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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended June 30, 2024
OR

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

Commission File Number: 001-36014

AGIOS PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-0662915**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
88 Sidney Street, Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 649-8600
(Registrant's Telephone Number, Including Area Code)

(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, Par Value $0.001 per share	**AGIO**	**Nasdaq Global Select 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 ☒

Number of shares of the registrant's Common Stock, $0.001 par value, outstanding on July 26, 2024: 56,893,130

AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2024

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited)

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
(Unaudited)

(In thousands, except share and per share data)	June 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 84,518	$ 88,205
Marketable securities	485,374	688,723
Accounts receivable, net	3,762	2,810
Inventory	23,937	19,076
Prepaid expenses and other current assets	34,536	35,021
Total current assets	632,127	833,835
Marketable securities	75,404	29,435
Operating lease assets	48,750	54,409
Property and equipment, net	12,726	15,382
Other non-current assets	4,056	4,057
Total assets	$ 773,063	$ 937,118
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,035	$ 9,780
Accrued expenses	36,742	43,167
Operating lease liabilities	15,860	15,008
Total current liabilities	62,637	67,955
Operating lease liabilities, net of current portion	48,760	56,988
Other non-current liabilities	1,156	1,156
Total liabilities	112,553	126,099
Stockholders' equity:		
Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued or outstanding at June 30, 2024 and December 31, 2023	—	—
Common stock, $0.001 par value; 125,000,000 shares authorized; 73,091,490 shares issued and 56,875,079 shares outstanding at June 30, 2024, and 72,161,489 shares issued and 55,945,078 shares outstanding at December 31, 2023	73	72
Additional paid-in capital	2,464,284	2,436,523
Accumulated other comprehensive loss	(1,045)	(441)
Treasury stock, at cost (16,216,411 shares at June 30, 2024 and December 31, 2023)	(802,486)	(802,486)
Accumulated deficit	(1,000,316)	(822,649)
Total stockholders' equity	660,510	811,019
Total liabilities and stockholders' equity	$ 773,063	$ 937,118

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations
(Unaudited)

(In thousands, except share and per share data)	Three Months Ended June 30, 2024	Three Months Ended June 30, 2023	Six Months Ended June 30, 2024	Six Months Ended June 30, 2023
Revenues:				
Product revenue, net	$ 8,615	$ 6,712	$ 16,804	$ 12,321
Total revenue	8,615	6,712	16,804	12,321
Operating expenses:				
Cost of sales	$ 1,495	$ 1,108	$ 2,122	$ 1,662
Research and development	77,401	68,895	146,021	136,196
Selling, general and administrative	35,536	30,409	66,550	58,776
Total operating expenses	114,432	100,412	214,693	196,634
Loss from operations	(105,817)	(93,700)	(197,889)	(184,313)
Interest income, net	8,120	8,254	17,009	16,345
Other income, net	1,579	1,640	3,213	3,144
Net loss	$ (96,118)	$ (83,806)	$ (177,667)	$ (164,824)
Net loss per share - basic and diluted	$ (1.69)	$ (1.51)	$ (3.14)	$ (2.97)
Weighted-average number of common shares used in computing net loss per share – basic and diluted	56,802,546	55,604,330	56,593,011	55,435,796

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss
(Unaudited)

(In thousands)	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	**2023**	**2024**	**2023**
Net loss	$ (96,118)	$ (83,806)	$ (177,667)	$ (164,824)
Other comprehensive income (loss)				
Unrealized gain (loss) on available-for-sale securities	42	(459)	(604)	3,665
Comprehensive loss	$ (96,076)	$ (84,265)	$ (178,271)	$ (161,159)

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(Unaudited)

(in thousands, except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Treasury Stock Shares	Treasury Stock Amount	Total Stockholders' Equity
Balance at December 31, 2023	72,161,489	$ 72	$ 2,436,523	$ (441)	$ (822,649)	(16,216,411)	$ (802,486)	$ 811,019
Unrealized loss on available-for-sale securities	—	—	—	(646)	—	—	—	(646)
Common stock issued under stock incentive plan and ESPP	806,433	1	5,863	—	—	—	—	5,864
Stock-based compensation expense	—	—	9,234	—	—	—	—	9,234
Net loss	—	—	—	—	(81,549)	—	—	(81,549)
Balance at March 31, 2024	72,967,922	$ 73	$ 2,451,620	$ (1,087)	$ (904,198)	(16,216,411)	$ (802,486)	$ 743,922
Unrealized gain on available-for-sale securities	—	—	—	42	—	—	—	42
Common stock issued under stock incentive plan and ESPP	123,568	—	1,099	—	—	—	—	1,099
Stock-based compensation expense	—	—	11,565	—	—	—	—	11,565
Net loss	—	—	—	—	(96,118)	—	—	(96,118)
Balance at June 30, 2024	73,091,490	$ 73	$ 2,464,284	$ (1,045)	$ (1,000,316)	(16,216,411)	$ (802,486)	$ 660,510

(in thousands, except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Treasury Stock Shares	Treasury Stock Amount	Total Stockholders' Equity
Balance at December 31, 2022	71,256,118	$ 71	$ 2,386,325	$ (12,535)	$ (470,561)	(16,216,411)	$ (802,486)	$ 1,100,814
Unrealized gain on available-for-sale securities	—	—	—	4,124	—	—	—	4,124
Common stock issued under stock incentive plan and ESPP	501,660	1	2,466	—	—	—	—	2,467
Stock-based compensation expense	—	—	10,139	—	—	—	—	10,139
Net loss	—	—	—	—	(81,018)	—	—	(81,018)
Balance at March 31, 2023	71,757,778	$ 72	$ 2,398,930	$ (8,411)	$ (551,579)	(16,216,411)	$ (802,486)	$ 1,036,526
Unrealized loss on available-for-sale securities	—	—	—	(459)	—	—	—	(459)
Common stock issued under stock incentive plan and ESPP	193,408	—	238	—	—	—	—	238
Stock-based compensation expense	—	—	11,737	—	—	—	—	11,737
Net loss	—	—	—	—	(83,806)	—	—	(83,806)
Balance at June 30, 2023	71,951,186	$ 72	$ 2,410,905	$ (8,870)	$ (635,385)	(16,216,411)	$ (802,486)	$ 964,236

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows
(Unaudited)

(In thousands)	Six Months Ended June 30, 2024	2023
Operating activities		
Net loss	$ (177,667)	$ (164,824)
Adjustments to reconcile net loss from operations to net cash used in operating activities:		
Depreciation and amortization	2,941	3,597
Stock-based compensation expense	20,799	21,876
Net accretion of discount on marketable securities	(5,136)	(5,738)
Gain on disposal of property and equipment	(39)	(150)
Non-cash operating lease expense	5,659	5,263
Realized gain on investments	(153)	—
Changes in operating assets and liabilities:		
Accounts receivable, net	(952)	(45)
Inventory	(4,861)	(7,179)
Prepaid expenses and other current and non-current assets	486	2,103
Accounts payable	268	(6,837)
Accrued expenses and other current liabilities	(6,425)	(1,161)
Operating lease liabilities	(7,376)	(6,713)
Other non-current liabilities	—	(2,123)
Net cash used in operating activities	(172,456)	(161,931)
Investing activities		
Purchases of marketable securities	(348,604)	(232,486)
Proceeds from maturities and sales of marketable securities	510,669	337,453
Purchases of property and equipment	(299)	(396)
Proceeds from sale of equipment	40	150
Net cash provided by investing activities	161,806	104,721
Financing activities		
Net proceeds from stock option exercises and employee stock purchase plan	6,963	2,704
Net cash provided by financing activities	6,963	2,704
Net change in cash and cash equivalents	(3,687)	(54,506)
Cash and cash equivalents at beginning of the period	88,205	139,259
Cash and cash equivalents at end of the period	$ 84,518	$ 84,753
Supplemental disclosure of non-cash investing and financing transactions		
Additions to property and equipment in accounts payable and accrued expenses	$ 42	$ 6
Net cash taxes (returned) paid	$ (603)	$ 801

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Overview and Basis of Presentation

References to Agios

Throughout this Quarterly Report on Form 10-Q, "Agios," "the company," "we," "us," and "our," and similar expressions, except where the context requires otherwise, refer to Agios Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our Board of Directors" refers to the board of directors of Agios Pharmaceuticals, Inc.

Overview

We are a biopharmaceutical company committed to transforming patients' lives through leadership in the field of cellular metabolism, with the goal of creating differentiated medicines for rare diseases, with a focus on classical hematology. With a history of focused study on cellular metabolism, we have a deep and mature understanding of this biology, which is involved in the healthy functioning of nearly every system in the body. Building on this expertise, these learnings can be rapidly applied to our clinical trials with the goal of developing medicines that can have a significant impact for patients. We accelerate the impact of our portfolio by cultivating connections with patient communities, healthcare professionals, partners and colleagues to discover, develop and deliver potential therapies for rare diseases. We are located in Cambridge, Massachusetts.

The lead product candidate in our portfolio, PYRUKYND® (mitapivat), is an activator of both wild-type and mutant pyruvate kinase, or PK, enzymes for the potential treatment of hemolytic anemias. In February 2022, the U.S. Food and Drug Administration, or FDA, approved PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States. In November 2022, we received marketing authorization from the European Commission for PYRUKYND® for the treatment of PK deficiency in adult patients in the European Union, or EU. In December 2022, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In addition, we are currently evaluating PYRUKYND® in clinical trials for the treatment of thalassemia, sickle cell disease, or SCD, and in pediatric patients with PK deficiency. We are also developing (i) AG-946 (tebapivat), a novel PK activator, for the potential treatment of lower-risk myelodysplastic syndrome, or LR MDS, and hemolytic anemias, and (ii) AG-181, our phenylalanine hydroxylase, or PAH, stabilizer for the potential treatment of phenylketonuria, or PKU.

In addition to the aforementioned development programs, in July 2023 we entered into a license agreement with Alnylam Pharmaceuticals, Inc., or Alnylam, for the development and commercialization of products containing or comprised of an siRNA preclinical development candidate discovered by Alnylam and targeting the transmembrane serine protease 6, or TMPRSS6, gene, and we have begun preclinical development of a product candidate for the potential disease-modifying treatment of patients with polycythemia vera, or PV, a rare blood disorder.

We are subject to risks common to companies in our industry including, but not limited to, uncertainties relating to conducting preclinical and clinical research and development, the manufacture and supply of products for clinical and commercial use, obtaining and maintaining regulatory approvals and pricing and reimbursement for our products, market acceptance, managing global growth and operating expenses, availability of additional capital, competition, obtaining and enforcing patents, stock price volatility, dependence on collaborative relationships and third-party service providers, dependence on key personnel, potential litigation, potential product liability claims and potential government investigations.

Alnylam License Agreement

On July 28, 2023, we entered into a license agreement with Alnylam under which we acquired the rights to develop and commercialize Alnylam's novel preclinical siRNA targeting the TMPRSS6 gene, as a potential disease-modifying treatment for patients with PV. Because the acquired assets do not meet the definition of a business in accordance with Accounting Standards Codification, or ASC, 805, *Business Combinations*, we accounted for the agreement as an asset acquisition.

In accordance with the license agreement, in the twelve months ended December 31, 2023, we made an up-front payment to Alnylam and recognized in-process research and development of $17.5 million. We will also pay Alnylam for certain expenses associated with the development of the TMPRSS6 program, and these will be recorded in our Consolidated Statements of Operations as incurred. Additionally, we are responsible to pay up to $130.0 million in potential development and regulatory milestones, in addition to sales milestones as well as tiered royalties on annual net sales, if any, of licensed products, which may be subject to specified reductions and offsets.

Sale of Oncology Business to Servier and Sale of Contingent Payments and Royalty Rights

On March 31, 2021, we completed the sale of our oncology business to Servier Pharmaceuticals, LLC, or Servier, which represented a discontinued operation. The transaction included the sale of our oncology business, including TIBSOVO®, our clinical-stage product candidates vorasidenib, AG-270 and AG-636, and our oncology research programs for a payment of approximately $1.8 billion in cash at the closing, subject to certain adjustments, and a payment of $200.0 million in cash, if, prior to January 1, 2027, vorasidenib is granted new drug application, or NDA, approval from the FDA with an approved label that permits vorasidenib's use as a single agent for the adjuvant treatment of patients with Grade 2 glioma that have an isocitrate dehydrogenase, or IDH, 1 or 2 mutation (and, to the extent required by such approval, the vorasidenib companion diagnostic test is granted an FDA premarket approval), or the Vorasidenib Milestone Payment, as well as a royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through loss of exclusivity, and a royalty of 15% of U.S. net sales of vorasidenib from the first commercial sale of vorasidenib through loss of exclusivity, or the Vorasidenib Royalty Rights. The Vorasidenib Milestone Payment, Vorasidenib Royalty Rights and royalty payments related to TIBSOVO® are referred to as contingent payments and recognized as income when realizable. Servier also acquired our co-commercialization rights for Bristol Myers Squibb's IDHIFA® and the right to receive a $25.0 million potential milestone payment under our prior collaboration agreement with Celgene Corporation, or Celgene, and following the sale Servier will conduct certain clinical development activities within the IDHIFA® development program.

In October 2022, we sold our rights to future contingent payments associated with the royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through the loss of exclusivity to entities affiliated with Sagard Healthcare Partners, or Sagard, and recognized income of $127.9 million within the gain on sale of contingent payments line item in our Consolidated Statements of Operations for the year ended December 31, 2022.

In February 2024, Servier announced that it received filing acceptance and priority review from the FDA for its NDA for vorasidenib for the treatment of certain IDH-mutant diffuse glioma and accelerated assessment from the European Medicines Agency, or EMA, for its Marketing Authorization Application, or MAA, for vorasidenib. The FDA assigned the NDA a Prescription Drug User Fee Act, or PDUFA, action date of August 20, 2024, and Servier anticipates that the European Commission will approve its MAA in the second half of 2024.

In May 2024, we entered into a purchase and sale agreement to sell the Vorasidenib Royalty Rights to Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, for $905.0 million in cash, which sale is contingent upon NDA approval of vorasidenib by the FDA on or before October 31, 2024, and other customary closing conditions. Upon consummation of the sale, Royalty Pharma will acquire 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in net sales for each calendar year. In addition, any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the rights to a 3% earn-out on those excess payments, or the Retained Earn-Out Rights. We retain our rights to the potential Vorasidenib Milestone Payment.

Basis of Presentation

The condensed consolidated balance sheet as of June 30, 2024, the condensed consolidated statements of operations, comprehensive loss and stockholders' equity for the three and six months ended June 30, 2024 and 2023, and the condensed consolidated statements of cash flows for the six months ended June 30, 2024 and 2023 are unaudited. The unaudited condensed consolidated financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of our management, reflect all adjustments, which include only normal recurring adjustments, necessary to fairly state our financial position as of June 30, 2024, our results of operations and stockholders' equity for the three and six months ended June 30, 2024 and 2023, and cash flows for the six months ended June 30, 2024 and 2023. The financial data and the other financial information disclosed in these notes to the condensed consolidated financial statements related to the three and six-month periods are also unaudited. The results of operations for the three and six months ended June 30, 2024 are not necessarily indicative of the results to be expected for the year ending December 31, 2024 or for any other future annual or interim period. The condensed consolidated balance sheet data as of December 31, 2023 was derived from our audited financial statements, but does not include all disclosures required by U.S. generally accepted accounting principles, or U.S. GAAP. The condensed consolidated interim financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2023 that was filed with the Securities and Exchange Commission, or SEC, on February 15, 2024.

Our condensed consolidated financial statements include our accounts and the accounts of our wholly owned subsidiaries. All intercompany transactions have been eliminated in consolidation. The condensed consolidated financial statements have been prepared in conformity with U.S. GAAP.

Use of Estimates

The preparation of our condensed consolidated financial statements requires us to make estimates, judgments and assumptions that may affect the reported amounts of assets, liabilities, equity, revenues and expenses and related disclosure of contingent assets and liabilities. On an ongoing basis we evaluate our estimates, judgments and methodologies. We base our estimates on historical experience and on various other assumptions that we believe are reasonable, the results of which form the basis for making judgments about the carrying values of assets, liabilities and equity and the amount of revenues and expenses. The full extent to which pandemics or public health emergencies, may in the future directly or indirectly impact our business, results of operations and financial condition, including expenses, reserves and allowances, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain.

Liquidity

As of June 30, 2024, we had cash, cash equivalents and marketable securities of $645.3 million. Although we have incurred recurring losses and expect to continue to incur losses for the foreseeable future, we expect our cash, cash equivalents and marketable securities to be sufficient to fund current operations for at least the next twelve months from the issuance of the financial statements. If we are unable to raise additional funds through equity or debt financings, we may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

2. Summary of Significant Accounting Policies

There have been no material changes to the significant accounting policies previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2023.

Recent Accounting Pronouncements

Accounting standards that have been issued by the Financial Accounting Standards Board or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our financial statements upon adoption.

3. Fair Value Measurements

We record cash equivalents and marketable securities at fair value. ASC 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and our own assumptions (unobservable inputs). The hierarchy consists of three levels:

Level 1 – Unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2 – Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, directly or indirectly, for substantially the full term of the asset or liability.

Level 3 – Unobservable inputs that reflect our own assumptions about the assumptions market participants would use in pricing the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

The following table summarizes our cash equivalents and marketable securities measured at fair value and by level on a recurring basis as of June 30, 2024:

(In thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 16,203	$ 29,474	$ —	$ 45,677
Total cash equivalents	16,203	29,474	—	45,677
Marketable securities:				
Certificates of deposit	$ —	$ 11,878	$ —	$ 11,878
U.S. Treasuries	—	102,260	—	102,260
Government securities	—	150,793	—	150,793
Corporate debt securities	—	295,847	—	295,847
Total marketable securities	—	560,778	—	560,778
Total cash equivalents and marketable securities	$ 16,203	$ 590,252	$ —	$ 606,455

Cash equivalents and marketable securities have been initially valued at the transaction price and are subsequently valued, at the end of each reporting period, utilizing third-party pricing services or other observable market data. The pricing services utilize industry standard valuation models, including both income and market-based approaches, and observable market inputs to

determine value. After completing our validation procedures, we did not adjust or override any fair value measurements provided by the pricing services as of June 30, 2024.

There have been no changes to the valuation methods during the six months ended June 30, 2024, and we had no financial assets or liabilities that were classified as Level 3 at any point during the six months ended June 30, 2024.

4. Marketable Securities

Our marketable securities are classified as available-for-sale pursuant to ASC 320, *Investments – Debt and Equity Securities*, and are recorded at fair value. Unrealized gains and losses are included as a component of accumulated other comprehensive loss in the condensed consolidated balance sheets and statements of stockholders' equity, and a component of total comprehensive loss in the condensed consolidated statements of comprehensive loss, until realized. Unrealized losses are evaluated for impairment under ASC 326, *Financial Instruments - Credit Losses*, to determine if the impairment is credit-related or noncredit-related. Credit-related impairment is recognized as an allowance on the condensed consolidated balance sheets with a corresponding adjustment to earnings, and noncredit-related impairment is recognized in other comprehensive income, net of taxes. Realized gains and losses are included in investment income on a specific-identification basis. There were no material realized gains or losses on marketable securities for the three and six months ended June 30, 2024 or 2023.

Marketable securities at June 30, 2024 consisted of the following:

(In thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 11,885	$ —	$ (7)	$ 11,878
U.S. Treasuries	77,271	—	(93)	77,178
Government securities	147,335	—	(311)	147,024
Corporate debt securities	249,719	1	(426)	249,294
Total Current	486,210	1	(837)	485,374
Non-current:				
U.S. Treasuries	25,132	8	(58)	25,082
Government securities	3,800	—	(31)	3,769
Corporate debt securities	46,681	5	(133)	46,553
Total Non-current	75,613	13	(222)	75,404
Total marketable securities	$ 561,823	$ 14	$ (1,059)	$ 560,778

Marketable securities at December 31, 2023 consisted of the following:

(In thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
U.S. Treasuries	$ 30,876	$ —	$ (56)	$ 30,820
Government securities	247,460	194	(695)	246,959
Corporate debt securities	411,045	874	(975)	410,944
Total Current	689,381	1,068	(1,726)	688,723
Non-current:				
U.S. Treasuries	4,802	30	—	4,832
Government securities	9,986	75	—	10,061
Corporate debt securities	14,430	112	—	14,542
Total Non-current	29,218	217	—	29,435
Total marketable securities	$ 718,599	$ 1,285	$ (1,726)	$ 718,158

As of June 30, 2024 and December 31, 2023, we held both current and non-current investments. Investments classified as current have maturities of less than one year. Investments classified as non-current are those that: (i) have a maturity of greater

than one year, and (ii) we do not intend to liquidate within the next twelve months, although these funds are available for use and, therefore, are classified as available-for-sale.

As of June 30, 2024 and December 31, 2023, we held 194 and 151 debt securities, respectively, that were in an unrealized loss position for less than one year. We did not record an allowance for credit losses as of June 30, 2024 and December 31, 2023 related to these securities. The aggregate fair value of debt securities in an unrealized loss position at June 30, 2024 and December 31, 2023 was $538.0 million and $513.5 million, respectively. There were no individual securities that were in a significant unrealized loss position as of June 30, 2024 and December 31, 2023. We regularly review the securities in an unrealized loss position and evaluate the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. We do not consider these marketable securities to be impaired as of June 30, 2024 and December 31, 2023.

5. Inventory

Inventory, which consists of commercial supply of PYRUKYND®, consisted of the following:

(In thousands)	June 30, 2024	December 31, 2023
Raw materials	$ 90	$ 51
Work-in-process	21,691	17,568
Finished goods	2,156	1,457
Total inventory	$ 23,937	$ 19,076

6. Leases

Our building leases are comprised of office and laboratory space under non-cancelable operating leases. These lease agreements have remaining lease terms of approximately four years and contain various clauses for renewal at our option. The renewal options were not included in the calculation of the operating lease assets and the operating lease liabilities as the renewal options are not reasonably certain of being exercised. The lease agreements do not contain residual value guarantees.

The components of lease expense and other information related to leases were as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Operating lease costs	$ 3,806	$ 3,806	$ 7,613	$ 7,613
Cash paid for amounts included in the measurement of operating lease liabilities	4,678	4,544	$ 9,331	$ 9,064

We have not entered into any material short-term leases or financing leases as of June 30, 2024.

In arriving at the operating lease liabilities as of June 30, 2024 and December 31, 2023, we applied the weighted-average incremental borrowing rate of 5.7% for both periods over a weighted-average remaining lease term of 3.7 and 4.2 years, respectively.

As of June 30, 2024, undiscounted minimum rental commitments under non-cancelable leases were as follows:

(In thousands)	
Remaining 2024	$ 7,810
2025	19,507
2026	20,151
2027	20,755
2028	3,479
Undiscounted minimum rental commitments	$ 71,702
Interest	(7,082)
Operating lease liabilities	$ 64,620

We provided our landlord a security deposit of $2.9 million as security for our leases, which is included within other non-current assets on our condensed consolidated balance sheet.

