, Suite 600
Stamford, CT 06901
Attention: Tim Bryant, General Counsel
Email: [***]

with a copy (which shall not constitute notice) to:

Morgan, Lewis & Bockius LLP
1701 Market Street
Philadelphia, Pennsylvania 19103-2921
Attn: Andrew R. Mariniello and Conor Larkin
E-mail: [***]

Each Party hereto may, by notice given in accordance herewith to the other Party hereto, designate any further or different address to which subsequent notices, consents, waivers and other communications shall be sent.

Section 12.4 Successors and Assigns. The provisions of this Agreement shall be binding upon and inure to the benefit of the Parties hereto and their respective successors and permitted assigns. The Company shall not be entitled to assign any of its obligations and rights under this Agreement without the prior written consent of the Investor Representative. The Investors may assign any of their obligations (other than those arising under Section 3.1, unless the assignee is an Affiliate of the Investors and has provided the Company with the

representations and warranties set forth in ARTICLE V) and rights hereunder to any other Person without the consent of the Company; provided that, if no Event of Default shall have occurred and be continuing, the Investors may not assign any of its rights and obligations hereunder to any other Person that is a direct competitor of Company or a vulture or distressed debt fund. The Investor Representative shall give notice of any such assignment to the Company promptly after the occurrence thereof. The Company shall maintain a "register" for the recordation of the names and addresses of, and the amounts owing to, each Investor from time to time. Notwithstanding anything to the contrary contained in this Agreement, no assignment of any interest of any Investor shall be effective until such assignment is recorded in the register and, consistent with the foregoing, the Company shall treat any Investor recorded in the register as an Investor under this Agreement, notwithstanding notice to the contrary. The Company shall be under no obligation to reaffirm any representations, warranties or covenants made in this Agreement or any of the other Transaction Documents. Any purported assignment of rights or obligations in violation of this Section 12.4 will be void.

Section 12.5 Independent Nature of Relationship. The relationship between the Company and the Investors is solely that of lender and borrower, and neither the Company nor any of the Investors has any fiduciary or other special relationship with the any of the Investors and their Affiliates on the one hand, or the Company and its Affiliates on the other hand. Nothing contained herein or in any other Transaction Document shall be deemed to constitute the Company and the Investors as a partnership, an association, a joint venture or any other kind of entity or legal form. The Parties agree that they shall not take any inconsistent position with respect to such treatment in a filing with any Governmental Authority.

Section 12.6 Entire Agreement. This Agreement, together with the Exhibits hereto (which are incorporated herein by reference) and the other Transaction Documents, constitute the entire agreement between the Parties hereto with respect to the subject matter hereof and supersede all prior agreements, understandings and negotiations, both written and oral, between the Parties hereto with respect to the subject matter of this Agreement. No representation, inducement, promise, understanding, condition or warranty not set forth herein (or in the Exhibits hereto or the other Transaction Documents) has been made or relied upon by either Party hereto.

Section 12.7 Governing Law.

(a) THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE INTERNAL SUBSTANTIVE LAWS OF THE STATE OF NEW YORK WITHOUT REFERENCE TO THE RULES THEREOF RELATING TO CONFLICTS OF LAW OR CHOICE OF FORUM OTHER THAN SECTIONS 5-1401 AND 5-1402 OF THE GENERAL OBLIGATIONS LAW OF THE STATE OF NEW YORK, AND THE OBLIGATIONS, RIGHTS AND REMEDIES OF THE PARTIES HEREUNDER SHALL BE DETERMINED IN ACCORDANCE WITH SUCH LAWS.

(b) Each of the Parties hereto hereby irrevocably and unconditionally submits, for itself and its property, to the exclusive jurisdiction of the Supreme Court of the State of New York sitting in New York County and of the United States District Court of the Southern District of New York, and any appellate court from any thereof, in any action or proceeding arising out of

or relating to this Agreement, or for recognition or enforcement of any judgment, and each of the Parties hereto hereby irrevocably and unconditionally agrees that all claims in respect of any such action or proceeding may be heard and determined in such New York State court or, to the extent permitted by Applicable Law, in such federal court. Each of the Parties hereto agrees that a final judgment in any such action or proceeding shall be conclusive and may be enforced in other jurisdictions by suit on the judgment or in any other manner provided by Applicable Law.

(c) Each of the Parties hereto hereby irrevocably and unconditionally waives, to the fullest extent it may legally and effectively do so, any objection that it may now or hereafter have to the laying of venue of any suit, action or proceeding arising out of or relating to this Agreement in any court referred to in Section 12.7(b). Each of the Parties hereto hereby irrevocably waives, to the fullest extent permitted by Applicable Law, the defense of an inconvenient forum to the maintenance of such action or proceeding in any such court.

(d) Each of the Parties hereto irrevocably consents to service of process in the manner provided for notices in Section 12.3. Nothing in this Agreement will affect the right of any Party hereto to serve process in any other manner permitted by Applicable Law. Each of the Parties hereto waives personal service of any summons, complaint or other process, which may be made by any other means permitted by New York Law.