In August 2021, we entered into a long-term sublease agreement for 13,000 square feet of the office space at 38 Sidney Street, Cambridge, Massachusetts, with the term of the lease running through December 2024. In April 2022, we entered into a long-term sublease agreement for 27,000 square feet of the office space at 64 Sidney Street, Cambridge, Massachusetts, with the term of the lease running through April 2025. In May 2023, we entered into a long-term sublease agreement for 7,407 square feet of office space on the first floor of 64 Sidney Street, Cambridge, Massachusetts, with the term of the lease running through April 2025. We recorded operating sublease income of $1.6 million and $1.4 million for the three months ended June 30, 2024 and 2023, respectively, and $3.2 million and $2.8 million for the six months ended June 30, 2024 and 2023, respectively, in other income, net in the condensed consolidated statements of operations. We hold security deposits from our sublessees of approximately $1.2 million which is recorded within other non-current assets on our condensed consolidated balance sheet.

As of June 30, 2024, the future minimum lease payments to be received under the long-term sublease agreements were as follows:

(In thousands)	
Remaining 2024	$ 2,565
2025	1,310
Total	$ 3,875

7. Accrued Expenses

Accrued expenses consisted of the following:

(In thousands)	June 30, 2024	December 31, 2023
Accrued compensation	$ 11,965	$ 23,232
Accrued research and development costs	19,265	15,463
Accrued professional fees	3,439	3,115
Accrued other	2,073	1,357
Total accrued expenses	$ 36,742	$ 43,167

8. Product Revenue

We sell PYRUKYND®, our wholly owned product, to a limited number of specialty distributors and specialty pharmacy providers, or collectively, the Customers. These Customers subsequently resell PYRUKYND® to pharmacies or dispense PYRUKYND® directly to patients. In addition to distribution agreements with Customers, we enter into arrangements with healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of PYRUKYND®.

The performance obligation related to the sale of PYRUKYND® is satisfied and revenue is recognized when the Customer obtains control of the product, which occurs at a point in time, typically upon delivery to the Customer.

Product revenue, net, were as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Product revenue, net	$ 8,615	$ 6,712	$ 16,804	$ 12,321

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price, or transaction price, which includes estimates of variable consideration for which reserves are established and result from contractual adjustments, government rebates, returns and other allowances that are offered within the contracts with our Customers, healthcare providers, payors and other indirect customers relating to the sale of our products.

Contractual Adjustments

We generally provide Customers with discounts, including prompt pay discounts, and allowances that are explicitly stated in the contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we receive sales order management, data and distribution services from certain Customers.

Chargebacks and discounts represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are estimated using the expected value method, based upon a range of possible outcomes that are probability-weighted for the estimated channel mix and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

Government Rebates

Government rebates include Medicare, TriCare, and Medicaid rebates, which we estimate using the expected value method, based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue. 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.

Returns / Replacement

We estimate the amount of product sales that may be returned by Customers or replaced by Agios and record this estimate as a reduction of revenue in the period the related product revenue is recognized. We currently estimate product return and replacement liabilities using the expected value method, based on available industry data, including our visibility into the inventory remaining in the distribution channel.

The following table summarizes balances and activity in each of the product revenue allowance and reserve categories for the six months ended June 30, 2024:

(In thousands)	Contractual Adjustments	Government Rebates	Returns/ Replacement	Total
Balance at December 31, 2023	$ 156	$ 1,084	$ 232	$ 1,472
Current provisions relating to sales in the current year	772	1,245	189	2,206
Adjustments relating to prior years	(39)	(49)	40	(48)
Payments/returns relating to sales in the current year	(632)	(306)	—	(938)
Payments/returns relating to sales in the prior years	(85)	(371)	(71)	(527)
Balance at June 30, 2024	$ 172	$ 1,603	$ 390	$ 2,165

Total revenue-related reserves above, included in our condensed consolidated balance sheets, are summarized as follows:

(In thousands)	June 30, 2024	December 31, 2023
Reduction of accounts receivable	$ 102	$ 151
Component of accrued expenses	2,063	1,321
Total revenue-related reserves	$ 2,165	$ 1,472

The following table presents changes in our contract assets during the six months ended June 30, 2024:

(In thousands)	December 31, 2023	Additions	Deductions	June 30, 2024
Contract assets[1]				
Accounts receivable, net	$ 2,810	$ 18,940	$ (17,988)	$ 3,762

(1) Additions to contract assets relate to amounts billed to Customers for product sales and deductions to contract assets primarily relate to collection of receivables during the reporting period.

9. Share-Based Payments

2023 Stock Incentive Plan and Inducement Grants

In June 2023, our stockholders approved the 2023 Stock Incentive Plan, or the 2023 Plan. The 2023 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, or RSUs, performance-based share units, or PSUs, and other stock-based awards to employees, advisors, consultants and non-employee directors.

Following the adoption of the 2023 Plan, we ceased granting equity awards under the 2013 Stock Incentive Plan, or the 2013 Plan. Any outstanding equity awards that were previously granted under the 2013 Plan continue to be governed by their terms. Following adoption of the 2013 Plan, we ceased granting equity awards under the 2007 Stock Incentive Plan, or the 2007 Plan. There are no outstanding equity awards under the 2007 Plan.

In connection with the start of employment of our Chief Executive Officer and Chief Financial Officer in 2022, and our Chief Commercial Officer in 2023, our board of directors granted each of them equity awards in the form of stock options, RSUs and PSUs, which awards were made outside our equity incentive plans as inducements material to their respective entry into employment with us in accordance with Nasdaq Listing Rule 5635(c)(4).

As of June 30, 2024, the maximum number of shares reserved under the 2013 Plan, the 2023 Plan and the inducement grants described above was 11,127,064, and we had 2,896,048 shares available for future issuance under the 2023 Plan.

Stock options

The following table presents stock option activity for the six months ended June 30, 2024:

	Number of Stock Options		Weighted-Average Exercise Price
Outstanding at December 31, 2023	5,263,681	$	44.94
Granted	960,488		33.39
Exercised	(184,331)		30.96
Cancelled/Forfeited	(21,063)		41.52
Expired	(22,750)		34.41
Outstanding at June 30, 2024	5,996,025	$	43.57
Exercisable at June 30, 2024	3,727,328	$	51.07
Vested and expected to vest at June 30, 2024	5,996,025	$	43.57

At June 30, 2024, there was approximately $36.8 million of total unrecognized compensation expense related to unvested stock option awards, which we expect to recognize over a weighted-average period of approximately 2.61 years.

Restricted stock units

The following table presents RSU activity for the six months ended June 30, 2024:

	Number of Stock Units		Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	1,346,701	$	29.67
Granted	1,054,565		31.23
Vested	(522,606)		33.04
Forfeited	(18,252)		29.17
Unvested shares at June 30, 2024	1,860,408	$	29.62

As of June 30, 2024, there was approximately $43.8 million of total unrecognized compensation expense related to RSUs, which we expect to recognize over a weighted-average period of approximately 2.14 years.

Performance-based stock units

The following table presents PSU activity for the six months ended June 30, 2024:

	Number of Stock Units		Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	362,133	$	30.66
Granted	183,000		32.27
Vested	(170,550)		35.04
Unvested shares at June 30, 2024	374,583	$	29.45

Stock-based compensation expense associated with these PSUs is recognized if the underlying performance condition is considered probable of achievement using our management's best estimates.

As of June 30, 2024, there was no unrecognized compensation expense related to PSUs with performance-based vesting criteria that are considered probable of achievement, and $11.0 million of total unrecognized compensation expense related to PSUs with performance-based vesting criteria that are considered not probable of achievement.

Market-based stock units

The following table presents market-based stock unit, or MSU, activity for the six months ended June 30, 2024:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2023	42,695	$ 41.50
Expired	(42,695)	41.50
Unvested shares at June 30, 2024	—	$ —

The fair value of MSUs are estimated using a Monte Carlo simulation model. Assumptions and estimates utilized in the model include the risk-free interest rate, dividend yield, expected stock volatility and the estimated period to achievement of the market condition. As of June 30, 2024, there was no remaining unrecognized compensation expense related to MSUs.

2013 Employee Stock Purchase Plan

In June 2013, our Board of Directors adopted, and in July 2013 our stockholders approved, the 2013 Employee Stock Purchase Plan, or the 2013 ESPP. We issued and sold 52,514 and 54,867 shares of common stock during the six months ended June 30, 2024 and 2023, respectively, under the 2013 ESPP. The 2013 ESPP provides participating employees with the opportunity to purchase up to an aggregate of 2,363,636 shares of our common stock. As of June 30, 2024, we had 1,633,525 shares of common stock available for future issuance under the 2013 ESPP.

Stock-based compensation expense

Stock-based compensation expense by award type included within the condensed consolidated statements of operations is as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Stock options	$ 4,361	$ 3,937	$ 8,432	$ 8,894
Restricted stock units	6,211	4,754	11,177	9,701
Performance-based stock units	750	2,784	750	2,784
Employee stock purchase plan	243	262	440	497
Total stock-based compensation expense	$ 11,565	$ 11,737	$ 20,799	$ 21,876

Expenses related to stock options and stock-based awards were allocated as follows in the condensed consolidated statements of operations:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Research and development expense	$ 4,460	$ 4,540	$ 8,235	$ 8,895
Selling, general and administrative expense	7,105	7,197	12,564	12,981
Total stock-based compensation expense	$ 11,565	$ 11,737	$ 20,799	$ 21,876

10. Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting the weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury stock method. For purposes of the dilutive net loss per share calculation, stock options, RSUs, PSUs and MSUs for which the performance and market vesting conditions, respectively, have been deemed probable, and 2013 ESPP shares are considered to be common stock equivalents, while PSUs and MSUs with performance and market vesting conditions, respectively, that were not deemed probable as of June 30, 2024 are not considered to be common stock equivalents.

We utilize the control number concept in the computation of diluted earnings per share to determine whether potential common stock equivalents are dilutive. The control number used is net loss from continuing operations. The control number concept requires that the same number of potentially dilutive securities applied in computing diluted earnings per share from continuing operations be applied to all other categories of income or loss, regardless of their anti-dilutive effect on such categories. Since we had a net loss for all periods presented, no dilutive effect has been recognized in the calculation of loss per share. Basic and diluted net loss per share was the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Three and Six Months Ended June 30,	
	2024	2023
Stock options	5,996,025	5,789,272
Restricted stock units	1,860,408	1,415,219
Employee stock purchase plan shares	39,381	50,942
Total common stock equivalents	7,895,814	7,255,433

11. Subsequent Events

In July 2024, we entered into a distribution agreement with NewBridge Pharmaceuticals FZ-LLC, or NewBridge, pursuant to which we granted NewBridge the right to commercialize PYRUKYND® in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates. We do not expect this agreement to have a material impact on our business, financial condition or results of operations for the fiscal year ending December 31, 2024.

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

Forward-looking Information

The following discussion of our financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements as of June 30, 2024 and for the three and six months ended June 30, 2024 and 2023, and related notes included in Part I, Item 1 of this Quarterly Report on Form 10-Q, as well as the audited consolidated financial statements and notes and Management's Discussion and Analysis of Financial Condition and Results of Operations, included in our Annual Report on Form 10-K for the year ended December 31, 2023 filed with the SEC on February 15, 2024. This Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on current expectations, estimates, forecasts and projections, and the beliefs and assumptions of our management, and include, without limitation, statements with respect to our expectations regarding our research, development and commercialization plans and prospects, results of operations, selling, general and administrative expenses, research and development expenses, and the sufficiency of our cash for future operations. Words such as "aim," "anticipate," "believe," "continue," "could," "estimate," "expect," "goal," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "strategy," "target," "vision," "will," "would" or the negatives of these words and similar expressions are intended to identify these forward-looking statements, although not all forward-looking statements contain these identifying words. Readers are cautioned that these forward-looking statements are predictions and are subject to risks, uncertainties and assumptions that are difficult to predict. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Among the important factors that could cause actual results to differ materially from those indicated by our forward-looking statements are those discussed under the heading "Risk Factors" in Part II, Item 1A and elsewhere in this report, and in our Annual Report on Form 10-K for the year ended December 31, 2023. We undertake no obligation to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events, except as required by law.

Overview

We are a biopharmaceutical company committed to transforming patients' lives through leadership in the field of cellular metabolism, with the goal of creating differentiated medicines for rare diseases, with a focus on classical hematology. With a history of focused study on cellular metabolism, we have a deep and mature understanding of this biology, which is involved in the healthy functioning of nearly every system in the body. Building on this expertise, these learnings can be rapidly applied to our clinical trials with the goal of developing medicines that can have a significant impact for patients. We accelerate the impact of our portfolio by cultivating connections with patient communities, healthcare professionals, partners and colleagues to discover, develop and deliver potential therapies for rare diseases.

The lead product candidate in our portfolio, PYRUKYND® (mitapivat), is an activator of both wild-type and mutant pyruvate kinase, or PK, enzymes for the potential treatment of hemolytic anemias. In February 2022, the U.S. Food and Drug Administration, or FDA, approved PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States. In November 2022, we received marketing authorization from the European Commission for PYRUKYND® for the treatment of PK deficiency in adult patients in the European Union, or EU. In December 2022, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In addition, we are currently evaluating PYRUKYND® in clinical trials for the treatment of thalassemia, sickle cell disease, or SCD, and in pediatric patients with PK deficiency. We are also developing (i) AG-946 (tebapivat), a novel PK activator, for the potential treatment of lower-risk myelodysplastic syndrome, or LR MDS, and hemolytic anemias, and (ii) AG-181, our phenylalanine hydroxylase, or PAH, stabilizer for the potential treatment of phenylketonuria, or PKU.

In addition to the aforementioned development programs, in July 2023 we entered into a license agreement with Alnylam Pharmaceuticals, Inc., or Alnylam, for the development and commercialization of products containing or comprised of an siRNA preclinical development candidate discovered by Alnylam and targeting the transmembrane serine protease 6, or TMPRSS6, gene, and we have begun preclinical development of a product candidate for the potential disease-modifying treatment of patients with polycythemia vera, or PV, a rare blood disorder.

Alnylam License Agreement

In accordance with the license agreement with Alnylam, in the year ended December 31, 2023, we made an up-front payment to Alnylam and recognized in-process research and development of $17.5 million. We will also pay Alnylam for certain expenses associated with the development of the TMPRSS6 program, and these will be recorded in our Consolidated Statements of Operations as incurred. Additionally, we are responsible to pay up to $130.0 million in potential development and regulatory milestones, in addition to sales milestones as well as tiered royalties on annual net sales, if any, of licensed products, which may

be subject to specified reductions and offsets. Because the acquired assets under the license agreement with Alnylam do not meet the definition of a business in accordance with ASC 805, *Business Combinations*, we accounted for the agreement as an asset acquisition.

Sale of Oncology Business to Servier and Sale of Contingent Payments and Royalty Rights

On March 31, 2021, we completed the sale of our oncology business to Servier Pharmaceuticals, LLC, or Servier, which represented a discontinued operation. The transaction included the sale of our oncology business, including TIBSOVO®, our clinical-stage product candidates vorasidenib, AG-270 and AG-636, and our oncology research programs for a payment of approximately $1.8 billion in cash at the closing, subject to certain adjustments, and a payment of $200.0 million in cash, if, prior to January 1, 2027, vorasidenib is granted new drug application, or NDA, approval from the FDA with an approved label that permits vorasidenib's use as a single agent for the adjuvant treatment of patients with Grade 2 glioma that have an isocitrate dehydrogenase, or IDH, 1 or 2 mutation (and, to the extent required by such approval, the vorasidenib companion diagnostic test is granted an FDA premarket approval), or the Vorasidenib Milestone Payment, as well as a royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through loss of exclusivity, and a royalty of 15% of U.S. net sales of vorasidenib from the first commercial sale of vorasidenib through loss of exclusivity, or the Vorasidenib Royalty Rights, with these royalties referred to as contingent payments and recognized as income when realizable. Servier also acquired our co-commercialization rights for Bristol Myers Squibb's IDHIFA® and the right to receive a $25.0 million potential milestone payment under our prior collaboration agreement with Celgene Corporation, or Celgene, and following the sale Servier will conduct certain clinical development activities within the IDHIFA® development program.

In October 2022, we sold our rights to future contingent payments associated with the royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through the loss of exclusivity to entities affiliated with Sagard Healthcare Partners, or Sagard, and recognized income of $127.9 million within the gain on sale of contingent payments line item in our consolidated statements of operations for the year ended December 31, 2022.

In February 2024, Servier announced that it received filing acceptance and priority review from the FDA for its NDA for vorasidenib for the treatment of certain IDH-mutant diffuse glioma and accelerated assessment from the European Medicines Agency, or EMA, for its Marketing Authorization Application, or MAA, for vorasidenib. The FDA assigned the NDA a Prescription Drug User Fee Act, or PDUFA, action date of August 20, 2024, and Servier anticipates that the European Commission will approve its MAA in the second half of 2024.

In May 2024, we entered into a purchase and sale agreement to sell the Vorasidenib Royalty Rights to Royalty Pharma Investments 2019 ICAV, or Royalty Pharma, for $905.0 million in cash, or the Upfront Payment, which sale is contingent upon NDA approval of vorasidenib by the FDA on or before October 31, 2024, and other customary closing conditions. Upon consummation of the sale, Royalty Pharma will acquire 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in net sales for each calendar year. In addition, any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the rights to a 3% earn-out on those excess payments, or the Retained Earn-Out Rights. We retain our rights to the potential Vorasidenib Milestone Payment.

Financial Operations Overview

General

Since inception, our operations have primarily focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in cellular metabolism and classical hematology, identifying potential product candidates, undertaking preclinical studies, conducting clinical trials, establishing a commercial infrastructure, preparing for and executing on the commercial launch of PYRUKYND® and, prior to the sale of our oncology business to Servier on March 31, 2021, marketing TIBSOVO® and IDHIFA®. Through March 31, 2021, we financed our operations primarily through proceeds from the sale of our royalty rights, commercial sales of TIBSOVO®, funding received from our collaboration agreements, private placements of our preferred stock, our initial public offering of our common stock and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings. Following the sale of our oncology business to Servier on March 31, 2021, we have financed and expect to continue to finance our operations primarily through cash on hand, royalty payments from Servier with respect to U.S. net sales of TIBSOVO® prior to the sale of these contingent payments to Sagard, proceeds from the sale of contingent payments to Sagard, a potential Upfront Payment from Royalty Pharma and a potential Vorasidenib Milestone Payment from Servier, both of which are contingent on if the NDA for vorasidenib is approved by the FDA, potential royalty payments with respect to the Retained Earn-Out Rights, the actual and potential future sales of PYRUKYND® and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings.

Additionally, since inception, we have historically incurred significant operating losses. Our net losses for the six months ended June 30, 2024 and 2023 were $177.7 million and $164.8 million, respectively. As of June 30, 2024, we had an accumulated deficit of $1.0 billion. We expect to incur significant expenses and net losses until such time we are able to report profitable results. Our net losses may fluctuate significantly from year to year. We expect that we will continue to incur significant expenses as we continue to advance and expand clinical development and commercialization activities for PYRUKYND®, including with respect to our anticipated regulatory submissions for the treatment of thalassemia; advance and expand clinical development of AG-946 (tebapivat); continue to advance AG-181, our PAH stabilizer; continue preclinical development of a licensed siRNA development candidate pursuant to our license agreement with Alnylam; expand and protect our intellectual property portfolio, including by in-licensing or acquiring assets for pipeline growth; and hire additional commercial and development personnel.

Revenues

Our wholly owned product, PYRUKYND®, received approval from the FDA on February 17, 2022, for the treatment of hemolytic anemia in adults with PK deficiency in the United States. Upon FDA approval of PYRUKYND® in the United States, we began generating product revenue from sales of PYRUKYND®. We sell PYRUKYND® to a limited number of specialty distributors and specialty pharmacy providers, or collectively, the Customers. These Customers subsequently resell PYRUKYND® to pharmacies or dispense PYRUKYND® directly to patients. In addition to distribution agreements with Customers, we enter into arrangements with healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of PYRUKYND®. In July 2024, we entered into a distribution agreement with NewBridge Pharmaceuticals FZ-LLC, or the NewBridge Agreement, pursuant to which we granted NewBridge the right to commercialize PYRUKYND® in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates. For further discussion of our revenue recognition policy, see Note 8, *Product Revenue*, to the condensed consolidated financial statements in this Quarterly Report on Form 10-Q.

In the future, we expect to continue to generate revenue from product sales, and we may potentially generate revenue from royalties on product sales, milestone payments, and upfront payments under existing arrangements or future collaborations or licensing agreements.

Cost of Sales

Cost of sales consists primarily of manufacturing costs for sales of PYRUKYND®. Based on our policy to expense costs associated with the manufacturing of our products prior to regulatory approval, certain of the manufacturing costs associated with product shipments of PYRUKYND® recorded during the three and six months ended June 30, 2024 and 2023 were expensed prior to February 17, 2022, and, therefore, are not included in costs of sales during the three and six months ended June 30, 2024 and 2023. The amounts excluded from cost of sales were not significant during the three and six months ended June 30, 2024 and 2023.

Inventories are reviewed periodically to identify excess or obsolete inventory based on projected sales activity as well as product shelf-life. Expired inventory is disposed of, and the related costs are recognized as cost of sales in our consolidated statements of operations, when, based on the expiry date, we do not believe we are able to sell the inventory. We have not reserved for excess or obsolete inventory during the three and six months ended June 30, 2024 and 2023.

Research and Development Expenses

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 related to our portfolio to increase as our product candidate development programs progress. However, the successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of and to commercialize these product candidates. We are unable to predict the amount of net cash inflows from PYRUKYND® or any of our product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- establishing an appropriate safety profile with an investigational new drug application, or IND, and/or NDA-enabling toxicology and clinical trials;
- successfully enrolling in, and completion of, clinical trials;
- receiving marketing approvals from applicable regulatory authorities;
- establishing compliant commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, in the United States or in other jurisdictions, whether alone or in collaboration with others, including pursuant to the NewBridge Agreement; and
- maintaining an acceptable safety profile of the products following approval.

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

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research and development and both preclinical and clinical activities on our behalf, and the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical and clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and the maintenance of facilities, insurance and other operating costs.

The following summarizes our most advanced programs:

PYRUKYND® (mitapivat): First-in-Class PK Activator

We are developing PYRUKYND® for the treatment of PK deficiency and other hemolytic anemias such as thalassemia and SCD. PYRUKYND® is an orally available small molecule and a potent activator of the wild-type and mutated PK enzymes.

In February 2022, the FDA approved PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States. In November 2022, we received marketing authorization from the European Commission for PYRUKYND® for the treatment of PK deficiency in adult patients in the EU. In December 2022, we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. In addition, we are currently evaluating PYRUKYND® in clinical trials for the treatment of thalassemia, SCD, and in pediatric patients with PK deficiency. We have worldwide development and commercial rights to PYRUKYND® and expect to fund the future development and commercialization costs related to this program. PYRUKYND® has been granted orphan drug designation for the treatment of PK deficiency by the FDA and the EMA. Additionally, PYRUKYND® has received orphan drug designation from the FDA for the treatment of thalassemia and SCD, and breakthrough medicine designation by the Saudi Food and Drug Authority for the treatment of thalassemia.

We have built our commercial infrastructure to support the commercial launch of PYRUKYND® in adult PK deficiency in the United States. In connection with our regulatory approvals in the EU and Great Britain, we are currently providing access to PYRUKYND® on a free of charge basis for eligible patients in those jurisdictions through a global managed access program. We provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions upon request through the global managed access program, on either a free of charge or for charge basis. Our global managed access program has not had a significant impact on our business, financial condition or results of operations. Beyond the global managed access program, we continue to evaluate options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities, such as the NewBridge Agreement which we entered into in July 2024.

We are evaluating PYRUKYND® in numerous clinical trials, including the following:

- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from ENERGIZE, our completed phase 3, double-blind, randomized, placebo-controlled multicenter study pivotal trial of PYRUKYND® in adults with non-transfusion-dependent alpha- or beta-thalassemia. We announced topline data for ENERGIZE in January 2024 and a more detailed analysis of the data in June 2024. A total of 194 patients were enrolled

in the study, with 130 randomized to PYRUKYND® 100 mg twice-daily, and 64 randomized to matched placebo. 122 patients (93.8%) in the PYRUKYND® arm and 62 patients (96.9%) in the placebo arm completed the 24-week double-blind period of the study. The study met the primary endpoint of hemoglobin response, where treatment with PYRUKYND® demonstrated a statistically significant increase in hemoglobin response compared to placebo, as 42.3% of patients in the PYRUKYND® arm achieved a hemoglobin response, compared to 1.6% of patients in the placebo arm (2-sided p<0.0001). Treatment with PYRUKYND® also demonstrated statistically significant improvements compared to placebo for both key secondary endpoints: (i) change from baseline in average Functional Assessment of Chronic Illness Therapy-Fatigue, or FACIT-Fatigue, subscale score from week 12 to week 24 and (ii) change from baseline in average hemoglobin concentration from week 12 to week 24. During the 24-week double-blind period, four (3.1%) subjects in the PYRUKYND® arm experienced adverse events, or AEs, leading to discontinuation, and there were no AEs in the placebo arm leading to discontinuation. We aim to submit an sNDA for PYRUKYND® in thalassemia to the FDA by the end of 2024.

- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from ENERGIZE-T, our completed phase 3, double-blind, randomized, placebo-controlled multicenter study evaluating the efficacy and safety of PYRUKYND® as a potential treatment for adults with transfusion-dependent alpha- or beta-thalassemia, defined as 6 to 20 red blood cell, or RBC, units transfused and ≤ six-week transfusion-free period during the 24-week period before randomization. The primary endpoint of the trial is percentage of patients with transfusion reduction response, defined as a ≥50% reduction in transfused RBC units with a reduction of ≥2 units of transfused RBCs in any consecutive 12-week period through week 48 compared with baseline. Secondary endpoints include additional transfusion reduction measures and percentage of participants with transfusion-independence. We announced topline data for ENERGIZE-T in June 2024. A total of 258 patients were enrolled in the study, with 171 randomized to PYRUKYND® 100 mg twice-daily and 87 randomized to matched placebo. 155 patients (90.6%) in the PYRUKYND® arm and 83 patients (95.4%) in the placebo arm completed the 48-week double-blind period of the study. The study met the primary endpoint of transfusion reduction response, where treatment with PYRUKYND® demonstrated a statistically significant reduction in transfusion burden compared to placebo, as 30.4% of patients achieved a transfusion reduction response, compared to 12.6% of patients in the placebo arm (2-sided p=0.0003). Treatment with PYRUKYND® also demonstrated a statistically significant reduction in additional measures of transfusion reduction response compared to placebo as assessed by the three key secondary endpoints: (i) ≥50% reduction in transfused RBC units in any consecutive 24-week period through week 48 compared with baseline, (ii) ≥33% reduction in transfused RBC units from week 13 through week 48 compared with baseline, and (iii) ≥50% reduction in transfused RBC units from week 13 through week 48 compared with baseline. In addition, a higher proportion of patients in the PYRUKYND® arm (9.9%) compared to the placebo arm (1.1%) achieved the secondary endpoint of transfusion independence (transfusion-free for ≥8 consecutive weeks through week 48). During the 48-week double-blind period, 5.8% of the patients in the PYRUKYND® arm experienced an AE leading to discontinuation, compared to 1.2% of patients in the placebo arm. As mentioned above, we aim to submit an sNDA for PYRUKYND® in thalassemia to the FDA by the end of 2024.
- RISE UP, a phase 2/3 study evaluating the efficacy and safety of PYRUKYND® in SCD patients who are 16 years of age or older, have had between two and 10 sickle cell pain crises in the past 12 months, and have hemoglobin within the range of 5.5 to 10.5 g/dL during screening. We enrolled 79 patients in the phase 2 portion of the trial, with 26 patients in the 50 mg twice daily mitapivat arm, 26 patients in the 100 mg twice daily mitapivat arm and 27 patients in the placebo arm. The primary endpoints of the phase 2 portion of the trial were hemoglobin response, defined as ≥ 1 g/dL increase in average hemoglobin concentration from week 10 to week 12 compared to baseline, and safety. In June 2023, we announced the phase 2 portion of this trial had achieved its primary endpoint of hemoglobin response in patients in both 50 mg and 100 mg twice daily mitapivat arms. 46.2% of patients (n=12) in the 50 mg twice daily mitapivat arm and 50.0% of patients (n=13) in the 100 mg twice daily mitapivat arm achieved a hemoglobin response, compared to 3.7% of patients (n=1) in the placebo arm (2-sided p=0.0003 and 0.0001, respectively). In December 2023, we announced the following additional results of the phase 2 portion of the trial: (i) the least-squares mean (95% confidence interval) for average change from baseline in hemoglobin levels, from week 10 through week 12, for patients in the 50 mg twice daily mitapivat, 100 mg twice daily mitapivat, and placebo arms, respectively, was 1.11 (0.77, 1.45) g/dL, 1.13 (0.79, 1.47) g/dL, and 0.05 (−0.28, 0.39) g/dL; (ii) we observed improvements in annualized rates of sickle cell pain crises as the annualized rate of sickle cell pain crises (95% confidence interval) for patients in the 50 mg twice daily and 100 mg twice daily mitapivat arms, respectively, was 0.83 (0.34, 1.99) and 0.51 (0.16, 1.59), compared to 1.71 (0.95, 3.08) for patients in the placebo arm; (iii) we observed improvement in patient-reported fatigue scores in the 50 mg twice daily mitapivat arm compared to the placebo arm, and the least-squares mean (95% confidence interval) for average changes from baseline in patient-reported fatigue score, from week 10 through week 12, for patients in the 50 mg twice daily mitapivat, 100 mg twice daily mitapivat, and placebo arms, respectively, was −3.80 (−7.16, −0.45), −0.10 (−3.27, 3.08), and −0.17 (−3.40, 3.07). The safety profile for mitapivat observed in the phase 2 portion of the trial was generally consistent with previously reported data in other studies of SCD and other hemolytic anemias. The most common

treatment-emergent adverse events, or TEAEs, in the 50 mg BID, 100 mg BID, and placebo arms, respectively, were: headache (n=6, 6, 7), arthralgia (n=3, 5, 9), dysmenorrhea (n=0, 3, 0), pain (n=3, 3, 2), pain in extremity (n=1, 3, 6), back pain (n=4, 2, 3), nausea (n=1, 2, 4), fatigue (n=4, 1, 5), and influenza-like illness (n=1, 1, 3). There were no serious TEAEs attributed to mitapivat and there were no AEs leading to drug reduction, discontinuation, interruption or death in either the mitapivat or the placebo arms. Of the 79 patients enrolled in the study, 73 continued into the Phase 2 open-label extension period. In October 2023, we enrolled the first patient in the phase 3 portion of this trial. The phase 3 portion includes a 52-week randomized, placebo-controlled period in which participants will be randomized in a 2:1 ratio to receive the recommended (100 mg twice daily) PYRUKYND® dose level or the placebo. The primary endpoints are hemoglobin response, defined as ≥1 g/dL increase in average hemoglobin from baseline to week 52, and annualized rate of sickle cell pain crises. Participants who complete either the phase 2 or phase 3 portion will have the option to move into a 216-week open-label extension period to continue to receive PYRUKYND®. We anticipate completing enrollment by the end of 2024 and announcing topline data for this trial in 2025.

- ACTIVATE-kids and ACTIVATE-kidsT, double-blind phase 3 studies evaluating the efficacy and safety of PYRUKYND® as a potential treatment for PK deficiency in not regularly transfused and regularly transfused patients between one and 18 years old, respectively.

  The primary endpoint of ACTIVATE-kidsT is transfusion reduction response, defined as ≥33% reduction in total RBC transfusion volume from week 9 through week 32 of the double-blind period. We announced topline data for ACTIVATE-kidsT in August 2024. Using Bayesian methodology, the prespecified statistical criterion for the primary endpoint in ACTIVATE-kidsT was not met using low or moderate borrowing of data from the ACTIVATE-T study in adults. In the study, 28.1% of patients in the mitapivat arm achieved the primary endpoint of transfusion reduction response, compared to 11.8% of patients in the placebo arm. Transfusion-free response and normal hemoglobin response were secondary endpoints in this study and only observed in patients in the mitapivat arm. In the 32-week double-blind treatment period, mitapivat was generally safe and well-tolerated, with safety results consistent with the safety profile for mitapivat previously observed in adults with PK deficiency who are regularly transfused. We plan to provide a more detailed analysis of the data from this trial at an upcoming medical meeting.

  The primary endpoint of ACTIVATE-kids is percentage of patients with hemoglobin response, defined as ≥1.5 g/dL increase in hemoglobin concentration from baseline that is sustained at two or more scheduled assessments at weeks 12, 16, and 20 during the double-blind period. ACTIVATE-kids has completed enrollment and we anticipate announcing topline data for this trial in 2025.

- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from ACTIVATE and ACTIVATE-T, our completed pivotal trials of PYRUKYND® in not regularly transfused and regularly transfused adult patients with PK deficiency.

- An extension study evaluating the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in patients from DRIVE PK, our completed global phase 2, first-in-patient, open-label safety and efficacy clinical trial of PYRUKYND® in adult, not regularly transfused patients with PK deficiency.

AG-946 (tebapivat): Novel PK Activator

We are developing AG-946 (tebapivat), a novel PK activator, for the potential treatment of LR MDS and hemolytic anemias. We are evaluating AG-946 (tebapivat) in a phase 1 trial of AG-946 (tebapivat) in healthy volunteers and in patients with SCD. We have presented data from the healthy volunteer cohorts, and we have initiated the SCD patient cohort of this phase 1 trial.

We initiated a phase 2a clinical trial of AG-946 (tebapivat) in adults with LR MDS in the third quarter of 2022, and the trial has completed enrollment with 22 patients, including 12 patients classified as non-transfused and 10 patients classified as low transfusion burden. Patients received 5 mg of AG-946 (tebapivat) once daily for up to 16 weeks. The two primary endpoints of the trial were transfusion independence (for patients classified as low transfusion burden), defined as transfusion-free for ≥ eight consecutive weeks during the 16-week treatment period, and hemoglobin response, defined as a ≥ 1.5 g/dL increase from baseline in the average hemoglobin concentration measured from week 8 through week 16.

In November 2023, we announced that we achieved clinical proof-of-concept in the phase 2a portion of the trial. We observed that four of the 10 patients with low transfusion burden achieved the transfusion independence endpoint, and one of the 22 patients achieved the hemoglobin response endpoint in the 16-week treatment period. The safety profile observed was consistent with data reported in the healthy volunteer study of AG-946 (tebapivat). 19 patients elected to enroll in the extension period for up to 156 weeks. We intend to complete a full evaluation of the phase 2a trial results and assess the impact of those results on the phase 2b portion of the protocol in 2024. Based on the data generated in the Phase 2a trial, we plan to increase the dosage levels evaluated in the upcoming Phase 2b trial, which we expect to initiate in mid-2024.

Other Programs

In addition to the aforementioned development programs, we are developing AG-181, a PAH stabilizer for the potential treatment of PKU, for which we filed an IND in December 2023. We initiated a phase 1 trial of AG-181 in healthy volunteers in the first quarter of 2024. Also, in July 2023, we entered into a license agreement with Alnylam for the development and commercialization of products containing or comprised of an siRNA preclinical development candidate discovered by Alnylam and targeting the TMPRSS6 gene, and we have begun preclinical development of a product candidate for the potential treatment of patients with PV.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, business development, commercial, legal, information technology and human resources functions. Other significant costs include facility-related costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our selling, general and administrative expenses will increase in the future to support continued research and development activities, and ongoing and future commercialization activities related to our portfolio, including the ongoing commercialization of PYRUKYND® and any of our other product candidates, which may include the hiring of additional personnel.

Critical Accounting Estimates

Our critical accounting estimates are those which require the most significant judgments and estimates in the preparation of our condensed consolidated financial statements. We have determined that our most critical accounting estimates are those relating to revenue recognition, accrued research and development expenses and stock-based compensation. As of June 30, 2024, there have been no material changes to our existing critical accounting estimates discussed in Part II, Item 7 of our Annual Report on Form 10-K for the year ended December 31, 2023.

Results of Operations

Comparison of the three and six months ended June 30, 2024 and 2023

Revenues

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Revenues:				
Product revenue, net	$ 8,615	$ 6,712	$ 16,804	$ 12,321
Total revenue	$ 8,615	$ 6,712	$ 16,804	$ 12,321

Total Revenue - Three Months Ended June 30, 2024 vs. Three Months Ended June 30, 2023 – The increase in total revenue of $1.9 million for the three months ended June 30, 2024 compared to the three months ended June 30, 2023 was due to increased product revenue associated with PYRUKYND®.

Total Revenue - Six Months Ended June 30, 2024 vs. Six Months Ended June 30, 2023 – The increase in total revenue of $4.5 million for the six months ended June 30, 2024 compared to the six months ended June 30, 2023 was due to increased product revenue associated with PYRUKYND®.

Total Operating Expenses

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Operating expenses:				
Cost of sales	$ 1,495	$ 1,108	$ 2,122	$ 1,662
Research and development	77,401	68,895	146,021	136,196
Selling, general and administrative	35,536	30,409	66,550	58,776
Total operating expenses	$ 114,432	$ 100,412	$ 214,693	$ 196,634

Total Operating Expenses - Three Months Ended June 30, 2024 vs. Three Months Ended June 30, 2023 – The increase in total operating expenses of $14.0 million for the three months ended June 30, 2024 compared to the three months ended June 30, 2023 was primarily due to an increase in research and development expenses of $8.5 million which is described below under

Research and Development Expenses, and an increase in selling, general and administrative expenses of $5.1 million, driven by an increase in commercial-related activities as we prepare for the potential approval of PYRUKYND® in thalassemia.

Total Operating Expenses - Six Months Ended June 30, 2024 vs. Six Months Ended June 30, 2023 – The increase in total operating expenses of $18.1 million for the six months ended June 30, 2024 compared to the six months ended June 30, 2023 was primarily due to an increase in research and development expenses of $9.8 million which is described below under Research and Development Expenses, and an increase in selling, general and administrative expenses of $7.8 million, driven by an increase in commercial-related activities as we prepare for the potential approval of PYRUKYND® in thalassemia.

Research and Development Expenses

Our research and development expenses, by major program, are outlined in the table below:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
PK activator (PYRUKYND®)	$ 27,968	$ 26,492	$ 54,004	$ 47,491
Novel PK activator (AG-946) (tebapivat)	4,488	4,129	6,383	7,597
Other research and platform programs	7,270	2,058	10,955	5,525
Total direct research and development expenses	39,726	32,679	71,342	60,613
Compensation and related expenses	27,476	26,263	55,110	55,954
Facilities and IT related expenses & other	10,199	9,953	19,569	19,629
Total indirect research and development expenses	37,675	36,216	74,679	75,583
Total research and development expense	$ 77,401	$ 68,895	$ 146,021	$ 136,196

Total Research and Development Expenses - Three Months Ended June 30, 2024 vs. Three Months Ended June 30, 2023 – The increase in total research and development expenses of $8.5 million for the three months ended June 30, 2024 compared to the three months ended June 30, 2023 was primarily due to a $7.0 million increase in our direct expenses. The increase in direct expenses was primarily due to an increase in other research and platform programs as a result of costs associated with the in-licensed siRNA TMPRSS6 program for polycythemia vera.

Total Research and Development Expenses - Six Months Ended June 30, 2024 vs. Six Months Ended June 30, 2023 – The increase in total research and development expenses of $9.8 million for the six months ended June 30, 2024 compared to the six months ended June 30, 2023 was primarily due to a $10.7 million increase in our direct expenses. The increase in direct expenses was primarily due to an increase in PYRUKYND® costs due to increased process development expenses and increased costs associated with clinical trials for patients with SCD, partially offset by lower costs associated with the phase 3 clinical trials of PYRUKYND® in patients with thalassemia, ENERGIZE and ENERGIZE-T, and an increase in other research and platform programs as a result of costs associated with the in-licensed siRNA TMPRSS6 program for polycythemia vera.

Other Income and Expense

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2024	2023	2024	2023
Interest income, net	$ 8,120	$ 8,254	17,009	16,345
Other income, net	1,579	1,640	3,213	3,144

Other Income and Expense - Three Months Ended June 30, 2024 vs. Three Months Ended June 30, 2023 – Interest income, net and other income, net in the three months ended June 30, 2024 were relatively consistent with the three months ended June 30, 2023.

Other Income and Expense - Six Months Ended June 30, 2024 vs. Six Months Ended June 30, 2023 – The increase in interest income, net was primarily attributable to an increase in interest rates. Other income, net in the six months ended June 30, 2024 was relatively consistent with the six months ended June 30, 2023.

Net Loss

(In thousands)	Three Months Ended June 30, 2024	Three Months Ended June 30, 2023	Six Months Ended June 30, 2024	Six Months Ended June 30, 2023
Net loss	$ (96,118)	$ (83,806)	$ (177,667)	$ (164,824)

Net Loss - Three Months Ended June 30, 2024 vs. Three Months Ended June 30, 2023 – The increase in net loss for the three months ended June 30, 2024 compared to the three months ended June 30, 2023 was primarily driven by the increase in research and development expenses discussed above under Research and Development Expenses and the increase in selling, general and administrative expenses discussed above under Total Operating Expenses, partially offset by the increase in revenue discussed above under Revenues.

Net Loss - Six Months Ended June 30, 2024 vs. Six Months Ended June 30, 2023 – The increase in net loss for the six months ended June 30, 2024 compared to the six months ended June 30, 2023 was primarily driven by the increase in research and development expenses discussed above under Research and Development Expenses and the increase in selling, general and administrative expenses discussed above under Total Operating Expenses, partially offset by the increase in revenue discussed above under Revenues and the increase in interest income, net discussed above under Other Income and Expense.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, and through March 31, 2021, we financed our operations primarily through proceeds from the sale of our royalty rights, commercial sales of TIBSOVO®, funding received from our collaboration agreements, private placements of our preferred stock, our initial public offering of our common stock and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings. Following the sale of our oncology business to Servier on March 31, 2021, we have financed and expect to continue to finance our operations primarily through cash on hand, royalty payments from Servier with respect to U.S. net sales of TIBSOVO® prior to the sale of these contingent payments to Sagard, proceeds from the sale of contingent payments to Sagard, a potential Upfront Payment from Royalty Pharma and a potential Vorasidenib Milestone Payment from Servier, both of which are contingent on if the NDA for vorasidenib is approved by the FDA, potential royalty payments with respect to the Retained Earn-Out Rights, the actual and potential future sales of PYRUKYND® and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings.

On March 31, 2021, we completed the sale of our oncology business to Servier. The transaction included the sale of our oncology business, including TIBSOVO®, our clinical-stage product candidates vorasidenib, AG-270 and AG-636, and our oncology research programs for a payment of approximately $1.8 billion in cash at the closing, subject to certain adjustments, and the right to a potential Vorasidenib Milestone Payment, as well as a royalty of 5% of U.S. net sales of TIBSOVO® from the close of the transaction through loss of exclusivity, and the potential Vorasidenib Royalty Rights. The Vorasidenib Milestone Payment, Vorasidenib Royalty Rights and royalty payments related to TIBSOVO® are referred to as contingent payments and recognized as income when realizable. Servier also acquired our co-commercialization rights for Bristol Myers Squibb's IDHIFA® and the right to receive a $25.0 million potential milestone payment under our prior collaboration agreement with Celgene, and following the sale Servier is responsible for conducting certain clinical development activities within the IDHIFA® development program. As discussed above in Note 1, Overview and Basis of Presentation, in October 2022, we sold our rights to the royalty on U.S. net sales of TIBSOVO® to Sagard for $131.8 million. We retained our rights to the Vorasidenib Milestone Payments and Vorasidenib Royalty Rights. In February 2024, Servier announced that it received filing acceptance and priority review from the FDA for its NDA for vorasidenib for the treatment of certain IDH-mutant diffuse glioma and accelerated assessment from the EMA, for its MAA for vorasidenib. The FDA assigned the NDA a PDUFA action date of August 20, 2024, and Servier anticipates that the European Commission will approve its MAA in the second half of 2024. In May 2024, we entered into a purchase and sale agreement with Royalty Pharma, pursuant to which we agreed to sell the Vorasidenib Royalty Rights for the Upfront Payment of $905.0 million. The consummation of the sale and payment of the purchase price are subject to approval of vorasidenib by the FDA on or before October 31, 2024, and other customary closing conditions. Upon consummation of the sale, Royalty Pharma will acquire 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in net sales for each calendar year. In addition, any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the Retained Earn-Out Rights. We also retain our rights to the potential Vorasidenib Milestone Payment.

Our cash, cash equivalents and marketable securities balance was $645.3 million at June 30, 2024. The potential Vorasidenib Milestone Payment, the Upfront Payment and the Retained Earn-Out Rights are our only committed potential external sources of funds. Whether the regulatory approval milestone for vorasidenib will be achieved is subject to various risks and

uncertainties, which are outside our control. Furthermore, we cannot predict what success, if any, Servier may have in the United States with respect to sales of vorasidenib, if approved, and consequently we cannot estimate the amount of payments, if any, we may receive on account of the Retained Earn-Out Rights.