Section 12.8 Waiver of Jury Trial. EACH PARTY HERETO HEREBY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY RIGHT IT MAY HAVE TO A TRIAL BY JURY IN ANY LEGAL PROCEEDING DIRECTLY OR INDIRECTLY ARISING OUT OF OR RELATING TO THIS AGREEMENT, OR THE TRANSACTIONS CONTEMPLATED HEREBY (WHETHER BASED ON CONTRACT, TORT OR ANY OTHER THEORY). EACH PARTY HERETO (A) CERTIFIES THAT NO REPRESENTATIVE, AGENT OR ATTORNEY OF THE OTHER PARTY HERETO HAS REPRESENTED, EXPRESSLY OR OTHERWISE, THAT THE OTHER PARTY HERETO WOULD NOT, IN THE EVENT OF LITIGATION, SEEK TO ENFORCE THE FOREGOING WAIVER AND (B) ACKNOWLEDGES THAT IT AND THE OTHER PARTY HERETO HAVE BEEN INDUCED TO ENTER INTO THIS AGREEMENT BY, AMONG OTHER THINGS, THE MUTUAL WAIVERS AND CERTIFICATIONS IN THIS SECTION 12.8.

Section 12.9 Severability. If one or more provisions of this Agreement are held to be invalid, illegal or unenforceable by a court of competent jurisdiction, such invalidity, illegality or unenforceability shall not affect any other provision of this Agreement, which shall remain in full force and effect, and the Parties hereto shall replace such invalid, illegal or unenforceable provision with a new provision permitted by Applicable Law and having an economic effect as close as possible to the invalid, illegal or unenforceable provision. Any provision of this Agreement held invalid, illegal or unenforceable only in part or degree by a court of competent jurisdiction shall remain in full force and effect to the extent not held invalid, illegal or unenforceable.

Section 12.10 Counterparts. This Agreement may be signed in any number of counterparts, each of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument. This Agreement shall become effective when each Party hereto shall have received a counterpart hereof signed by the other Party hereto. Any

counterpart may be executed by facsimile or electronic transmission, and such facsimile or electronic transmission shall be deemed an original.

Section 12.11 Amendments; No Waivers. Neither this Agreement nor any term or provision hereof may be amended, supplemented, restated, waived, changed or modified except with the written consent of the Company and the Investor Representative. No failure or delay by either Party hereto in exercising any right, power or privilege hereunder shall operate as a waiver thereof nor shall any single or partial exercise thereof preclude any other or further exercise thereof or the exercise of any other right, power or privilege. No notice to or demand on either Party hereto in any case shall entitle it to any notice or demand in similar or other circumstances. No waiver or approval hereunder shall, except as may otherwise be stated in such waiver or approval, be applicable to subsequent transactions. No waiver or approval hereunder shall require any similar or dissimilar waiver or approval thereafter to be granted hereunder. The rights and remedies herein provided shall be cumulative and not exclusive of any rights or remedies provided by Applicable Law.

Section 12.12 No Third Party Rights. Other than the Parties, no Person will have any legal or equitable right, remedy or claim under or with respect to this Agreement. This Agreement may be amended or terminated, and any provision of this Agreement may be waived, without the consent of any Person who is not a Party. The Company shall enforce any legal or equitable right, remedy or claim under or with respect to this Agreement for the benefit of the Company Indemnified Parties and the Investor Representative shall enforce any legal or equitable right, remedy or claim under or with respect to this Agreement for the benefit of the Investor Indemnified Parties.

Section 12.13 Table of Contents and Headings. The Table of Contents and headings of the Articles and Sections of this Agreement have been inserted for convenience of reference only, are not to be considered a part hereof and shall in no way modify or restrict any of the terms or provisions hereof.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year first written above.

RHYTHM PHARMACEUTICALS, INC.

By: /s/ David Meeker
Name: David P. Meeker
Title: President and Chief Executive Officer

[*Signature Page to Revenue Interest Financing Agreement*]

HEALTHCARE ROYALTY PARTNERS IV, L.P.

By: HealthCare Royalty GP IV, LLC,
its general partner

By: /s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

HCRP OVERFLOW FUND, L.P.

By: HCRP Overflow GP, LLC
its general partner

By: /s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

HCR STAFFORD FUND, L.P.

By: HCR Stafford Fund GP, LLC,
its general partner

By: /s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

HCR CANARY FUND, L.P.

By: HCR Canary Fund GP, LLC,
its general partner

By: /s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

HCR POTOMAC FUND, L.P.

By: HCR Potomac Fund GP, LLC,
its general partner

By: /s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

HCR MOLAG FUND, L.P.