Cash flows

The following table provides information regarding our cash flows for the six months ended June 30, 2024 and 2023:

	Six Months Ended June 30,	
(In thousands)	2024	2023
Net cash used in operating activities	$ (172,456)	$ (161,931)
Net cash provided by investing activities	161,806	104,721
Net cash provided by financing activities	6,963	2,704
Net change in cash and cash equivalents	$ (3,687)	$ (54,506)

Net cash used in operating activities. Cash used in operating activities of $172.5 million during the six months ended June 30, 2024 was primarily due to operating expenses driven by research and development costs described above under Research and Development Expenses, partially offset by cash received from interest income of $19.3 million and product revenues of $17.6 million.

Cash used in operating activities of $161.9 million during the six months ended June 30, 2023 was primarily due to operating expenses driven by research and development costs described above under Research and Development Expenses, partially offset by cash received from interest income of $15.6 million and product revenues of $13.6 million.

Net cash provided by investing activities. Cash provided by investing activities of $161.8 million during the six months ended June 30, 2024 was primarily due to higher proceeds from maturities and sales of marketable securities than purchases of marketable securities.

Cash provided by investing activities of $104.7 million during the six months ended June 30, 2023 was primarily due to higher proceeds from maturities and sales of marketable securities than purchases of marketable securities.

Net cash provided by financing activities. Cash provided by financing activities of $7.0 million during the six months ended June 30, 2024, was the result of net proceeds received from stock option exercises and purchases made pursuant to our 2013 Employee Stock Purchase Plan, or 2013 ESPP.

Cash provided by financing activities of $2.7 million during the six months ended June 30, 2023 was the result of net proceeds received from stock option exercises and purchases made pursuant to our 2013 ESPP.

Funding requirements

We expect our expenses to increase as we continue the research, development and clinical trials of, seek marketing approvals for, and commercialize our product candidates in our portfolio, including as we continue to commercialize PYRUKYND®. If we obtain additional marketing approvals for PYRUKYND® in thalassemia or in other indications, or outside of the United States or for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

We expect that our existing cash, cash equivalents and marketable securities as of June 30, 2024, together with anticipated product revenue, interest income and the potential Vorasidenib Milestone Payment and Upfront Payment, will provide the financial independence to prepare for potential PYRUKYND® launches in thalassemia and SCD, and to opportunistically expand our pipeline through both internally and externally discovered assets. Our future capital requirements will depend on many factors, including:

- the amount and timing of future revenue received from commercial sales of PYRUKYND® or any of our product candidates for which we may receive marketing approval;
- whether vorasidenib is approved by the FDA and the sale of the Vorasidenib Royalty Rights to Royalty Pharma is consummated;
- the amount of payments, if any, we may receive on account of the Retained Earn-Out Rights;
- the costs and timing of our ongoing commercialization activities, including product manufacturing, sales, marketing and distribution for PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in approved jurisdictions;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs associated with in-licensing or acquiring assets for pipeline growth, including the amount and timing of future milestone and royalty payments potentially payable to Alnylam pursuant to the license agreement;

- the costs, timing and outcome of regulatory review of our product candidates, including with respect to our anticipated regulatory submissions for PYRUKYND® for the treatment of thalassemia;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for any of our product candidates for which we may receive marketing approval;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- our ability to successfully execute on our strategic plans;
- operational delays due to public health epidemics, including the COVID-19 pandemic; and
- operational delays, disruptions and/or increased costs associated with global economic developments, rising global energy prices or energy shortages or rationing.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs primarily through cash on hand, the potential Vorasidenib Milestone Payment and Upfront Payment, potential Retained Earn-Out Rights, the actual and potential future sales of PYRUKYND® and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings. We do not have any committed external source of funds other than the potential Vorasidenib Milestone Payment, Upfront Payment and Retained Earn-Out Rights. 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, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends.

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

Contractual Obligations

During the six months ended June 30, 2024, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2023.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of June 30, 2024 and December 31, 2023, we had cash, cash equivalents and marketable securities of $645.3 million and $806.4 million, respectively, consisting primarily of investments in U.S. Treasuries, government securities, corporate debt securities and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are primarily in short-term marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we do not believe an immediate and uniform 100 basis point change in interest rates would have a material effect on the fair market value of our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates. We have contracts with CROs and contract manufacturing organizations that are located in Asia and Europe and are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of June 30, 2024 and December 31, 2023, we had minimal or no liabilities denominated in foreign currencies.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of June 30, 2024, our principal executive officer and

principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports it files or submits under the Exchange Act is accumulated and communicated to its management, including its principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

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 fiscal quarter ended June 30, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1A. Risk Factors

The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 16 of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to the Discovery, Development, and Commercialization of our Products and Product Candidates

If we do not successfully commercialize PYRUKYND® and other products for which we receive approval, our prospects may be substantially harmed.

In February 2022, we obtained marketing approval from the FDA for PYRUKYND® (mitapivat) for the treatment of hemolytic anemia in adults with PK deficiency in the United States. In November 2022, we received marketing authorization from the European Commission for PYRUKYND® for the treatment of PK deficiency in adult patients in the EU and in December 2022 we received marketing authorization in Great Britain for PYRUKYND® for the treatment of PK deficiency in adult patients under the European Commission Decision Reliance Procedure. PYRUKYND® is the first product in our rare disease portfolio that has received marketing approval and is our first product following the sale of our oncology business to Servier in March 2021. Our ability to generate meaningful revenue from PYRUKYND® will depend heavily on our successful development and commercialization of the product. In connection with our regulatory approvals in the EU and Great Britain, we are currently providing access to PYRUKYND® on a free of charge basis for eligible patients in those jurisdictions through a global managed access program. We provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions upon request through the global managed access program, on either a free of charge or for charge basis. Beyond the global managed access program, we continue to evaluate options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities, such as the NewBridge Agreement.

The development and commercialization of PYRUKYND® could be unsuccessful if:

- the medical community and third-party payors do not accept PYRUKYND® as safe, efficacious and cost-effective for the treatment of adults with PK deficiency in the approved jurisdictions;
- we fail to maintain the necessary financial resources and expertise to manufacture, market and sell PYRUKYND®;
- we fail to develop, implement and maintain effective marketing, sales and distribution strategies and operations for the development and commercialization of PYRUKYND®;
- we fail to continue to develop, validate and maintain a commercially viable manufacturing process for PYRUKYND® that is compliant with current good manufacturing practices, or cGMP;
- we fail to successfully obtain third party reimbursement and generate commercial demand that results in expected sales of PYRUKYND®;
- PYRUKYND® may become subject to unfavorable pricing regulations and third-party reimbursement practices;
- we encounter any third-party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to PYRUKYND®;
- we fail to comply with regulatory and legal requirements applicable to the sale of PYRUKYND®;
- competing drug products are approved for the same indications as PYRUKYND®;
- significant safety, manufacturing and/or quality risks are identified;
- PYRUKYND® fails to gain and/or maintain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community;
- a significant number of eligible patients with PK deficiency are not prescribed PYRUKYND® and, if they are, such patients do not stay on treatment; or
- PYRUKYND® does not demonstrate acceptable safety and efficacy in current or future clinical trials, or otherwise does not meet applicable regulatory standards for approval in other indications.

If we experience significant delays or an inability to successfully develop and commercialize PYRUKYND® our business would be materially harmed.

We depend heavily on the success of our clinical-stage product candidates, including the potential approval of PYRUKYND® for use in thalassemia or in indications other than PK deficiency and in other jurisdictions. Clinical trials of our product candidates may not be successful for a number of important reasons. If we or our collaborators are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification of our product candidates and the development of our most advanced clinical programs, including PYRUKYND®. Our ability to generate meaningful product revenue will depend heavily on the successful clinical development and eventual commercialization of our current and any future product candidates, including PYRUKYND®. While we obtained marketing approval of PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States and marketing authorization of PYRUKYND® for the treatment of adults with PK deficiency in the EU and Great Britain, we cannot be certain that we will obtain marketing approval of PYRUKYND® in thalassemia or in indications other than PK deficiency or in other jurisdictions.

We, and any collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements in foreign jurisdictions. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development. Moreover, we, or any collaborators, may experience any of a number of possible unforeseen adverse events in connection with clinical trials, many of which are beyond our control, including:

- we, or our collaborators, may fail to demonstrate efficacy in a clinical trial or across a broad population of patients;
- it is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. For example, many compounds that initially showed promise in earlier stage testing for treating specific indications have later been found to cause side effects that prevented further development of the compound;
- our product candidates may have undesirable side effects or other unexpected characteristics or otherwise expose participants to unacceptable health risks, causing us, our collaborators or our investigators, regulators or institutional review boards or the data safety monitoring board for such trial to halt, delay, interrupt, suspend or terminate the trials or cause us, or any collaborators, to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective;
- if our product candidates have undesirable side effects, it could result in a more restrictive label, or it could result in the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities;
- clinical trials of our product candidates may produce negative or inconclusive results, and we, or our collaborators, may decide, or regulators may require us, to conduct additional clinical trials, including testing in more subjects, or abandon product development programs;
- regulators or institutional review boards may not authorize us, our collaborators or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we or our collaborators may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment in these clinical trials, which may be particularly challenging for some of the orphan diseases we target in our rare disease programs, may be slower than we anticipate; or participants may drop out of these clinical trials at a higher rate than we anticipate;
- third-party contractors used by us or our collaborators may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all;
- significant preclinical study or clinical trial delays could shorten any periods during which we, or any collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any collaborators, to bring products to market before we, or any collaborators, do;
- the cost of clinical trials of our product candidates may be greater than anticipated; and

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

In December 2016, we withdrew our IND for AG-519, our second PK activator, following verbal notification of a clinical hold from the FDA relating to a previously disclosed case of drug-induced cholestatic hepatitis which occurred in our phase 1 clinical trial of AG-519 in healthy volunteers. Although these decisions and this hepatic adverse event finding do not affect our ongoing clinical trials for PYRUKYND®, our first PK activator, we cannot provide any assurances that there will not be other treatment-related severe adverse events in our other clinical trials, or that our other trials will not be placed on clinical hold in the future.

Our failure to successfully begin and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates could result in additional costs to us, or any collaborators, would impair our ability to generate revenue from product sales, regulatory and commercialization milestones and royalties and would significantly harm our business.

We may engage in in-licensing transactions or acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

We have and may in the future enter into additional transactions to in-license products, technologies or assets or to acquire other products, technologies, assets or businesses. As part of the evolution of our research organization, we plan to prioritize in-licensing or acquiring assets for future pipeline growth. For example, in July 2023, we entered into a license agreement with Alnylam for the development and commercialization of products containing or comprised of an siRNA development candidate discovered by Alnylam and targeting the TMPRSS6 gene, and we have begun preclinical development of a product candidate for the potential treatment of PV.

Our ability to successfully in-license or acquire assets and develop product candidates following such transactions is unproven. If we do identify additional suitable candidates or assets for in-licensing transactions or acquisitions, we may not be able to make such transactions on favorable terms, or at all. Such transactions may require us to relinquish rights to develop product candidates in certain indications, limit our ability to pursue certain targets or require us to make significant milestone or royalty payments to third parties upon achievement of certain events. For example, we are responsible to pay up to $130.0 million in potential development and regulatory milestones, in addition to sales milestones as well as tiered royalties on annual net sales, if any, of any licensed products, under the license agreement with Alnylam. Further, any in-licensing transaction or acquisitions we undertake may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or an in-licensing transaction or issue our common stock or other equity securities to the stockholders of the counterparty, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business, product or technology that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Such transactions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot ensure that following any transaction we would achieve the expected synergies to justify the transactions. We cannot predict the number, timing or size of future transactions or the effect that any such transactions might have on our operating results.

Public health epidemics or pandemics may affect our ability to initiate or continue our planned, ongoing and future preclinical studies and clinical trials, disrupt regulatory activities, disrupt our ability to maintain a commercial infrastructure for our product or have other adverse effects on our business and operations.

Public health emergencies or pandemics could adversely affect our business, financial condition, results of operations, and prospects. We may face delays, disruptions or shortages as a result of such pandemics that may affect our ability to initiate and complete preclinical studies and clinical trials or impact our commercialization efforts. We have previously experienced disruptions to certain clinical and research activities at our CROs due to the COVID-19 pandemic. Any future pandemic or public health emergency could result in delays or pauses in site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis due to changes in hospital or university policies, federal, state or local regulations, diversion of hospital resources or other reasons related to a public health emergency. If a pandemic or public health emergency arises in the future, we may face difficulties recruiting or retaining patients in our ongoing clinical trials, and patients enrolled in our clinical trials may be unable or unwilling to visit clinical trial sites which may impact the collection of important clinical trial data and may necessitate remote data verification. In addition, limitations on the ability to visit sites may affect our enrollment timelines for our clinical trials, and may adversely affect the timing of completion of our clinical trials or our ability to complete clinical trials in a fully compliant manner. Additionally, the potential

suspension of clinical trial activity at clinical trial sites or reduced availability of CRO personnel may have an adverse impact on our clinical trial plans and timelines.

The public health emergency declarations related to COVID-19 ended on May 11, 2023. The FDA ended a number of COVID-19 related policies and retained a number of COVID-19 related policies. It is unclear how, if at all, these developments will impact our efforts to develop and commercialize our product candidates.

We cannot be certain what the overall impact of future health emergencies or pandemics will be on our business.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate, continue or complete clinical trials for our product candidates if we or they are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States. Furthermore, enrollment had previously been particularly challenging in light of the COVID-19 pandemic.

Patient enrollment is also affected by other factors including:

- prevalence and severity of the disease under investigation;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Utilizing our precision medicine approach, we generally focus our development activities on genetically or biomarker defined patients most likely to respond to our therapies. As a result, the potential patient populations for our clinical trials are narrowed, and we may experience difficulties in identifying and enrolling a sufficient number of patients in our clinical trials.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug product. These plans are meant to encourage enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. If we are not able to adhere to these new requirements, our ability to conduct clinical trials may be delayed or halted.

In addition, some of our competitors may have ongoing or planned clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. For example, Rocket Pharma LTD, or Rocket Pharma, is developing a gene therapy targeting PK deficiency; Novo Nordisk A/S, or Novo Nordisk, is developing molecules for the treatment of alpha and beta thalassemia, SCD and LR MDS; Pfizer Inc., or Pfizer, is developing molecules for the treatment of SCD; Fulcrum Therapeutics Inc., or Fulcrum, is developing a treatment for SCD; Keros Therapeutics, or Keros, is developing KER-050 for the treatment of anemia in LR MDS; PTC Therapeutics, Inc., or PTC, and Jnana Therapeutics, Inc., or Jnana, and Homology Medicines Inc., or Homology, are developing therapies to treat PKU; and Protagonist Therapeutics, or Protagonist, with Takeda Pharmaceutical Company Limited, or Takeda, Ionis Pharmaceuticals, Inc., or Ionis, Silence Therapeutics, or Silence, and Merck & Co., Inc., or Merck, are developing therapies to treat PV. Competition for eligible patients may make it particularly difficult for us to enroll a sufficient number of patients to complete our clinical trials for our product candidates in a timely and cost-effective manner.

In addition, we have a small number of clinical trial sites for certain clinical trials in the Middle East, including in Lebanon and Israel, that could be affected by the current armed conflict in the region.

We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. Our or our collaborators' 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, or result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Results of preclinical studies and early clinical trials may not be predictive of results of later-stage clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier stages of development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. While we obtained marketing approval of PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States and marketing authorization of PYRUKYND® for the treatment of adults with PK deficiency in the EU and Great Britain, we cannot be certain that we will obtain marketing approval of PYRUKYND® in other indications. The results of clinical trials of PYRUKYND® for the treatment of PK deficiency and thalassemia are not predictive of results of our ongoing clinical trials of PYRUKYND® in other indications, such as SCD. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. We are prioritizing investment in advancing our late lead-optimization research, while continuing to progress our registration-enabling clinical programs in thalassemia, SCD and pediatric PK deficiency, our phase 2 trial in LR MDS, our phase 1 trial for AG-181, our PAH stabilizer for the potential treatment of PKU, and our development of a licensed siRNA development candidate under our license agreement with Alnylam. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We or others may later discover that PYRUKYND®, or any of our product candidates that may receive marketing approval in the future, is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any collaborators, to market the product.

It is possible that our clinical trials, or those of any collaborators, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, including PYRUKYND®, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements;
- we, or any collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;

- we, or any collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

PYRUKYND®, or any of our product candidates that may receive marketing approval in the future, may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

PYRUKYND®, or any of our product candidates that may receive marketing approval in the future, may fail to gain and/or maintain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. If PYRUKYND® or any of our product candidates that may receive marketing approval do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of PYRUKYND® and any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- ensuring uninterrupted product supply;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If we are unable to maintain sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing PYRUKYND® or any of our product candidates if they are approved.

We have limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for approved medicines for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to other third parties. We have established sales and marketing capabilities to support our commercial launch of PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States. In addition, in connection with our regulatory approvals in the EU and Great Britain, we are currently providing access to PYRUKYND® free of charge for eligible patients in those jurisdictions through a global managed access program. We provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions upon request through the global managed access program, on either a free of charge or for charge basis. Beyond the global managed access program, we continue to evaluate options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities, including the NewBridge Agreement.

We may need to further build our sales and marketing infrastructure, either directly or with third-party partners, to maintain our ongoing commercialization efforts and to commercialize PYRUKYND® in other indications or outside of the United States or to commercialize any of our other product candidates for which we obtain marketing approval.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our medicines on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;

- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of product revenue to us are likely to be lower than if we were to market and sell any medicines that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing PYRUKYND® or any of our product candidates for which we obtain marketing approval.

We provide certain development estimates related to the development and regulatory approval of PYRUKYND® and our product candidates. If we do not achieve our projected development or regulatory approval estimates in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we provide estimates related to the development of PYRUKYND® and our product candidates. We also estimate the timing of the anticipated accomplishment of various scientific, preclinical, clinical, regulatory and other product development goals. These estimates may include the commencement or completion of clinical trials, the timing for reporting clinical trial results and the timing of submission of regulatory filings in various jurisdictions. From time to time, we may publicly announce our estimates, including the timing of certain milestones related to our product candidates. All of these estimates are and will be based on numerous assumptions. The actual results and timing of our preclinical studies, clinical trials and regulatory submissions can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If our estimates change or we do not meet the timing of our estimates as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

We face competition with respect to PYRUKYND® and our current product candidates, and we will face competition with respect to any product candidates that we may seek to develop or commercialize in the future. Potential competitors may include major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the indications for which we are developing our product or our product candidates, such as PK deficiency, thalassemia, SCD, LR MDS, PKU, and PV. For example, Merck and Bristol-Myers Squibb Company, or BMS, are marketing a therapy to treat beta thalassemia and LR MDS and are conducting clinical trials for alpha thalassemia and LR MDS patients that are ESA naïve and non-transfusion dependent; Geron Corporation recently announced FDA approval of a treatment for adults with LR MDS with transfusion-dependent anemia; Novartis International AG, or Novartis, Emmaus Life Sciences, and Pfizer are each marketing therapies to treat SCD, with Pfizer continuing to conduct clinical trials for therapies in SCD; BioMarin Pharmaceutical Inc., or BioMarin, is marketing and conducting clinical trials for therapies to treat PKU; Novo Nordisk is conducting clinical trials for the treatment of alpha and beta thalassemia, SCD and LR MDS; bluebird is marketing a gene therapy to treat transfusion-dependent beta-thalassemia and SCD; Vertex, with CRISPR, is marketing a gene therapy targeting SCD and transfusion-dependent beta-thalassemia; Fulcrum is conducting clinical trials for a potential treatment for SCD; Keros is conducting a clinical trial for potential treatments for LR MDS; PTC and Jnana and are conducting clinical trials for potential treatments for PKU; PharmaEssentia Corp, or PharmaEssentia, and Incyte Corporation, or Incyte, are marketing therapies to treat PV, and Protagonist with Takeda, Ionis, Italfarmaco S.p.A., Disc Medicine, Inc., and Silence are developing therapies to treat PV; and a number of other biotechnology companies have product candidates in clinical development in similar indications as ours.

There are a variety of treatment options available, including a number of marketed enzyme replacement therapies, or ERTs, for treating patients with rare diseases. In addition to currently marketed therapies, there are also a number of products that are either ERTs, gene therapies or PK activators in various stages of clinical development to treat rare diseases. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies or for which there are no approved treatments. As a result, they may provide significant competition for any of our product candidates for which we obtain marketing approval.

There are also a number of product candidates in preclinical or clinical development by third parties to treat rare diseases by targeting similar mechanisms of action or target indications as our product candidates. These companies include large

pharmaceutical companies, such as Novartis, Novo Nordisk, Pfizer, BMS, Merck and Vertex as well as biotechnology companies of various sizes, such as BioMarin, bluebird, PTC and Rocket Pharma.

Our competitors may develop products that are more effective, safer, more convenient or less costly than PYRUKYND® or any product candidates that we are developing or that would render PYRUKYND® or our product candidates obsolete or non-competitive. In addition, our competitors may discover biomarkers that more efficiently measure metabolic pathways than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and globally marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and clinical stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring or in-licensing technologies complementary to, or necessary for, our programs.

If the FDA does not grant our products, if and when approved, appropriate periods of data exclusivity before approving generic or follow-on versions of our products, the sales of our products could be adversely affected.

With FDA approval of an NDA, the product covered by the application is specified as a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States.

In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the sponsor generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any reference-listed drug may be typically lost to the generic product.

A manufacturer may also submit an NDA under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, that references the FDA's prior approval of the innovator product or preclinical studies and/or clinical trials that were not conducted by, or for, the sponsor and for which the sponsor has not obtained a right of reference. A 505(b)(2) NDA product, or follow-product, may be for a new or improved version of the original reference listed drug.

The FDA may not approve an ANDA or 505(b)(2) NDA until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The FDCA provides a period of five years of new chemical entity exclusivity for a new drug containing a new active moiety. Specifically, in cases where such exclusivity has been granted, an ANDA or a 505(b)(2) NDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the sponsor may submit its application four years following approval of the reference-listed drug. The FDCA also provides a period of three years of new clinical investigation data exclusivity in connection with the approval of a supplemental indication for the product for which a clinical trial is deemed by the FDA as essential for approval.

In the event that a generic or follow-on manufacturer is somehow able to obtain FDA approval without adherence to these periods of data exclusivity, the competition that our approved products may face from generic and follow-on versions could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

In addition, if there are patents listed for our drug products in the Orange Book, ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the sponsor intends to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic or follow-on competitor would address such patents, whether we would sue on any such patents or the outcome of any such suit.

Product liability lawsuits against us or any collaborators could cause us or our collaborators to incur substantial liabilities and could limit commercialization of any medicines that we or they may develop.

We and any collaborators face a risk of product liability exposure related to our product candidates in human clinical trials and face an even greater risk as we or they commercially sell any medicines, including PYRUKYND®. If we or any collaborators cannot successfully defend ourselves or themselves against claims that our product candidates or medicines caused injuries, we or they could incur substantial costs and liabilities. Regardless of merit or eventual outcome, liability claims may also result in, among other things, decreased demand for any product candidates or medicines that we may develop, reputational harm and lost revenue.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur.

Our internal information technology systems, or those of any third parties with which we contract, may fail or suffer security breaches, loss of data or other disruptions which could result in a material disruption of our product development programs, compromise sensitive information related to our business or prevent us from accessing critical information, trigger legal obligations, potentially exposing us to liability, competitive or reputational harm or otherwise adversely affecting our business and financial results.

Despite the implementation of security measures, our internal information technology systems and those of third parties with which we contract are vulnerable to damage from computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber incidents by malicious third parties. Cybersecurity incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cybersecurity incidents could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cybersecurity incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. Attackers may use artificial intelligence and machine learning to launch more automated, targeted and coordinated attacks against targets. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies.

System failures, accidents, cybersecurity incidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed or future trials 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 were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and our product research, development and commercialization efforts could be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, and, as a result, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain processes, systems and controls designed to prevent these events from occurring, and we have a process to assess, identify and manage threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. We cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to prevent any cyber-attacks or security breaches.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the United States, EU and United Kingdom. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. Enforcement activity by the U.S. Department of Health & Human Services, or HHS, can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In addition to potential enforcement by HHS, we are also potentially subject to privacy enforcement from the Federal Trade Commission, or FTC. The FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act of 1914, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements.

States are also active in creating specific rules relating to the processing of personal information. In 2018, California passed into law the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act, or CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities.

In addition to California, a number of other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime over the next several years. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or are in the process of enacting privacy laws that will go into effect in 2024 and beyond. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Similar to the laws in the United States, there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

The GDPR places restrictions on the cross-border transfer of personal data from the EU to countries that have not been found by the European Commission to offer adequate data protection legislation, such as the United States. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. This CJEU decision has resulted in increased scrutiny on data transfers generally and may increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business internationally.

Following Brexit, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the United Kingdom and the EU have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The United Kingdom and the U.S. are also in discussions to develop a US-UK "data bridge", which would function similarly to the EU-U.S. Data Privacy Framework and provide an additional legal mechanism for companies to transfer data from the United Kingdom to the U.S. In addition to the United Kingdom, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK "data bridge" in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws

may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the United States regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Risks Related to Our Financial Position

We face new challenges as a smaller, less diversified company following the sale of our oncology business to Servier.

We developed most of our initial products and product candidates for the treatment of various types of cancer. The sale of our oncology business to Servier in 2021, including our approved products at the time of sale, TIBSOVO® and IDHIFA®, has resulted in us being a smaller, less diversified company with a more limited business concentrated on products and product candidates for the treatment of rare diseases. The success of the rare disease business is subject to various risks and uncertainties, including the possibility that we may not be able to successfully commercialize PYRUKYND®, the possibility that PYRUKYND® is not approved for thalassemia or in indications other than PK deficiency, the possibility of adverse clinical and other developments in respect of PYRUKYND® or our other product candidates of the rare disease business, and unanticipated changes in applicable laws and regulations that may adversely affect the rare disease business.

We may be more susceptible to changing market conditions, including fluctuations and risks particular to the markets for patients with rare diseases, than a more diversified company, which could adversely affect our business, financial condition and results of operations. In addition, even with the FDA approval of PYRUKYND® for PK deficiency, the diversification of our revenues, costs and cash flows has diminished following the sale of our oncology business. Our results of operations, cash flows, working capital and financing requirements may be subject to increased volatility and our ability to fund capital expenditures and investments or satisfy other financial commitments may be diminished.

The amount of contingent consideration we will receive with respect to vorasidenib is subject to various risks and uncertainties.

As part of the sale of our oncology business to Servier, Servier agreed to pay to us:

- $200.0 million in cash if, prior to January 1, 2027, vorasidenib is granted approval for an NDA from the FDA with an approved label that permits vorasidenib's use as a single agent for the adjuvant treatment of patients with Grade 2 glioma that have an IDH1 or IDH2 mutation (and, to the extent required by such approval, the vorasidenib companion diagnostic test is granted an FDA premarket approval), or the Vorasidenib Milestone Payment; and
- a royalty payment of 15% of the U.S. net sales (as defined in the purchase agreement with Servier) of vorasidenib from its first commercial sale through loss of exclusivity of vorasidenib, or the Vorasidenib Royalty Rights.

In May 2024, we entered into a purchase and sale agreement with Royalty Pharma, pursuant to which we agreed to sell the Vorasidenib Royalty Rights to Royalty Pharma for an upfront payment of $905.0 million in cash, or the Upfront Payment. The consummation of the sale and payment of the purchase price are subject to approval of vorasidenib by the FDA on or before October 31, 2024, and other customary closing conditions. Upon the consummation of the sale, Royalty Pharma will acquire 100% of the Vorasidenib Royalty Rights payments made by Servier on account of up to $1.0 billion in net sales for each calendar year. Any such Vorasidenib Royalty Rights payments made by Servier on account of U.S. net sales in each calendar year in excess of $1.0 billion will be split, with Royalty Pharma having the rights to a 12% earn-out on those excess payments and Agios retaining the Retained Earn-Out Rights. We also retained our rights to the Vorasidenib Milestone Payment.

The contingent consideration described above is subject to various risks and uncertainties. Although the FDA assigned Servier's NDA for vorasidenib a Prescription Drug User Fee Act action date of August 20, 2024, there is no guarantee that vorasidenib will be approved by the FDA, and that, as such we will receive the Vorasidenib Milestone Payment, the Upfront Payment from Royalty Pharma or any potential royalties on sales of vorasidenib.

If the sale to Royalty Pharma is consummated, we will only be entitled to royalty payments on U.S. net sales of vorasidenib if such sales are in excess of $1.0 billion in a calendar year. We cannot predict what success, if any, Servier may have in the United States with respect to future sales of vorasidenib, if approved, or whether Servier will have more than $1.0 billion in net

sales in any calendar year, and, therefore, we cannot predict the amount of royalty payments that we may receive prior to the loss of exclusivity of vorasidenib, if any.

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

Until such time, if ever, as we can generate substantial product revenue, including from sales of PYRUKYND®, we expect to finance our cash needs primarily through cash on hand, a potential Upfront Payment from Royalty Pharma if vorasidenib is approved by the FDA, a potential Vorasidenib Milestone Payment from Servier, potential royalty payments with respect to the Retained Earn-Out Rights, and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings. We do not have any committed external source of funds other than the potential Upfront Payment, the Vorasidenib Milestone Payment and the Retained Earn-Out Rights described above. 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, may require us to enter into agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

If our existing capital is insufficient to fund our operating expenses and capital expenditures, we will need to raise capital, and if we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to incur significant expenses as we continue to advance our ongoing activities. Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities to be available to fund our operating expenses and capital expenditures is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds. Our future capital requirements will depend on many factors, including:

- the amount and timing of future revenue received from commercial sales of PYRUKYND® and any of our other product candidates for which we may receive marketing approval;
- whether vorasidenib is approved by the FDA and the sale of the Vorasidenib Royalty Rights to Royalty Pharma is consummated;
- the amount of payments, if any, we may receive on account of the Retained Earn-Out Rights;
- the costs and timing of our ongoing commercialization activities, including product manufacturing, sales, marketing and distribution, for PYRUKYND® for the treatment of adults with PK deficiency in the approved jurisdictions;
- the anticipated cost-savings associated with the evolution of our research organization;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs associated with in-licensing or acquiring assets for pipeline growth, including the amount and timing of future milestone and royalty payments payable to Alnylam pursuant to the license agreement;
- the costs, timing and outcome of regulatory review of our product candidates, including with respect to our anticipated regulatory submissions for PYRUKYND® for the treatment of thalassemia;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for any of our product candidates for which we may receive marketing approval;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- our ability to successfully execute on our strategic plans;
- operational delays due to public health epidemics, including the COVID-19 pandemic; and

- operational delays, disruptions and/or increased costs associated with global economic developments, rising global energy prices or energy shortages or rationing.

We have historically incurred operating losses. We expect to incur losses in the future and may never achieve or maintain profitability.

We have a history of incurring operating losses. Our net losses for the six months ended June 30, 2024 and 2023 were $177.7 million and $164.8 million, respectively. As of June 30, 2024, we had an accumulated deficit of $1.0 billion. Prior to the sale of our oncology business to Servier in March 2021, we had generated only modest revenue from sales of TIBSOVO® and, prior to our sale to Royalty Pharma of our royalty rights to IDHIFA®, from royalties on sales of IDHIFA®. Following receipt of marketing approval in February 2022, we have begun to commercialize PYRUKYND® for the treatment of hemolytic anemia in adults with PK deficiency in the United States. We are currently providing access to PYRUKYND® free of charge for eligible patients in the EU and Great Britain through a global managed access program, and we provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions through the global managed access program on either a free of charge or for charge basis. Beyond the global managed access program, we continue to evaluate options for the commercialization of PYRUKYND® outside of the United States, including through exploring potential partnership opportunities, such as the NewBridge Agreement.

PYRUKYND® is the first product we have received marketing approval for following the sale of our oncology business. We have neither obtained marketing approval for PYRUKYND® in any other indications nor have we obtained marketing approval for any of our other product candidates, all of which are in preclinical or clinical development stages.

Following the sale of our oncology business, we have financed and expect to continue to finance our operations primarily through cash on hand, royalty payments from Servier with respect to U.S. net sales of TIBSOVO® prior to the sale of these royalty rights to Sagard, proceeds from the sale of our rights to the royalty on U.S. net sales of TIBSOVO® to Sagard, a potential Upfront Payment from Royalty Pharma if vorasidenib is approved by the FDA, a potential Vorasidenib Milestone Payment from Servier, potential royalty payments with respect to the Retained Earn-Out Rights, and, potentially, collaborations, strategic alliances, licensing arrangements and other nondilutive strategic transactions. In addition, we may pursue opportunistic debt offerings, and equity or equity-linked offerings. We expect to continue to incur significant expenses and net losses until such time as we are able to report profitable results. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that we will incur significant expenses if and as we:

- commercially launch PYRUKYND® for approved indications in approved jurisdictions;
- continue to establish and maintain a sales, marketing and distribution infrastructure to commercialize PYRUKYND® and other product candidates for which we may obtain marketing approval;
- initiate and continue clinical trials for our products and product candidates, including PYRUKYND® in other indications;
- continue our research and preclinical development of our product candidates and seek to identify additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials, including our anticipated regulatory submissions for PYRUKYND® for the treatment of thalassemia;
- require the manufacture of larger quantities of product candidates for clinical development and commercialization;
- maintain, expand and protect our intellectual property portfolio;
- add additional personnel to support our product research and development and planned future commercialization efforts and our operations;
- add equipment and physical infrastructure to support our research and development; and
- acquire or in-license other product candidates, medicines and technologies.

To become and remain profitable, we must develop and successfully commercialize medicines with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those medicines for which we may obtain marketing approval and satisfying any post-marketing requirements. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or the Tax Act, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The Tax Act, among other things, contained significant changes to corporate taxation.

As part of Congress' response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021. Such legislation contains numerous tax provisions. In addition, the Inflation Reduction Act of 2022, or IRA, was signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded corporations. The 1% excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. Regulatory guidance under the IRA, the Tax Act, and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the IRA, the Tax Act, and additional tax legislation.

Risks Related to Our Dependence on Third Parties

We rely and expect to continue to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We do not independently conduct clinical trials of any of our product candidates. We rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. In addition, we currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time. If any of our relationships with these third parties terminate, we may not be able to enter into similar arrangements with alternative third-parties or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional cost and requires management time and focus. As a result, delays may occur in our product development activities. Although we seek to carefully manage our relationships with our CROs, we could encounter such challenges or delays that could have a material adverse impact on our business, financial condition and prospects.

Our reliance on third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our responsibility to comply with any such standards. We and these third parties are required to comply with current good clinical practices, or cGCP, which are regulations and guidelines enforced by the FDA, the competent authorities of the member states of the EEA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you a given regulatory authority will determine that any of our clinical trials comply with cGCP regulations. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, clinicaltrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. We are exposed to risk of fraud or other misconduct by such third parties.

Furthermore, third parties on whom we rely may also have relationships with other entities, some of which may be our competitors. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going clinical, nonclinical, and preclinical programs.

If these third parties 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 is compromised, our clinical trials may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to successfully commercialize our medicines.

If either we or any third parties on which we rely are adversely impacted by rising global energy costs or energy shortages or rationing, delays may occur in our product development activities, which delays could have a material adverse impact on our business, financial condition and prospects.

We also rely and expect to continue to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and for commercialization.

We do not have any manufacturing or supply chain-related facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the materials and manufacture of our product candidates for preclinical and clinical testing and for commercial supply of PYRUKYND® and any product candidate for which we obtain marketing approval.

Although we have entered into long-term supply agreements for commercial supply of PYRUKYND® with third-party manufacturers, we may be unable to establish similar long-term supply agreements with third-party manufacturers with respect to our other product candidates or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance, quality assurance, environmental and safety and pharmacovigilance reporting;
- the possible breach of the manufacturing agreement by the third party; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMPs, regulations or similar regulatory requirements on a global basis. Our failure, or the failure of our third-party manufacturers, to comply with currently applicable regulations, or regulations or specifications to which we become subject in the future, could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

In addition, we currently rely on foreign third-party manufacturers and/or CROs, including those in China, and will likely continue to rely on foreign third-party manufacturers and/or CROs in the future. Foreign third-party manufacturers and/or CROs may be subject to U.S. legislation, including sanctions, trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material or services available to us, delay the procurement or supply of such material or services or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. Moreover, in January 2024, the U.S. House of Representatives introduced the BIOSECURE Act (H.R. 7085) and the Senate advanced a substantially similar bill (S.3558), which legislation, if passed and enacted into law, would have the potential to restrict the ability of U.S. biopharmaceutical companies like us to purchase services or products from, or otherwise collaborate with, certain Chinese biotechnology companies "of concern," without losing the ability to contract with, or otherwise receive funding from, the U.S. government. It is possible some of our contractual counterparties could be impacted by this legislation.

If either we or any third parties on which we rely are adversely impacted by restrictions resulting from the COVID-19 pandemic, the emergence of another public health epidemic, by rising global energy costs or energy shortages or rationing and/or the impacts of the Russia-Ukraine war, our supply chain may be disrupted, limiting our ability to manufacture our product candidates for our clinical trials and research and development operations and our product for commercialization.

Any performance failure on the part of our existing or future manufacturers could delay preclinical development, clinical development, marketing approval or our commercialization efforts. Due to the volatility of the supply networks globally, we have obtained regulatory approval for redundant supply of raw materials and active pharmaceutical ingredient for PYRUKYND®, and have an ongoing program to monitor supply, including establishing safety stocks. While we maintain a broad safety stock of drug product, we do not currently have arrangements in place for redundant supply for drug product. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product or our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We may depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek collaborations for the development and commercialization of our product candidates, such as the NewBridge Agreement, with large and mid-size pharmaceutical companies and biotechnology companies. We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate and document. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. Collaborators may have rights that restrict us from entering into future agreements on certain terms with potential collaborators.

If we enter into any such arrangements with collaborators, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities. Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing, which may result in a need for additional capital to pursue further development or commercialization of the applicable product candidate. Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources. In addition, our ability to enter into arrangements with collaborators in specific regions, such as the Middle East, may be affected by localized geopolitical unrest or military conflict, such as the current armed conflict in the region.

Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent or trade secret protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary medicines and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and medicines that are important to our business. We do not yet have issued patents for all our most advanced product candidates in all markets in which we intend to commercialize but we continue to actively pursue patent protection for our assets around the world.

The patent prosecution process is costly and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify and/or file patent applications on every aspect of our research and development output that is or may be eligible for patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who may have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. There is also the possibility that loss or theft of data or records may jeopardize the ability to seek patent protection or impede the progress or drafting of patent applications.

We have licensed patent rights, and in the future may license additional patent rights, from third parties. Such licenses may be accompanied by milestone and/or royalty payment obligations. These licensed patent rights may be valuable to our business, and we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In

addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or medicines or that effectively prevent others from commercializing competitive technologies and medicines. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to make the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. Beginning in March 2013, the United States transitioned to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of the patent or in one or more patent claims being narrowed or invalidated, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and medicines. Given the significant amount of time required for the discovery, development, preclinical and clinical testing and regulatory review and approval of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. In such circumstances we would be relying primarily on regulatory or marketing exclusivity to exclude others from commercializing a generic version of our products.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, 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 proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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.

Third parties may initiate legal proceedings alleging that we or our collaborators are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product and product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. We have in the past, are and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our medicines and technology, including opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference

proceedings before the USPTO or other patent offices around the world. For example, two of the European patents in our mitapivat portfolio, neither being the primary compound patent, have been challenged in opposition proceedings in the European Patent Office. The revocation of either of these European patents could potentially allow additional competitor drugs, if approved, to enter the European marketplace earlier than anticipated.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we or one of our collaborators are found to infringe a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we or our collaborators may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our collaborators were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We or our collaborators could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we or our collaborators could be found liable for monetary damages. A finding of infringement could prevent us or our collaborators from commercializing our product and product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we or our collaborators have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Many of our employees, consultants or advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our organization.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our confidential information related to our proprietary platforms and technology, our business and competitive position could be harmed.

In addition to seeking patents for some of our technology and medicines, we also rely on maintaining the confidentiality of unpatented know-how, technology and other proprietary information, to maintain our competitive position. For example, we consider the confidential information and know-how related to our cellular metabolism technology platform to be our primary intellectual property assets in this space. Unpatented proprietary technical information and know-how can be difficult to protect.

We seek to protect this proprietary technical information and know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive and time-consuming, and the outcome is unpredictable. If any of our proprietary technical information and know-how were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. Moreover, we anticipate

that with respect to this platform, at least some of this technical information and know-how will, over time, be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

The FDA, EMA and other foreign regulatory authorities have substantial discretion in the approval process. Accordingly, it is possible that the FDA or EMA may refuse to accept for substantive review any NDA, supplemental NDA or MAA that we submit for our product candidates, or may conclude after review of our data that our marketing application is insufficient to obtain marketing approval of our product candidates. If the FDA or EMA does not accept or approve our applications for any of our product candidates, the applicable regulator may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before reconsidering our applications. Depending on the extent of these or any other FDA- or EMA-required trials or studies, approval of any marketing applications that we submit may be delayed by several years, or may require us to expend more resources than we planned. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA or EMA to approve any marketing applications. We may not be successful in obtaining FDA or EMA approval of our product candidates on a timely basis, or ever. We have limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process, and failure to obtain marketing approval for our product candidates will prevent us from commercializing the product candidate in the applicable jurisdictions.

Further, the process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application.

Disruptions at the FDA and other agencies may prolong the time necessary for regulatory submissions to be reviewed and/or new drugs to be 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 employees and stop critical activities. If a prolonged government shutdown were to occur, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. For example, should the FDA determine that an inspection is necessary for approval of a regulatory submission and an inspection cannot be completed during the review cycle, and the FDA does not determine a remote interactive evaluation to be adequate, the FDA has stated that it generally intends to issue a complete response letter or defer action on the regulatory submission until an inspection can be completed.

Several significant administrative law cases were decided by the U.S. Supreme Court in 2024, most notably *Loper Bright Enterprises v. Raimondo*, which overruled *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc*. Since 1984, *Chevron* had required that courts defer to reasonable agency interpretations of statutes and agency action. In *Loper Bright*, the Supreme Court held that the U.S. Administrative Procedure Act requires courts to exercise their independent judgment when

deciding whether an agency has acted within its statutory authority, and that courts may not defer to an agency interpretation solely because a statute is ambiguous. These decisions may result in additional legal challenges to regulations and guidance issued by federal regulatory agencies, including the FDA and CMS, that we have relied on and intend to rely on in the future. Any such challenges, if successful, could have an impact on our business, and any such impact could be material. In addition to potential changes to regulations and agency guidance as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays in and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations.

Finally, our ability to develop and market new drug products may be impacted if litigation challenging the FDA's approval of another company's drug continues. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS.

The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market, but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that the FDA authorized in 2016 and 2021 were arbitrary and capricious. In June 2024, the Supreme Court reversed and remanded that decision after unanimously finding that the plaintiffs did not have standing to bring this legal action against the FDA. Depending on the outcome of this litigation, if it continues, our ability to develop new drug product candidates and to maintain approval of existing drug products and measures adopted under a REMS is at risk and our efforts to develop and market new drug products could be delayed, undermined or subject to protracted litigation.

If we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our medicines from being marketed in such jurisdictions and any of our medicines that are approved for marketing in such jurisdiction will be subject to risk associated with foreign operations.

In order to market and sell our medicines in the EU and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval 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, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Moreover, approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. Although we have received marketing authorization for PYRUKYND® for the treatment of adults with PK deficiency in the EU and Great Britain, we may not be able to file for additional marketing approvals and may not receive necessary approvals to commercialize our medicines in any other foreign market.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the withdrawal of the United Kingdom from the EU on December 31, 2020, commonly referred to as Brexit. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, the consequences of Brexit and the impact on the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom remains unclear. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to EU rules under the Northern Ireland Protocol. The United Kingdom and the EU have however agreed to the Windsor Framework which fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the United Kingdom. Once implemented, the changes introduced by the Windsor Framework will result in the MHRA being responsible for approving all medicinal products destined for the United Kingdom market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may prevent us from commercializing any product candidates in the United Kingdom and/or the EU and may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, 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. The European Commission's proposal for revision of several legislative instruments related to medicinal products (including potentially reducing the duration of regulatory data protection and revising the eligibility for expedited pathways) was published in April 2023, and the European Parliament has requested several amendments. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States. In addition, we do not have experience commercializing products outside of the United States and such efforts may depend on our ability to find a suitable collaborator.

Fast track designation and/or priority review designation by the FDA or PRIME designation in the EU may not actually lead to a faster development or regulatory review or approval process, nor does it assure approval of the product candidate by the FDA or the EMA.

We may seek fast track designation, priority review designation and/or PRIME designation for our product candidates.

If a product candidate is intended for the treatment of a serious or life-threatening disease or condition and the product candidate demonstrates the potential to address unmet medical needs for this disease or condition, the drug sponsor may apply for FDA fast track designation.

Further, if the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or thereafter.

The FDA has broad discretion on whether to grant fast track designation and/or priority review designation to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Even if our product candidates receive fast track designation and/or priority review designation, we may not experience a faster development process, review or approval, if at all, compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

In addition, in the EU, the PRIME designation program focuses on product candidates that target conditions for which there exists no satisfactory method of treatment in the EU or product candidates that may offer a major therapeutic advantage over existing treatments. The benefits of a PRIME designation include, among other things, the potential to qualify product for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME designation enables a sponsor to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if our product candidates receive PRIME designation, we may not experience a faster development process, review or approval compared to conventional EMA procedures and it does not assure or increase the likelihood of the EMA's grant of a marketing authorization.