By: HCR Molag Fund GP, LLC,
its general partner

By: /s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

INVESTOR REPRESENTATIVE:

HCR COLLATERAL MANAGEMENT, LLC

By:/s/ Clarke B. Futch
Name: Clarke B. Futch
Title: Chairman & Chief Executive Officer

DISCLOSURE SCHEDULES

of

RHYTHM PHARMACEUTICALS, INC.

pursuant to that certain

REVENUE INTEREST FINANCING AGREEMENT

dated as of June 16, 2022

by and among

RHYTHM PHARMACEUTICALS, INC.,

ENTITIES MANAGED BY HEALTHCARE ROYALTY MANAGEMENT, LLC

and

HCR COLLATERAL MANAGEMENT, LLC

The following schedules are delivered pursuant to that certain Revenue Interest Financing Agreement (the "Agreement"), dated as of June 16, 2022, by and among RHYTHM PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), the entities managed by HEALTHCARE ROYALTY MANAGEMENT, LLC, as listed on the signature pages thereto (the "Investors") and HCR COLLATERAL MANAGEMENT, LLC, a Delaware limited liability company (the "Investor Representative"), solely in its capacity as agent for, and representative of, the Investors. Nothing contained in these schedules is intended to broaden the scope of any representation or warranty contained in the Agreement or to create any covenant unless clearly and explicitly specified in the contrary herein.

Notwithstanding any materiality qualifications in any representations or warranties in the Agreement, for administrative ease, certain items have been included herein which are not considered by the Company to be material to its business, assets (including intangible assets), financial condition, prospects or results of operations. No reference to or disclosure of any item or other matter in these schedules shall be construed as an admission or indication that such item or other matter is material (nor shall it establish a standard of materiality for any purpose whatsoever) or that such item or other matter is required to be referred to or disclosed herein.

The information set forth in these schedules is disclosed solely for the purposes of the Agreement, and nothing in these schedules constitute an admission by any party hereto of any liability or obligation of the Company to any Third Party of any matter whatsoever, or an admission against the Company interests. The inclusion of any matters not required by the Agreement to be reflected in these schedule is set forth for informational purposes and does not necessarily include other matters of a similar informational nature. In disclosing the information in these schedules,

the Company expressly does not waive any attorney-client privilege associated with such information or any protection afforded by the work-product doctrine with respect to any of the matters disclosed or discussed herein.

The information contained in these schedules is in all respects subject to ARTICLE IX of the Agreement. These schedules and the information, descriptions and disclosures included herein are intended to qualify and limit the representations, warranties, and covenants of the Company contained in the Agreement. The headings used in these schedules are inserted for convenience only and shall not create a different standard for disclosure than the language set forth in the Agreement. Capitalized terms used herein but not otherwise defined herein shall have the meanings ascribed thereto in the Agreement.

SCHEDULE 1

[***]

SCH 1

SCHEDULE 1.1-1

[***]

SCHEDULE 1.1-2

[***]

SCHEDULE 1.1-3

[***]

SCHEDULE 1.1-4

[***]

SCHEDULE 3.2

[***]

SCHEDULE 4.6

[***]

SCHEDULE 4.8

[***]

SCHEDULE 4.10

[***]

SCH. 4.10

SCHEDULE 4.12(a)

[***]

SCH. 4.12(a)

SCHEDULE 4.14(c)

[***]

SCH. 4.14(c)

SCHEDULE 4.15

[***]

SCH. 4.15

SCHEDULE 4.20

[***]

SCH. 4.20

SCHEDULE 4.26(b)

[***]

SCH. 4.26(b)

SCHEDULE 6.2

[***]

SCH. 6.2

SCHEDULE 8.3(a)(vi)

[***]

SCH. 8.3(a)(vi)

EXHIBIT A

[***]

EXH. A

EXHIBIT B

[***]

EXH. B

EXHIBIT C

[***]

EXH. C

EXHIBIT D

[***]

EXH. D

Exhibit 31.1

CERTIFICATION

I, David P. Meeker, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Rhythm Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 3, 2022

/s/ David P. Meeker, M.D.
Name: David P. Meeker, M.D.
Title: President and Chief Executive Officer
(*Principal Executive Officer*)

Exhibit 31.2

CERTIFICATION

I, Hunter C. Smith, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Rhythm Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 3, 2022

/s/ Hunter C. Smith
Name: Hunter C. Smith
Title: Chief Financial Officer and Treasurer
(*Principal Financial Officer*)

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, David P. Meeker, M.D., certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge, the Quarterly Report on Form 10-Q of Rhythm Pharmaceuticals, Inc. for the fiscal quarter ended June 30, 2022 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, and the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of Rhythm Pharmaceuticals, Inc.

/s/ David P. Meeker, M.D.
Name: David P. Meeker, M.D.
Title: President and Chief Executive Officer
(*Principal Executive Officer*)

August 3, 2022

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Hunter C. Smith, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge, the Quarterly Report on Form 10-Q of Rhythm Pharmaceuticals, Inc. for the fiscal quarter ended June 30, 2022 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of Rhythm Pharmaceuticals Inc.

/s/ Hunter C. Smith
Name: Hunter C. Smith
Title: Chief Financial Officer and Treasurer
(*Principal Financial Officer*)

August 3, 2022