We, or any collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our drug candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing drugs.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the United States and currently ten years in Europe. The European exclusivity period can be reduced to six years if a product no

longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA 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. Moreover, even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

In addition, even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. We do not know if, when, or how the FDA or Congress may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Any product or product candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

Any product or product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and record keeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we market our medicines for uses other than their respective approved indications, we may be subject to enforcement actions for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws, which violations may result in the imposition of significant administrative, civil and criminal penalties.

Our relationships with healthcare providers, physicians and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of PYRUKYND® and any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute PYRUKYND® and any other medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false

or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;

- HIPAA imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals and other covered recipients; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are 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 significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of member states of the EU, or the EU Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

PYRUKYND® or any product candidate that we commercialize may become subject to unfavorable pricing regulations and third-party reimbursement practices, which would harm our business.

We have built our commercial infrastructure to support the commercial launch of PYRUKYND® in adult PK deficiency in the United States. We are providing access to PYRUKYND® free of charge for eligible patients in the EU and Great Britain through a global managed access program, and we provide access to PYRUKYND® for adult patients with PK deficiency in other jurisdictions through the global managed access program on either a free of charge or for charge basis. The commercial success of PYRUKYND® or of any of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any collaborators, may not be able to successfully commercialize PYRUKYND® or our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and 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 will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. 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 our product candidates 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.

As a result, we, or any collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any collaborators, to commercialize PYRUKYND® or any of our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any collaborators to sell PYRUKYND® or our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenue. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for PYRUKYND® or any product candidate that we, or any collaborator, may commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for PYRUKYND® or any of our product candidates for which we, or any collaborator, may obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Current and future healthcare reform legislation may increase the difficulty and cost for us and any collaborators to obtain reimbursement and commercialize our drug candidates.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell PYRUKYND® or any other product for which we, or they, obtain marketing approval. 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 collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the ACA. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This legislation resulted in aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect for six months into fiscal year 2032. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On November 10, 2020, the Supreme Court heard oral arguments as to whether the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. On June 17, 2021, the Supreme Court struck down the lower court rulings, finding that the plaintiffs did not have standing to challenge the ACA's minimum essential coverage provision at issue in the case.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked these orders and issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. This Executive Order also directs the HHS to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic. We cannot predict how federal agencies will respond to such executive orders.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we obtain for our drug products, if and when approved, and/or the sustainability of those prices.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States.

To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and Medicaid. To those ends, President Trump issued several executive orders intended to lower the costs of prescription products. Certain provisions of these orders have been reflected in promulgated regulations, including an interim final rule implementing a most favored nation model for prices, which would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries. Such final rule has been subject to a nationwide preliminary injunction, and, on December 29, 2021, Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With the issuance of this rule, CMS stated it will explore all options to incorporate value into payments for Medicare Part B drugs and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Several states have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the IRA, has been delayed by Congress to January 1, 2032.

The IRA has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to

penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Medicare Part D drugs in 2027, 15 Medicare Part B or Part D drugs in 2028, and 20 Medicare Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

In June 2023, Merck filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce and pharmaceutical companies, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. There have been various decisions by the courts considering these cases since they were filed. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

Accordingly, while it is currently unclear how the IRA will be effectuated, 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.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. 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 product or product candidates or additional pricing pressures.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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 or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If

reimbursement of our product is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We are subject to U.S. and foreign export control, import, sanctions, anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with such laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

With the passage of the CREATES Act, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications.

In December 2019, former President Trump signed legislation intended to facilitate the development of generic and biosimilar products. The bill, previously known as the Creating and Restoring Equal Access to Equivalent Samples Act of 2019, or the CREATES Act, authorizes sponsors of ANDAs and 505(b)(2) applications to file lawsuits against companies holding NDAs that decline to provide sufficient quantities of an approved reference drug on commercially reasonable, market-based terms. Drug products on FDA's drug shortage list are exempt from these new provisions unless the product has been on the list for more than six continuous months or the FDA determines that the supply of the product will help alleviate or prevent a shortage. For the purposes of the statute, the term "commercially reasonable, market-based terms" is defined as (1) the nondiscriminatory price at or below the most recent wholesale acquisition cost for the product, (2) a delivery schedule that meets the statutorily defined timetable, and (3) no additional conditions on the sale.

To bring an action under the statute, an ANDA or 505(b)(2) sponsor must take certain steps to request the reference product, which, in the case of products covered by a Risk Evaluation and Mitigation Strategy with elements to assure safe use, include obtaining authorization from the FDA for the acquisition of the reference product. If the sponsor does bring an action for failure to provide a reference product, there are certain affirmative defenses available to the NDA holder, which must be shown by a preponderance of evidence. If the sponsor prevails in litigation, it is entitled to a court order directing the NDA holder to provide, without delay, sufficient quantities of the applicable product on commercially reasonable, market-based terms, plus reasonable attorney fees and costs.

Additionally, the statutory provisions authorize a federal court to award the product developer an amount "sufficient to deter" the NDA holder from refusing to provide sufficient product quantities on commercially reasonable, market-based terms if the court finds, by a preponderance of the evidence, that the NDA holder did not have a legitimate business justification to delay providing the product or failed to comply with the court's order.

Although we intend to fully comply with the terms of these new statutory provisions, we are still exposed to potential litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of ANDAs and 505(b)(2) applications. Such litigation would subject us to additional costs, damages and reputational harm, which could lead to lower revenues. The CREATES Act

may enable generic competition with PYRUKYND® and any of our product candidates, if approved, which could impact our ability to maximize product revenue.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our key executives and scientific leadership and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams, each of whom is employed "at will," meaning we or they may terminate the employment relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We cannot predict the likelihood, timing or effect of future transitions among our executive leadership.

Recruiting and retaining qualified scientific, clinical, manufacturing, regulatory 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 and universities and research institutions for similar personnel. Our consultants and advisors, including our scientific co-founders, who assist us in formulating our research and development and commercialization strategy 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. Furthermore, our flexible workplace policy which allows employees to work from home may make it difficult for us to maintain our corporate culture.

In the future we may experience growth in the number of our development, regulatory and sales and marketing personnel. To manage any anticipated future growth, 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. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations or regulations in other jurisdictions, provide accurate information to the FDA or other regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately, disclose unauthorized activities to us, or comply with securities laws. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, including for illegal insider trading activities, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective 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 be in compliance with such 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 and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Our Common Stock and Other Matters

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing the members of our management team, 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. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our Board of Directors;
- limit the manner in which stockholders can remove directors from our Board of Directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our Board of Directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a shareholder rights plan, or so-called "poison pill," that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The price of our common stock is likely to be volatile, which could result in substantial losses for purchasers of our common stock.

The trading price of our common stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. For example, since January 1, 2015 the closing price of our common stock on the Nasdaq Global Select Market has ranged from $17.06 per share to $135.01 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. While the full extent of the economic impact of the recent increases in inflation rates (particularly as it relates to clinical- or manufacturing-related costs) may be difficult to assess or predict, such impacts have already caused, and are likely to result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms. If we are unable to raise additional funds through equity or debt financings when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

The market price for our common stock may be influenced by many factors, including:

- our success in launching and commercializing PYRUKYND®;
- the decision to focus our efforts on our rare disease business;
- the evolution of our research organization;
- whether the sale of the Vorasidenib Royalty Rights to Royalty Pharma will be consummated;

- announcements by us or our competitors of significant acquisitions, in-licensing arrangements, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of product candidates, or our competitors' product candidates;
- regulatory actions with respect to our product or product candidates or our competitors' products and product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our products, product candidates or development programs;
- the results of our efforts to develop additional product candidates and products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders, including shares issuable upon exercise of outstanding stock options and upon vesting of stock units under our stock incentive plans;
- variations in our financial results or results of companies that are perceived to be similar to us;
- changes in estimates, evaluations or recommendations by securities analysts, that cover our stock or the failure by one or more securities analysts to continue to cover our stock;
- changes in the structure of healthcare payment systems;
- the societal and economic impact of public health epidemics or pandemics, such as the COVID-19 pandemic and any recession, depression or sustained market event resulting from such epidemics or pandemics;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert managements' attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

We also cannot guarantee that an active trading market for our shares will be sustained. An inactive trading market for our common stock may impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Our financial condition and operating results also may fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of June 30, 2024, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. 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 persons could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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

Under Section 382 of the Code and corresponding provisions of state law, if a company undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership by certain stockholders over a three-year period, the company's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income may be limited. Our prior equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership

change. We completed a review of our changes in ownership through December 31, 2023, and determined that we did not have a qualified ownership change since our last review as of December 31, 2022. Future ownership changes under Section 382 may limit the amount of net operating loss and tax credit carryforwards that we could potentially utilize to reduce future tax liabilities.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. The Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons we may be unable to use a material portion of our net operating losses and other tax attributes.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different from previous periods or our current expectations due to numerous factors, including as a result of changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors may result in tax obligations in excess of amounts accrued in our financial statements.

We incur costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

We have incurred and will continue to incur significant legal, accounting and other expenses as a public company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select 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. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations. Our management and other personnel devote, and will need to continue to devote, a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Item 5. Other Information

(c) ***Director and Officer Trading Arrangements***

A significant portion of the compensation of our directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) is in the form of equity awards and, from time to time, directors and officers engage in open-market transactions with respect to the securities acquired pursuant to such equity awards or other of our securities, including to satisfy tax withholding obligations when equity awards vest or are exercised, and for diversification or other personal reasons.

Transactions in our securities by directors and officers are required to be made in accordance with our insider trading policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in our securities in a manner that avoids concerns about initiating transactions while in possession of material nonpublic information.

None of our directors or officers terminated a Rule 10b5-1 trading arrangement or adopted or terminated a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the quarterly period covered by this report.

Item 6. Exhibits

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation	8-K	001-36014	July 30, 2013	3.1	
3.2	Third Amended and Restated By-Laws	8-K	001-36014	March 3, 2023	3.1	
10.1†	Purchase and Sale Agreement, dated May 24, 2024, by and between the Registrant and Royalty Pharma Investments 2019 ICAV					X
31.1	Certification of principal executive officer pursuant to Rule 13a 14(a)/15d 14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1*	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2*	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are not embedded within the Inline XBRL document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Label Linkbase Document					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101.INS)					X

* This certification will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

† Portions of this exhibit 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.

AGIOS PHARMACEUTICALS, INC.

August 1, 2024 By: /s/ Brian Goff

Brian Goff
Chief Executive Officer
(principal executive officer)

August 1, 2024 By: /s/ Cecilia Jones

Cecilia Jones
Chief Financial Officer
(principal financial officer)

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

PURCHASE AND SALE AGREEMENT

dated as of May 24, 2024

by and between

AGIOS PHARMACEUTICALS, INC.,

as SELLER

and

ROYALTY PHARMA INVESTMENTS 2019 ICAV,

as PURCHASER

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PURCHASE AND SALE AGREEMENT

This PURCHASE AND SALE AGREEMENT (this "Purchase and Sale Agreement") dated as of May 24, 2024 is by and among Agios Pharmaceuticals, Inc., a Delaware corporation and the Person defined as "Seller" in the Counterparty Agreement (the "Seller"), and Royalty Pharma Investments 2019 ICAV (the "Purchaser").

W I T N E S E T H:

WHEREAS, the Seller has the right to receive fifteen percent (15.0%) of Net Sales of the Earn-Out Product (vorasidenib) (as defined below) in the US Territory under the Counterparty Agreement;

WHEREAS, the Seller desires to sell, contribute, assign, transfer, convey and grant to the Purchaser, and the Purchaser desires to purchase, acquire and accept from the Seller its rights, title and interest in and to the Purchased Assets (as defined below), upon and subject to the terms and conditions set forth in this Purchase and Sale Agreement;

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

ARTICLE I
DEFINED TERMS AND RULES OF CONSTRUCTION

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

"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 Voting Securities, by contract or otherwise, and the terms "controlled" and "controlling" have meanings correlative to the foregoing.

"Annual Net Sales Statement" has the meaning set forth in Section 2.13(a)(iv) of the Counterparty Agreement.

"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 Percentage" means, in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring in the US Territory during each calendar year, 100.0% until the Purchaser has actually received $150 million in Vorasidenib Receivables hereunder in respect of such Net Sales occurring in the US Territory during such calendar year, and, for the remainder of

such calendar year, 80.0%. For clarity, with respect to Net Sales of the Earn-Out Product (vorasidenib) occurring in the US Territory during each calendar year as described in the prior sentence, the "Vorasidenib Receivables" constitute 15.0% of such Net Sales until the Purchaser has actually received $150 million in Vorasidenib Receivables hereunder in respect of such Net Sales occurring in the US Territory during such calendar year, and, for the Net Sales occurring in the US Territiory during the remainder of such calendar year, 12.0% of such Net Sales.

"Applicable Patent Rights" means the "Earn-Out Patent Rights" with respect to the Earn-Out Product (vorasidenib) described in sub-part (b) of the definition of "Earn-Out Patent Right" in Section 1.1 of the Counterparty Agreement.

"Audit Reports" means any reports, summaries of preliminary conclusions, and final conclusions of any Independent Accounting Firm pursuant to Section 2.13(e) of the Counterparty Agreement.

"Bankruptcy Event" means the occurrence of any of the following in respect of a Person: (a) (i) an admission in writing by such Person of its inability to pay its debts generally as they become due or (ii) a general assignment by such Person for the benefit of creditors; (b) the filing of any petition 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) whether with or without the consent or acquiescence of such Person, the entering of an order for relief or approving 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, with or without the consent or acquiescence of such Person, the entering 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 [**] from entry thereof.

"Bill of Sale" means that certain bill of sale effective as of the Closing Date executed by the Seller and the Purchaser substantially in the form of Exhibit A.

"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.

"Capital Securities" means, with respect to any Person, all shares, interests, participations or other equivalents (however designated, whether voting or non-voting) of such Person's capital, whether now outstanding or issued after the Effective Date, including common shares, ordinary shares, preferred shares, membership interests or share capital in a limited liability company or other Person, limited or general partnership interests in a partnership, beneficial interests in trusts or any other equivalent of such ownership interest or any options, warrants and other rights to acquire such shares or interests, including rights to allocations and distributions, dividends, redemption payments and liquidation payments.

"Closing" means the sale, contribution, assignment, transfer, conveyance and grant of the Purchased Assets contemplated hereunder.

"Closing Date" means the date on which the Closing occurs pursuant to Section 2.1(a).

"Counterparty" means each of Servier and Servier SAS, and their permitted successors and assigns (collectively, the "Counterparties").

"Counterparty Agreement" means that certain Purchase and Sale Agreement, dated as of December 20, 2020, by and among Seller and the Counterparties, as amended, modified or otherwise supplemented from time to time, including pursuant to the Counterparty Consent.

"Counterparty Consent" means that certain Consent Agreement dated May 23, 2024 between Seller and Counterparty, a true, correct and complete copy of which is attached hereto as Exhibit F.

"Counterparty Instruction" means the irrevocable direction to each Counterparty substantially in the form of Exhibit B.

"Credit Event" means any insolvency, bankruptcy, receivership, assignment for the benefit of creditors, or similar proceeding, following or as a result of which any Counterparty fails to pay amounts owing under the Counterparty Agreement in respect of the Vorasidenib Receivables as a result of the Counterparty's financial distress, creditworthiness, or insolvency.

"Deposit Account" means the bank account described on the Schedule 1.2 under the heading "Deposit Account" for the benefit of the Purchaser, as such bank account may be changed by the Purchaser in its sole discretion from time to time upon prior written notice to the Seller in accordance with Section 5.4(b).

"Disclosure Schedule" means the Disclosure Schedule, attached hereto as Exhibit E and dated as of the date hereof and delivered by the Seller to the Purchaser.

"Disputed Amount" has the meaning set forth in Section 2.13(j) of the Counterparty Agreement.

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

"Earn-Out Product (vorasidenib)" means an isocitrate dehydrogenase-1 & 2 (IDH1 & 2) inhibitor that has the compound AG-881 as its active ingredient.

"Earn-Out Product Transaction" has the meaning set forth in Section 2.13(g) of the Counterparty Agreement.

"Effective Date" means the date of this Agreement.

"Excluded Liabilities and Obligations" has the meaning set forth in Section 2.3.

"FD&C Act" means the United States Federal Food, Drug, and Cosmetic Act.

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

"FDA Approval" means Regulatory Approval from FDA for the Earn-Out Product (vorasidenib).

"FDA Approval Date" means the date FDA Approval is received.

"GAAP" means generally accepted accounting principles in effect in the United States from time to time.

"Governmental Authority" means the government of the United States, any other nation or any political subdivision thereof, whether state or local, 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.

"Independent Accounting Firm" has the meaning set forth in the Counterparty Agreement.

"Knowledge" means, with respect to the Seller, the actual knowledge of [**], or any successor to any such individuals holding the same or substantially similar officer positions at the applicable time, after internal due inquiry with such individuals (and excluding, for the avoidance of doubt, any inquiries with the Counterparty or any other third party, it being understood that, since consummation of the transactions contemplated by the Counterparty Agreement in December 20, 2020, Seller's knowledge of the Earn-Out Product (vorasidenib) and related issues is limited and indirect).

"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, or any other restriction on transfer.

"Loss" means any loss, damage, assessment, award, cause of action, claim, charge, cost, expense, fine, judgment, liability, obligation, penalty or, solely for purposes of Section 7.1 but

not for Section 7.2, Receivables Reduction for which, in the case of any Receivables Reduction, Seller is liable under Section 5.4(d) and as to which Seller has not paid Purchaser in accordance with Section 5.4(d).

"Material Adverse Change" means (i) a material adverse effect on the legality, validity or enforceability of the Transaction Documents or the Counterparty Agreement (as it relates to the Purchased Assets), (ii) a material adverse effect on the ability of the Seller to perform any of its obligations under the Transaction Documents, (iii) a material adverse effect on the rights of the Seller or the Purchaser under the Counterparty Agreement with respect to the Purchased Assets, other than as a result of a Permitted Deduction or Credit Event, (iv) a material adverse effect on the validity or enforceability of any of the Applicable Patent Rights that, if adversely determined, would reasonably be expected to adversely affect in any material respect the timing, amount or duration of the payments to be made to the Purchaser in respect of the Purchased Assets, provided that acts or omissions of Seller after December 20, 2020, shall not be the basis for any Material Adverse Change under this clause (iv) unless any such act or omission was taken (or not) with the intent or knowledge that such action or omission would reasonably be likely to have such effect, or (v) an adverse effect in any material respect on the timing, amount or duration of the payments to be made to the Purchaser in respect of the Vorasidenib Receivables or the right of the Purchaser to receive such payments, other than as a result of a Permitted Deduction or Credit Event.

"Net Sales" has the meaning set forth in Section 1.1 of the Counterparty Agreement.

"Net Sales Term" has the meaning set forth in Section 1.1 of the Counterparty Agreement as it relates to the Earn-Out Product (vorasidenib).

"Permitted Deductions" means (i) the deductions set forth in items (a)-(k) of the definition of "Permitted Deductions" in Section 1.1 of the Counterparty Agreement to the extent such deductions are actually taken by the Counterparty in the calculation of "Net Sales" for sales of the Earn-Out Product (vorasidenib) that are made in the US Territory from and after the FDA Approval Date, (ii) offsets permitted under clause (B) of the second sentence of 2.13(a)(iv) and Section 2.13(e)(B) of the Counterparty Agreement resulting from Counterparty overpayment of Vorasidenib Receivables to the Purchaser, in each case in respect of "Net Sales" of the Earn-Out Product (vorasidenib) made in the US Territory from and after the FDA Approval Date, and (iii) any deductions or withholdings for Taxes required under Applicable Law in accordance with and subject to Section 5.7(b). For the avoidance of doubt, no other right of set-off, off-set, counterclaim, deduction, withholding, or credit, by contract or otherwise (including offsets or reductions in respect of Third Party License Payments pursuant to Section 2.13(a)(ii) of the Counterparty Agreement and any offset or reduction taken on account of any Disputed Amounts under Section 2.13(j) of the Counterparty Agreement) is a Permitted Deduction.

"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.

"Purchase and Sale Agreement" has the meaning set forth in the preamble.

"Purchase Price" has the meaning set forth in Section 2.2.

"Purchased Assets" means, collectively, (a) the Seller's right, title and interest in, to and under the Counterparty Agreement with respect to the Vorasidenib Receivables and the Receivables Reports, and (b) the right to transfer, assign or pledge the foregoing, in whole or in part, and the payments, accounts, proceeds and income of, and the rights to enforce, each of the foregoing. The Purchased Assets do not include any other rights under the Counterparty Agreement or otherwise including, for the avoidance of doubt, Seller's right, title and interest in the other assets transferred pursuant to the Sagard Agreement.

"Purchaser Indemnified Party" has the meaning set forth in Section 7.1.

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

"Qualified Assignee" means: (i) [**]; or (ii) any other Person designated as such in writing by mutual agreement of the Seller and the Purchaser.

"Quarterly Net Sales Statement" has the meaning set forth in Section 2.13(a)(iii) of the Counterparty Agreement.

"Receivables Reduction" means any right of set-off, off-set, counterclaim, deduction, withholding, or credit, by contract or otherwise, including pursuant to Section 2.13(a)(ii) or Section 2.13(j) of the Counterparty Agreement, other than any Permitted Deductions.

"Receivables Reports" mean Seller's right to: (i) receive the Quarterly Net Sales Statements produced by Counterparty pursuant to Section 2.13(a)(iii) of the Counterparty Agreement in respect of Net Sales of the Earn-Out Product (vorasidenib), (ii) receive the Annual Net Sales Statements produced by Counterparty pursuant to Section 2.13(a)(iv) of the Counterparty Agreement in respect of Net Sales of the Earn-Out Product (vorasidenib), and (iii) receive a summary of preliminary conclusions of any Independent Accounting Firm and to provide comments thereon pursuant to Section 2.13(e) of the Counterparty Agreement and receive the final conclusions of such Independent Accounting Firm pursuant to Section 2.13(e) of the Counterparty Agreement.

"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" mean, collectively, all regulatory approvals, registrations, certificates, authorizations, permits and supplements thereto, as well as associated materials (including the product dossier) pursuant to which the Earn-Out Product (vorasidenib) may be marketed, sold and distributed in a jurisdiction, issued by the appropriate Regulatory Agency.

"Retained Percentage" means, in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring in the US Territory during each calendar year, 0.0% until the Purchaser has actually received $150 million in Vorasidenib Receivables hereunder in respect of such Net Sales occurring in the US Territory during such calendar year, and, for Net Sales occurring in the US Territory during the remainder of such calendar year, 20.0%. For clarity, with respect to Net Sales of the Earn-Out Product (vorasidenib) occurring in the US Territory during each calendar year as described in the prior sentence, the "Retained Receivables" constitute 0.0% of such Net Sales until the Purchaser has actually received $150 million in Vorasidenib Receivables hereunder in respect of such Net Sales occurring in the US Territory during such calendar year, and, for Net Sales occurring in the US Territory during the remainder of such calendar year, 3.0% of such Net Sales.

"Retained Receivables" means, without duplication:

(a) the Retained Percentage of all amounts or fees due, paid or payable, owed or owing, accrued or otherwise to be paid to the Seller or any of its Affiliates under Section 2.13(a)(i)(B) of the Counterparty Agreement in respect of aggregate annual Net Sales of the Earn-Out Product (vorasidenib) made in the US Territory from and after the FDA Approval Date and during the Net Sales Term, and any amounts payable by Counterparty to Seller under the Counterparty Agreement in lieu thereof, but in each case without giving effect to any offsets or reductions in respect of Third Party License Payments pursuant to Section 2.13(a)(ii) of the Counterparty Agreement or any offsets or reductions taken on account of any Disputed Amounts under Section 2.13(j) of the Counterparty Agreement;

(b) all amounts payable resulting from Counterparty underpayments in respect of the Retained Percentage of Net Sales of the Earn-Out Product (vorasidenib) made in the US Territory from and after the FDA Approval Date pursuant to (i) Section 2.13(a)(iii)(B) of the Counterparty Agreement, (ii) clause (B) of the first sentence in Section 2.13(a)(iv) of the Counterparty Agreement, and (iii) Section 2.13(e) of the Counterparty Agreement (in each case (b)(i)-(b)(iii) above, regardless of whether Seller furnishes an invoice to Counterparty for such amounts);

(c) all indemnity payments, guarantees, recoveries, damages or awards or settlement amounts payable by Counterparty to the Seller or any of its Affiliates after the FDA Approval Date as a result of a breach by either Counterparty of the provisions of the Counterparty Agreement related to the Purchased Assets in respect of the amounts described in clause (a) and (b) above, including pursuant to Section 10.3, Section 10.5, and Section 11.15 of the Counterparty Agreement (other than for any unreimbursed costs payable to Seller pursuant to the Counterparty Agreement) related to the period after the FDA Approval Date;

(d) any payments payable to Seller under Section 2.13(i) of the Counterparty Agreement in respect of the payments described in clauses (a)-(c) above related to the period after the FDA Approval Date;

(e) all other amounts paid or payable by Counterparty or any other Person to the Seller or any of its Affiliates arising out of, related to or resulting from the amounts described in clauses (a), (b), (c) and (d) above;

(f) all accounts (as defined under the UCC) evidencing the rights to the payments and amounts described in clauses (a)-(e) above; and

(g) all proceeds (as defined under the UCC) of any of the foregoing.

"Sagard Agreement" means that certain Purchase and Sale Agreement, dated as of October 27, 2022, by and among Seller, Sagard Healthcare Royalty Partners, LP and Sagard Healthcare Partners Co-Invest Designated Activity Company, as amended, modified or otherwise supplemented from time to time not in violation of this Agreement.

"Sale Date" means the "Closing Date" as defined in the Counterparty Agreement, which was March 31, 2021.

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

"Seller Account" means the account described on Schedule 1.2 (or to such other account as the Seller shall notify, the Purchaser in writing from time to time).

"Seller Indemnified Party" has the meaning set forth in Section 7.2.

"Servier" means Servier Pharmaceuticals, LLC, a Delaware limited liability company and the Person defined as "Purchaser" in the Counterparty Agreement.

"Servier SAS" means Servier S.A.S., a French *societe par actions simplifiee* and the Person defined as "Purchaser Guarantor" in the Counterparty Agreement.

"Specified Indemnity Claim" has the meaning set forth in Section 2.13(j) of the Counterparty Agreement, and herein shall be limited to any such claim related to the Purchased Assets or the Earn-Out Product (vorasidenib).

"Specified Tax Withholding" has the meaning set forth in Section 5.7(b).

"Sublicensee" means any licensee or sublicensee of Counterparty in respect of the Earn-Out Product (vorasidenib).

"Subsidiary" means, with respect to any Person, any other Person of which more than 50% of the outstanding Voting Securities of such other Person (irrespective of whether at the time Capital Securities of any other class or classes of such other Person shall or might have voting power upon the occurrence of any contingency) is at the time directly or indirectly owned or controlled by such Person, by such Person and one or more other Subsidiaries of such Person or by one or more other Subsidiaries of such Person.

"Tax" or "Taxes" means any federal, state, local or foreign income, gross receipts, license, payroll, employment, excise, severance, occupation, premium, windfall profits, environmental, customs duties, capital stock, franchise, profits, withholding, social security, unemployment, disability, real property, personal property, abandoned property, value added, alternative or add-on minimum, estimated or other tax of any kind whatsoever, including any interest, penalty or addition thereto, whether disputed or not.

"Third Party License Payments" has the meaning set forth in Section 1.1 of the Counterparty Agreement.

"Transaction Documents" means this Purchase and Sale Agreement, the Bill of Sale and the Counterparty Instruction.

"UCC" means the Uniform Commercial Code as in effect from time to time in the State of Delaware; 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 backup security interest or any portion thereof granted pursuant to Section 2.1(f) is governed by the Uniform Commercial Code as in effect in a jurisdiction of the United States other than the State of Delaware, 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 Purchase and Sale Agreement and any financing statement relating to such perfection or effect of perfection or non-perfection.

"Upstream License Agreement" means that certain Exclusive License Agreement by and among The Johns Hopkins University, Duke University, and the Seller, dated as of November 7, 2009, which agreement was transferred by the Seller to the Counterparty in connection with the Counterparty Agreement on the Sale Date.

"U.S." or "United States" means the United States of America, its 50 states, each territory thereof and the District of Columbia.

"US Territory" has the meaning set forth in Section 1.1 of the Counterparty Agreement.

"Vorasidenib Receivables" means, without duplication:

(a) the Applicable Percentage of all amounts or fees due, paid or payable, owed or owing, accrued or otherwise to be paid to the Seller or any of its Affiliates under Section 2.13(a)(i)(B) of the Counterparty Agreement in respect of aggregate annual Net Sales of the Earn-Out Product (vorasidenib) made in the US Territory from and after the FDA Approval Date and during the Net Sales Term, and any amounts payable by Counterparty to Seller under the Counterparty Agreement in lieu thereof, but in each case without giving effect to any offsets or reductions in respect of Third Party License Payments pursuant to Section 2.13(a)(ii) of the Counterparty Agreement or any offsets or reductions taken on account of any Disputed Amounts under Section 2.13(j) of the Counterparty Agreement;

(b) all amounts payable resulting from Counterparty underpayments in respect of the Applicable Percentage of Net Sales of the Earn-Out Product (vorasidenib) made in the US Territory from and after the FDA Approval Date pursuant to (i) Section 2.13(a)(iii)(B) of the Counterparty Agreement, (ii) clause (B) of the first sentence in Section 2.13(a)(iv) of the Counterparty Agreement, and (iii) Section 2.13(e) of the Counterparty Agreement (in each case (b)(i)-(b)(iii) above, regardless of whether Seller furnishes an invoice to Counterparty for such amounts);

(c) all indemnity payments, guarantees, recoveries, damages or awards or settlement amounts payable by Counterparty to the Seller or any of its Affiliates after the FDA Approval Date as a result of a breach by either Counterparty of the provisions of the Counterparty Agreement related to the Purchased Assets in respect of the amounts described in clause (a) and (b) above, including pursuant to Section 10.3, Section 10.5, and Section 11.15 of the Counterparty Agreement (other than for any unreimbursed costs payable to Seller pursuant to the Counterparty Agreement) related to the period after the FDA Approval Date;

(d) any payments payable to Seller under Section 2.13(i) of the Counterparty Agreement in respect of the payments described in clauses (a)-(c) above related to the period after the FDA Approval Date;

(e) all other amounts paid or payable by Counterparty or any other Person to the Seller or any of its Affiliates arising out of, related to or resulting from the amounts described in clauses (a), (b), (c) and (d) above;

(f) all accounts (as defined under the UCC) evidencing the rights to the payments and amounts described in clauses (a)-(e) above; and

(g) all proceeds (as defined under the UCC) of any of the foregoing.

"Voting Securities" means, with respect to any Person, Capital Securities of any class or kind ordinarily having the power to vote for the election of directors, managers or other voting members of the governing body of such Person.

Section 1.1 Rules of Construction. Unless the context otherwise requires, in this Purchase and Sale Agreement:

a. A term has the meaning assigned to it and an accounting term not otherwise defined has the meaning assigned to it in accordance with GAAP.

b. Unless otherwise defined, all terms that are defined in the UCC shall have the meanings stated in the UCC.

c. Words of the masculine, feminine or neuter gender shall mean and include the correlative words of other genders.

d. The definitions of terms shall apply equally to the singular and plural forms of the terms defined.

e. The terms “include”, “including” and similar terms shall be construed as if followed by the phrase “without limitation”.

f. 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) and include any annexes, exhibits and schedules attached thereto.

g. References to any Applicable Law shall include such Applicable Law as from time to time in effect, including any amendment, modification, codification, replacement or reenactment thereof or any substitution therefor.

h. 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.

i. The word “will” shall be construed to have the same meaning and effect as the word “shall”.

j. The words “hereof”, “herein”, “hereunder” and similar terms when used in this Purchase and Sale Agreement shall refer to this Purchase and Sale 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 Purchase and Sale Agreement unless otherwise specified.

k. 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”.

l. Any interpretation of whether an action or consent (or refusal to act or consent) or any instruction by any Purchaser or the Seller is “reasonable,” shall take into the account the relative economic interests of the Seller, on the one hand, and the Purchaser, on the other, in the reasonably expected future amounts due, paid or payable, owed or owing, accrued or otherwise to be paid by Counterparty or any of its Affiliates under Section 2.13(a)(i)(B) of the Counterparty Agreement in respect of Net Sales of the Earn-Out Product (vorasidenib).

m. Where any payment is to be made, any funds are to be applied or any calculation is to be made under this Purchase and Sale Agreement on a day that is not a Business Day, unless this Purchase and Sale 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.

n. Any reference herein to a term that is defined by reference to its meaning in the Counterparty Agreement shall refer to such term's meaning in the Counterparty Agreement as in existence on the date hereof and provided to the Purchaser as set forth in Section 3.14(b) (and not to any new, substituted, amended, modified or supplemented version thereof unless the Purchaser has consented thereto in writing).

ARTICLE II
PURCHASE AND SALE OF THE PURCHASED ASSETS

Section 2.1 Purchase and Sale; Closing.

a. Subject to the satisfaction (or waiver by the party so entitled to waive) of the conditions set forth in Article VI, the Closing shall take place remotely via the exchange of documents and signatures within [**] following FDA Approval.

b. On the Closing Date, the Seller shall sell, contribute, assign, transfer, convey and grant to the Purchaser, and the Purchaser shall purchase, acquire and accept from the Seller, all of the Seller's rights, title and interest in and to the Purchased Assets, free and clear of any and all Liens, other than those Liens created in favor of the Purchaser by Sections 2.1(f) hereof.

c. The Seller and the Purchaser intend and agree that the sale, contribution, assignment, transfer, conveyance and granting of the Purchased Assets under this Purchase and Sale Agreement shall be, and are, a true, complete, absolute and irrevocable assignment and sale by the Seller to the Purchaser of the Purchased Assets and that such assignment and sale shall provide the Purchaser (or its respective permitted assigns) with the full benefits of ownership of the Purchased Assets. Neither the Seller nor the Purchaser intend the transactions contemplated hereby to be, or for any purpose characterized as, a loan from the Purchaser to the Seller or a pledge or assignment or a security agreement. The Seller waives any right to contest or otherwise assert that this Purchase and Sale Agreement does not constitute a true, complete, absolute and irrevocable sale and assignment by the Seller to the Purchaser of the Purchased Assets under Applicable Law, which waiver shall be enforceable against the Seller in any Bankruptcy Event in respect of the Seller. The sale, contribution, assignment, transfer, conveyance and granting of the Purchased Assets shall be reflected on the Seller's financial statements and other records as a sale of assets to the Purchaser (except to the extent GAAP require otherwise with respect to the Seller's consolidated financial statements).

d. The Seller hereby authorizes the Purchaser or its designee to, from and after the Closing Date, execute, record and file, and consents to the Purchaser or its designee executing, recording and filing, at the Purchaser's sole cost and expense, financing statement, in forms to be agreed by the parties hereto, in the appropriate filing offices under the UCC (and continuation statements with respect to such financing statements or other amendments deemed necessary by the Purchaser, if and when applicable) naming the Purchaser as the "Buyer" of the Purchased Assets and the Secured Party thereunder, and amendments thereto or assignments thereof, in such manner and in such jurisdictions as are necessary or appropriate to evidence or

perfect the sale, contribution, assignment, transfer, conveyance and grant by the Seller to the Purchaser, and the purchase, acquisition and acceptance by the Purchaser from the Seller, of the Purchased Assets and to perfect the security interest in the Purchased Assets granted by the Seller to Purchaser pursuant to Section 2.1(f).

e. The Purchaser's right, title and interest to the Purchased Assets shall commence as of the Closing Date. For the avoidance of doubt, following the Closing, payments on account of the Purchased Assets shall be owned by and payable to the Purchaser regardless of whether such payments are made by the Counterparty during the same calendar year in which the Net Sales related to such payments are generated or in any other calendar year.

f. Notwithstanding that the Seller and the Purchaser expressly intend for the sale, contribution, assignment, transfer, conveyance and granting of the Purchased Assets to be a true, complete, absolute and irrevocable sale and assignment, and, conditioned only upon the occurrence of the Closing, the Seller hereby assigns, conveys, grants and pledges to the Purchaser, as security for its obligations created hereunder in the event that the transfer contemplated by this Purchase and Sale Agreement is held not to be a sale, a first priority security interest in all of the Seller's right, title and interest in, to and under the Purchased Assets, and, in such event, this Purchase and Sale Agreement shall constitute a security agreement.

Section 2.2 Purchase Price. In full consideration for the sale, contribution, assignment, transfer, conveyance and granting of the Purchased Assets, and subject to the terms and conditions set forth herein, on the Closing Date, the Purchaser shall pay (or cause to be paid) to the Seller the purchase price of $905,000,000 (the "Purchase Price") in immediately available funds by wire transfer to the Seller Account. Following the Closing Date, the parties hereto shall, acting reasonably, agree to an allocation of the Purchase Price among the Purchased Assets and memorialize this allocation in a separate writing. The parties hereto agree not to take any position that is inconsistent with the allocation set forth in such writing on any Tax return or in any audit or other Tax-related administrative or judicial proceeding, unless taking such a position is required by Applicable Law.

Section 2.3 No Assumed Liabilities or Obligations. Notwithstanding any provision in this Purchase and Sale Agreement to the contrary, the Purchaser will purchase, acquire and accept only the Purchased Assets and is not assuming any liability or obligation of the Seller or any of the Seller's Affiliates of whatever nature, whether presently in existence or arising or asserted hereafter (including any liability or obligation of the Seller under the Counterparty Agreement, the Sagard Agreement or otherwise). All such liabilities and obligations shall be retained by and remain liabilities and obligations of the Seller or the Seller's Affiliates, as the case may be (the "Excluded Liabilities and Obligations").

Section 2.4 Excluded Assets. The Purchaser does not, by purchase, acquisition or acceptance of the rights, title or interest granted hereunder or otherwise pursuant to any of the Transaction Documents, purchase, acquire or accept any assets or contract rights of the Seller under the Counterparty Agreement, other than the Purchased Assets, or any other assets of the Seller, including, for the avoidance of doubt, (a) the assets sold pursuant to the Sagard Agreement, (b) payments under Section 2.13(b) of the Counterparty Agreement, and (c) the Retained Receivables. For the avoidance of

doubt, payments on account of the Retained Receivables shall be owned by and payable to the Seller regardless of whether such payments are made by the Counterparty during the same calendar year in which the Net Sales related to such payments are generated or in any other calendar year.

Section 2.5 Receivables Reports. Effective immediately upon the sale of the Purchased Assets hereunder and payment of the Purchase Price, the Purchaser shall have the right to receive the Receivables Reports pursuant to the Counterparty Agreement in accordance with the Counterparty Consent, provided that the Seller shall also retain the right to receive the Receivables Reports directly from the Counterparty and, if requested, from the Purchaser.

ARTICLE III

REPRESENTATIONS AND WARRANTIES OF THE SELLER

The Seller hereby represents and warrants to the Purchaser that:

Section 3.1 Organization. The Seller is a corporation duly organized, validly existing and in good standing under the laws of the State 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 and to exercise its rights and to perform its obligations under the Counterparty Agreement. The Seller 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 be a Material Adverse Change). Neither the Purchaser nor any of its partners, members or controlling Persons is an Affiliate of the Seller or any Subsidiary of the Seller.

Section 3.2 No Conflicts.

a. None of the execution and delivery by the Seller of any of the Transaction Documents to which the Seller is party, the performance by the Seller 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, termination of or loss of benefit under, 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 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 Seller 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 Seller or any of its Subsidiaries is a party or by which the Seller or any of its Subsidiaries or any of their respective assets or properties is bound or committed (including the Counterparty Agreement, after giving effect to the Counterparty Consent) to the extent it would reasonably be expected to result in a Material Adverse Change or (C) any term or provision of any of the organizational documents of the Seller or any of its Subsidiaries; (ii) give rise to any additional right of termination, cancellation or acceleration of any right or obligation of the Seller or any of

its Subsidiaries to the extent it would reasonably be expected to result in a Material Adverse Change; or (iii) 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 Earn-Out Product (vorasidenib), the Counterparty Agreement or the Purchased Assets.

b. Except for the Lien created in favor of the Purchaser under Section 2.1(f) of this Purchase and Sale Agreement, the Seller has not granted, nor does there exist, any Lien on or relating to the Counterparty Agreement (other than under or in respect of the Sagard Agreement and not related to Purchased Assets) or the Purchased Assets.

Section 3.3 Authorization. The Seller 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 Seller is party and the performance by the Seller of its obligations hereunder and thereunder have been duly authorized by all necessary corporate action on the part of the Seller. Each of the Transaction Documents to which the Seller is party has been duly executed and delivered by an authorized officer of the Seller. Each of the Transaction Documents to which the Seller is party constitutes the legal, valid and binding obligation of the Seller, enforceable against the Seller in accordance with its respective terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium or similar Applicable Laws affecting creditors' rights generally and general equitable principles.

Section 3.4 Ownership. The Seller is the exclusive owner of the entire right, title (legal and equitable) and interest in, to and under the Purchased Assets and has good, valid and marketable title thereto, free and clear of all Liens, other than Liens to be created in favor of the Purchaser under Section 2.1(f) of this Purchase and Sale Agreement. The Purchased Assets to be sold, contributed, assigned, transferred, conveyed and granted to the Purchaser have not been pledged, sold, contributed, assigned, transferred, conveyed or granted by the Seller to any other Person. The Seller has full right to sell, contribute, assign, transfer, convey and grant the Purchased Assets to the Purchaser. Upon the sale, contribution, assignment, transfer, conveyance and granting by the Seller of the Purchased Assets to the Purchaser, the Purchaser shall acquire good and marketable title to the Purchased Assets free and clear of all Liens, other than Liens created in favor of the Purchaser under Section 2.1(f) of this Purchase and Sale Agreement, and shall be the exclusive owner of the Purchased Assets. The Purchaser shall have the same rights as the Seller would have with respect to the Purchased Assets (if the Seller were still the owner of such Purchased Assets) against any other Person.

Section 3.5 Governmental and Third Party Authorizations. The execution and delivery by the Seller of the Transaction Documents to which the Seller is party, the performance by the Seller of its obligations hereunder and thereunder and the consummation of any of the transactions contemplated hereunder and thereunder (including the sale, contribution, assignment, transfer, conveyance and granting of the Purchased Assets to the Purchaser) 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 the filing of UCC financing statements, the notice to the Counterparties contained in the Counterparty Instruction and any such consent, approval, license, order,

authorization or declaration, notice, action or registration the failure of which to obtain would not reasonably be expected to result in a Material Adverse Change.

Section 3.6 No Litigation. There is no (a) action, suit, arbitration proceeding, claim, demand, citation, summons, subpoena, investigation or other proceeding (whether civil, criminal, administrative, regulatory, investigative or informal) pending or, to the Knowledge of the Seller, threatened against the Seller or any of its Subsidiaries, relating to the Counterparty, the Earn-Out Product (vorasidenib) or the Purchased Assets, at law or in equity, or (b) inquiry or investigation (whether civil, criminal, administrative, regulatory, investigative or informal) by or before a Governmental Authority pending or, to the Knowledge of the Seller, threatened against the Seller or any of its Subsidiaries relating to the Counterparty or the Counterparty Agreement as they relate to the Earn-Out Product (vorasidenib) or otherwise as to the Earn-Out Product (vorasidenib) or the Purchased Assets, that, in each case, (i) if adversely determined, could reasonably be expected to result in a Material Adverse Change, 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 Seller is party. To the Knowledge of the Seller, no event has occurred or circumstance exists that may give rise to or serve as a basis for the commencement of any such action, suit, arbitration, claim, investigation, proceeding or inquiry.

Section 3.7 Solvency. The Seller has determined that, and by virtue of its entering into the transactions contemplated by the Transaction Documents to which the Seller is party and its authorization, execution and delivery of the Transaction Documents to which the Seller is party, the Seller'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 Seller's assets will be greater than the sum of its debts, liabilities and other obligations, including contingent liabilities, (b) the present fair saleable value of the Seller'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 contingent liabilities, as they become absolute and matured, (c) the Seller will be able to realize upon its assets and pay its debts, liabilities and other obligations, including contingent obligations, as they mature, (d) the Seller will not be rendered insolvent, 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 Seller 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 Seller will not have become subject to any Bankruptcy Event and (g) the Seller will not have been rendered insolvent within the meaning of Section 101(32) of Title 11 of the United States Code. No step has been taken or is intended by the Seller or, so far as it is aware, any other Person to make the Seller subject to a Bankruptcy Event.

Section 3.8 Tax Matters. No deduction or withholding for or on account of any Tax has been made, or was required under Applicable Law to be made, from any payment to the Seller under the Counterparty Agreement with respect to the Purchased Assets. Seller has received no notice from any Counterparty of any intention to deduct or withhold any tax from any future payments to the Seller with respect to the Counterparty Agreement with respect to the Purchased Assets. The Seller has filed (or caused to be filed) all income and other material tax returns and reports required by Applicable Law to

have been filed by it with respect to the Purchased Assets, and all such tax returns were true, correct and complete in all material respects, and the Seller has paid (or caused to be paid) all taxes required to be paid by it with respect to the Purchased Assets. There are no existing Liens for Taxes on the Purchased Assets (or any portion thereof) other than Liens for Taxes not yet due and payable.

Section 3.9 No Brokers' Fees. The Seller 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 Purchase and Sale Agreement, except for [**], which are the sole responsibility of the Seller.

Section 3.10 [Reserved].

Section 3.11 Compliance with Laws. None of the Seller or any of its Subsidiaries (a) has violated or is in violation of, or, to the Knowledge of the Seller, is under investigation with respect to or has been threatened to be charged with or been given notice of any violation of, any Applicable Law or any judgment, order, writ, decree, injunction, stipulation, consent order, permit or license granted, issued or entered by any Governmental Authority 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 would be a Material Adverse Change. Each of the Seller and any Affiliate of the Seller is in compliance with the requirements of all Applicable Laws, a breach of any of which would be a Material Adverse Change.

Section 3.12 Earn-Out Product (vorasidenib).

a. There is no injunction, claim, suit, action, citation, summons, subpoena, hearing, inquiry, investigation, complaint, arbitration, mediation, demand, decree or other dispute, disagreement, proceeding or claim by or with any Person against the Seller involving the Earn-Out Product (vorasidenib) that, if adversely determined, would reasonably be expected to result in a Material Adverse Change.

b. To the Knowledge of the Seller, there is no pending or threatened (in writing), and no event has occurred or circumstance exists that (with or without notice or lapse of time, or both) could reasonably be expected to give rise to or serve as a basis for any, action, suit or proceeding, or any investigation or claim by any Person to which the Seller or, to the Knowledge of the Seller, to which Counterparty, any Affiliate of Counterparty or any Sublicensee is or could be a party, and the Seller 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 Earn-Out Product (vorasidenib) by Counterparty, any Affiliate of Counterparty or any Sublicensees does or could infringe on any patent or other intellectual property rights of any other Person or constitute misappropriation of any other Person's trade secrets or other intellectual property rights. To the Knowledge of the Seller, there are no pending patent applications owned by any third party that, if issued, would limit or prohibit, in any material respect, the manufacture, use or sale of the Earn-Out Product by Counterparty, any Affiliate of Counterparty or any Sublicensees. To the Knowledge of the Seller, Counterparty is the sole and exclusive owner, or exclusive licensee, of all intellectual property rights underlying the Earn-Out Product (vorasidenib). The Seller has not received any notice of any, and to the

Knowledge of the Seller, there is no, infringement of any of the intellectual property rights underlying the Earn-Out Product (vorasidenib).

Section 3.13 Regulatory Matters.

a. All applications, submissions, information and data related to the Earn-Out Product (vorasidenib) submitted or utilized as the basis for any request to any Regulatory Agency by or on behalf of the Seller prior to the Sale Date were true and correct in all material respects as of the date of such submission or request, and, to the Knowledge of the Seller, any material updates, changes, corrections or modifications to such applications, submissions, information or data required to have been made under applicable laws or regulations have been submitted to the necessary Regulatory Agencies.

b. Neither the Seller, nor, to the Knowledge of the Seller, the Counterparty or any of its or their officers, employees, contractors or agents, is the subject of any pending or, to the Knowledge of the Seller, threatened investigation by the FDA or any other Regulatory Agency with regard to the Earn-Out Product (vorasidnib) that would reasonably be expected to result in a Material Adverse Change.

c. None of the Seller, any of its Subsidiaries and, to the Knowledge of the Seller, any third party manufacturer for the Earn-Out Product (vorasidenib), has received from the FDA a "Warning Letter", Form FDA-483, "Untitled Letter", or similar material written correspondence or notice alleging violations of applicable laws and regulations enforced by the FDA, or any comparable material written correspondence from any other Regulatory Agency with regard to the Earn-Out Product (vorasidenib) or the manufacture, processing, packaging or holding thereof, the subject of which communication is unresolved and if determined adversely would, individually or in the aggregate, reasonably be expected to result in a Material Adverse Change.

d. Neither the Seller nor any of its officers, employees, contractors or agents made an untrue statement of material fact on, or material omissions from, any notifications, applications, approvals, reports and other submissions to the FDA or any similar Regulatory Agency with respect to the Earn-Out Product (vorasidenib).

e. Prior to entering into the Counterparty Agreement, the Seller was in compliance with all applicable laws administered or issued by the FDA or any similar Regulatory Agency, including the FD&C Act, applicable requirements in FDA regulations, and any orders issued by the FDA or similar Regulatory Agencies, and all other laws regarding ownership, developing, testing, manufacturing, packaging, storage, import, export, disposal, marketing, distributing, promoting, and complaint handling or adverse event reporting for the Earn-Out Product (vorasidenib), except to the extent that such failure to comply with such applicable laws would not be a Material Adverse Change.

Section 3.14 Counterparty Agreement.

a. Other than the Transaction Documents, the Counterparty Agreement, the Upstream License Agreement, and the Sagard Agreement, there is no contract, agreement or other arrangement (whether written or oral) to which the Seller or any of its Subsidiaries is a party or by which any of their respective assets or properties is bound or committed (i) that creates a Lien on, affects or otherwise relates to the Purchased Assets, the Earn-Out Product (vorasidenib) or the Counterparty Agreement, or (ii) for which breach, nonperformance, cancellation or failure to renew would be a Material Adverse Change.

b. Attached as Exhibit D hereto is a true, correct and complete copy of the Counterparty Agreement in effect on the Effective Date. The Seller has provided to the Purchaser true, correct and complete copies of (i) any confidentiality agreement between Seller and Counterparty relating thereto that is currently in effect (excluding any such agreement entered into solely for the purpose of Counterparty considering a purchase of the Vorasidenib Receivables), and (ii) all material notices and material correspondences delivered to, or by, the Seller pursuant to the Counterparty Agreement relating to the Purchased Assets or the Earn-Out Product (vorasidenib) since the Sale Date.

c. The Counterparty Agreement is in full force and effect and is the legal, valid and binding obligation of the Seller and Counterparty, enforceable against the Seller and Counterparty in accordance with its terms, subject, as to enforcement of remedies, to bankruptcy, insolvency, reorganization, moratorium or similar Applicable Laws affecting creditors' rights generally and general equitable principles. The execution and delivery of, and performance of obligations under, the Counterparty Agreement were and are within the powers of the Seller and, to the Knowledge of the Seller, Counterparty. The Counterparty Agreement was duly authorized by all necessary action on the part of, and validly executed and delivered by, the Seller and to the Knowledge of the Seller, Counterparty. The Seller is not in breach or violation of or in default under the Counterparty Agreement. There is to Seller's Knowledge no event or circumstance that, upon notice or the passage of time, or both, would constitute or give rise to any breach or default in the performance of the Counterparty Agreement by the Seller or Counterparty.

d. The Seller has not waived any rights or defaults under the Counterparty Agreement or released Counterparty, in whole or in part, from any of its obligations under the Counterparty Agreement. There are no oral waivers or modifications (or pending requests therefor) in respect of the Counterparty Agreement. Neither the Seller nor Counterparty has agreed to amend or waive any provision of the Counterparty Agreement, other than the Counterparty Consent.

e. To the Knowledge of the Seller, no event has occurred that would give the Seller or Counterparty the right to terminate the Counterparty Agreement or allow Counterparty to cease paying Vorasidenib Receivables thereunder or reduce any such payments other than in connection with Permitted Deductions. The Seller has not received any notice of an intention by Counterparty to terminate or breach the Counterparty Agreement, in whole or in part, or challenging the validity or enforceability of the Counterparty Agreement or the obligation to pay the Vorasidenib Receivables under the Counterparty Agreement, or alleging that the Seller or

Counterparty is in default of its obligations under the Counterparty Agreement. To the Knowledge of the Seller, there has been no default, violation or breach by Counterparty under the Counterparty Agreement that would reasonably be expected to result in a Material Adverse Change. The Seller has no intention of terminating the Counterparty Agreement and has not given Counterparty any notice of termination of the Counterparty Agreement, in whole or in part.

f. The amount of the Vorasidenib Receivables paid under the Counterparty Agreement has not been and, to the Knowledge of the Seller, the amount of the Vorasidenib Receivables due and payable under the Counterparty Agreement is not, as of the date hereof, subject to any claim against the Seller pursuant to any Receivables Reduction. To the Knowledge of the Seller, no event or condition currently exists that, upon notice, passage of time or otherwise, would permit Counterparty to make, or have the right to make, any Receivables Reduction against the Vorasidenib Receivables. The Seller is not a party to any agreement (other than the Counterparty Agreement) providing for a sharing of, or providing for or permitting any Receivables Reduction against the Vorasidenib Receivables payable under the Counterparty Agreement to the Seller. Counterparty has no express right of set-off under any contract or other agreement against the Vorasidenib Receivables or any other amounts payable to the Seller under the Counterparty Agreement, other than rights of set-off expressly set forth in the Counterparty Agreement.

g. Seller has not consented to an assignment by Counterparty of any of Counterparty's rights or obligations under the Counterparty Agreement, and the Seller does not have Knowledge of any such assignment by Counterparty. Other than the Liens created in favor of the Purchaser set forth in Section 2.1(f) of this Purchase and Sale Agreement, or under or in respect of the Sagard Agreement (but not as to any Purchased Assets), the Seller has not assigned, in whole or in part, and has not granted, incurred or suffered to exist any Lien on the Counterparty Agreement or the Purchased Assets.

h. None of the Seller, Counterparty or any other Person has made any claim of indemnification under the Counterparty Agreement in respect of the Purchased Assets.

i. The Seller has not exercised its rights to conduct an audit under Section 2.13(e) of the Counterparty Agreement as to the Purchased Assets.

j. To the Knowledge of the Seller, Counterparty has not granted any sublicenses relating to the Earn-Out Product (vorasidenib).

k. To the Knowledge of the Seller, none of Counterparty nor any of its Affiliates has entered into any Earn-Out Product Transaction.

l. To the Knowledge of the Seller, there has been no actual or alleged Specified Indemnity Claim and there exist no facts or circumstances that would reasonably be expected to result in a Specified Indemnity Claim.

m. Counterparty has no grounds to reduce, take an offset against, or otherwise withhold payment of the Vorasidenib Receivables, whether pursuant to Section 2.13(a)(ii) of the

Counterparty Agreement, Section 2.13(j) of the Counterparty Agreement or otherwise, other than deductions set forth in clause (i) of the definition of "Permitted Deductions".

n. To the Knowledge of the Seller, there are no Third Party License Payments that are required to be made to any third party with respect to the Earn-Out Product (vorasidenib); provided that, for avoidance of doubt, this representation does not include payments under the Upstream License Agreement, which are not, pursuant to the Counterparty Agreement, Third Party License Payments.

o. The Seller has not received any written notice advising the Seller that the obligation of Counterparty to pay Vorasidenib Receivables will end before the expiration of the last to expire Applicable Patent Rights relating to the Earn-Out Product (vorasidenib).

Section 3.15 Intellectual Property.

a. Schedule 3.15(a) of the Disclosure Schedule lists all Applicable Patent Rights. To the Knowledge of the Seller, Servier is the exclusive owner of the Applicable Patent Rights.

b. To the Knowledge of the Seller, there are no pending or threatened litigations, interferences, reexamination, oppositions, inter-partes review, post-grant review, derivation proceedings, or like procedures involving any Applicable Patent Rights.

c. To the Knowledge of the Seller, all of the Applicable Patent Rights are in full force and effect and have not lapsed, expired or otherwise terminated. To the Knowledge of the Seller, each issued claim within the Applicable Patent Rights is valid and enforceable. The Seller has not received any written notice relating to the lapse, expiration or other termination of any of the issued Applicable Patent Rights, or any written legal opinion that alleges that any issued claim of the Applicable Patent Rights is invalid or unenforceable.

d. There is no Person who is, or who prior to the Sale Date claimed to be, and, to the Knowledge of the Seller, there is no person who on or after the Sale Date has claimed to be, an inventor under any of the Applicable Patent Rights who is not a named inventor thereof.

e. Seller has not, and, to the Knowledge of the Seller, Counterparty has not, received any written notice of any claim by any Person challenging inventorship or ownership of, the rights of the Seller (prior to the Sale Date) or rights of Counterparty (on or after the Sale Date), as applicable, in and to, or the patentability, validity or enforceability of, any issued claim of the Applicable Patent Rights, or asserting that the development, manufacture, importation, sale, offer for sale or use of the Earn-Out Product (vorasidenib) infringes or would reasonably be expected to infringe any patent or other intellectual property rights of such Person.

f. To the Knowledge of the Seller, the discovery, development and commercialization of the Earn-Out Product (vorasidenib) did not and has not infringed, violated or misused any patent or other intellectual property rights owned by any third party.

g. To the Knowledge of the Seller, the manufacture, use, marketing, sale, offer for sale, importation or distribution of the Earn-Out Product (vorasidenib) will not infringe, misappropriate or otherwise violate any patent rights or other intellectual property rights owned by any other Person.

h. To the Knowledge of the Seller, there has been no infringement of the Applicable Patent Rights by any third party.

i. To the Knowledge of the Seller as of the Sale Date, all required maintenance fees, annuities and like payments with respect to the Applicable Patent Rights had been timely paid.

Section 3.16 UCC Matters. The Seller's exact legal name is, and for the preceding 10 years has been, "Agios Pharmaceuticals, Inc." The Seller's principal place of business is, and for the preceding 10 years has been, located in Cambridge, Massachusetts. The Seller's jurisdiction of organization is, and for the preceding 10 years has been, the State of Delaware. The Seller's organizational identification number (within the meaning of Section 9-516(b)(5)(C)(iii) of the UCC) is 4403099.

ARTICLE IV
REPRESENTATIONS AND WARRANTIES OF THE PURCHASER

The Purchaser hereby represents and warrants to the as follows:

Section 4.1 Organization. The Purchaser is duly formed or organized and, to the extent such concepts exist in its jurisdiction of organization, validly existing and in good standing under the laws of its jurisdiction of organization 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 4.2 No Conflicts. None of the execution and delivery by the Purchaser of any of the Transaction Documents to which the Purchaser is party, the performance by the Purchaser 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 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 the Purchaser 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 the Purchaser is a party or by which the Purchaser or any of its assets or properties is bound or committed or (iii) any term or provision of any of the organizational documents of the Purchaser.

Section 4.3 Authorization. The Purchaser has all necessary 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 Purchaser is a party and the performance by the Purchaser of its obligations hereunder and thereunder have been duly authorized by the Purchaser. Each of the Transaction Documents to which the Purchaser is party has been duly executed and delivered by the Purchaser. Each of the Transaction Documents to which the Purchaser is party constitutes the legal, valid and binding obligation of the Purchaser, enforceable against the Purchaser in accordance with its respective terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium or similar Applicable Laws affecting creditors' rights generally and general equitable principles.

Section 4.4 Governmental and Third Party Authorizations. The execution and delivery by the Purchaser of the Transaction Documents to which the Purchaser is party, the performance by the Purchaser of its obligations hereunder and thereunder and the consummation of any of the transactions contemplated hereunder and thereunder by the Purchaser does 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 as described in Section 3.5.

Section 4.5 No Financing. The Purchaser will have sufficient cash on hand or other sources of immediately available funds to pay the Purchase Price on the Closing Date. The Purchaser acknowledges that its obligations under this Purchase and Sale Agreement are not contingent on obtaining financing.

Section 4.6 No Litigation. There is no (a) action, suit, arbitration proceeding, claim, demand, citation, summons, subpoena, investigation or other proceeding (whether civil, criminal, administrative, regulatory, investigative or informal) pending or, to the knowledge of the Purchaser, threatened by or against the Purchaser, at law or in equity, or (b) inquiry or investigation (whether civil, criminal, administrative, regulatory, investigative or informal) by or before a Governmental Authority pending or, to the knowledge of the Purchaser, threatened against the Purchaser, that, in each case, challenges or seeks to prevent or delay the consummation of any of the transactions contemplated by any of the Transaction Documents to which the Purchaser is party.

ARTICLE V
COVENANTS

The parties hereto covenant and agree as follows:

Section 5.1 Books and Records; Notices.

a. From and after the Effective Date, promptly (but in no event more than [**]) after receipt by the Seller of written notice of, or related to, any action, suit, claim, demand, dispute, investigation, arbitration or other proceeding (commenced or threatened in writing) relating to (i) any Transaction Document or the Counterparty Agreement or the transactions contemplated hereunder or thereunder, (ii) the Purchased Assets or (iii) any default or termination by Counterparty under the Counterparty Agreement, the Seller shall (x) inform the Purchaser in writing of the receipt of such notice and the substance thereof and (y) if such notice is in writing, furnish the Purchaser with a copy of such notice and any related materials with respect thereto.

b. Each of the Seller and the Purchaser shall keep and maintain, or cause to be kept and maintained, at all times full and accurate books and records adequate to reflect accurately all financial information it has received from Counterparty related to the Purchased Assets, and all amounts paid or received under the Counterparty Agreement related to the Purchased Assets. Notwithstanding the foregoing or anything in the Transaction Documents to the contrary, Seller shall have no obligation to keep or maintain information it or Counterparty delivers to the Purchaser, except as required under Applicable Law, and Purchaser shall have no obligation to keep or maintain information it or Counterparty delivers to the Seller, except as required under Applicable Law. For avoidance of doubt, Purchaser shall have no rights hereunder in respect of, and Seller shall have no obligations hereunder in respect of, assets purchased under the Sagard Agreement.

c. From and after the Effective Date, promptly (but in no event more than [**]) following receipt by the Seller from Counterparty, any of its Affiliates or any Sublicensees of any material communication, whether in the form of a written notice, certificate, offer, proposal, material correspondence or report, in each case relating to or affecting the Purchased Assets, the Seller shall (i) inform the Purchaser in writing of such receipt and (ii) furnish the Purchaser with a copy of such notice, certificate, offer, proposal, correspondence, report or other communication. [**]. The Seller shall promptly furnish to the Purchaser a copy of any material communication relating to or affecting the Purchased Assets sent by the Seller to Counterparty, any of its Affiliates or any Sublicensees.

d. From and after the Effective Date, the Seller shall provide the Purchaser with written notice as promptly as practicable (and in any event within [**]) after obtaining Knowledge of any of the following: (i) the occurrence of a Bankruptcy Event in respect of the Seller; (ii) any material breach or default by the Seller or Counterparty of or under any covenant, agreement or other provision of any Transaction Document to which it is party; (iii) any representation or warranty made by the Seller in any of the Transaction Documents or in any certificate delivered to the Purchaser pursuant to this Purchase and Sale Agreement shall prove to be untrue, inaccurate or incomplete in any material respect on the date as of which made; (iv) any change, effect, event, occurrence, state of facts, development or condition that would reasonably likely to result in a Material Adverse Change, (v) any allegation or claim by a third party that the making, having made, using, importing, offering for sale or selling of any Earn-Out Product (vorasidenib) infringes any intellectual property rights of such third party; or (vi) any third party making, having made, using, importing, offering for sale or selling of any product in a manner that infringes any intellectual property rights underlying the Earn-Out Product (vorasidenib).

e. The Seller shall notify the Purchaser in writing not less than [**] prior to any change in, or amendment or alteration of, the Seller's (i) legal name, (ii) form or type of organizational structure, (iii) jurisdiction of organization or (iv) organizational identification number (within the meaning of Section 9-516(b)(5)(C)(iii) of the UCC).

f. From and after the Effective Date, subject to applicable confidential restrictions (including Section 5.10) and Applicable Laws relating to securities matters, the Seller

shall make available such other information within Seller's Knowledge as the Purchaser may, from time to time, reasonably request with respect to (i) the Purchased Assets, (ii) the Counterparty Agreement as to any matter related to the Purchased Assets, (iii) the Vorasidenib Receivables, and (iv) the Earn-Out Product (vorasidenib).

Section 5.2 Public Announcement. Except for a press release previously approved in form and substance by the Seller and the Purchaser or any other public announcement using substantially the same text as such press release or other public disclosure permitted hereunder, neither the Purchaser nor the Seller shall, and each party hereto shall cause its respective Affiliates not to, issue a press release or other public announcement or otherwise make any public disclosure with respect to the Transaction Documents, or the subject matter or any terms hereof or thereof (including the identity of any of the parties hereto), without the prior written consent of the other parties hereto (which consent shall not be unreasonably withheld or delayed), except as may be required by applicable law or stock exchange rule (in which case the party hereto required to make the press release or other public announcement or disclosure shall allow the other parties hereto reasonable time to comment on, and, if applicable, reasonably direct the disclosing party to seek confidential treatment in respect of portions of, such press release or other public announcement or disclosure in advance of such issuance).

Section 5.3 Efforts; Further Assurances.

a. Subject to the terms and conditions of this Purchase and Sale Agreement, from and after the Effective Date, each of the Seller and the Purchaser shall use its reasonable best efforts to take, or cause to be taken, all actions and to do, or cause to be done, all things necessary under Applicable Laws to consummate the transactions contemplated by the Transaction Documents to which the Seller or the Purchaser, as applicable, is party, including to perfect the sale, contribution, assignment, transfer, conveyance and granting of the Purchased Assets to the Purchaser pursuant to this Purchase and Sale Agreement. Following the Effective Date, the Purchaser and the Seller agree to take, or cause to be taken, all actions and to do, or cause to be done, all things necessary under Applicable Laws to (i) execute and deliver such other documents, certificates, instruments, agreements and other writings and to take such other actions as may be necessary or desirable, or reasonably requested by the other party hereto, in order to consummate or implement expeditiously the transactions contemplated by any Transaction Document to which the Seller or the Purchaser, as applicable, is party, (ii) perfect, protect, more fully evidence, vest and maintain in the Purchaser's good, valid and marketable rights and interests in and to the Purchased Assets on and after the Closing Date free and clear of all Liens (other than those Liens created in favor of the Purchaser pursuant to Section 2.1(f) hereof), (iii) create, evidence and perfect the Purchaser's first priority back-up security interests granted pursuant to Sections 2.1(f), and (iv) enable the Purchaser to exercise or enforce the Purchaser's rights under any Transaction Document to which the Seller or the Purchaser as applicable, is party, including following the Effective Date.

b. From and after the Effective Date, the Seller and the Purchaser shall cooperate and provide assistance as reasonably requested by any other party hereto, at the expense of such other party hereto (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 other party hereto, 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 Documents, the Purchased Assets or the transactions described herein or therein but in all cases excluding any litigation brought by the Seller (for itself or on behalf of any of its Affiliates and any and all of their respective partners, directors, managers, members, officers, employees, agents and controlling Persons) against the Purchaser or brought by the Purchaser (for itself or on behalf of its Affiliates and any and all of their respective partners, directors, managers, members, officers, employees, agents and controlling Persons) against the Seller.

c. Without limiting any other obligation of the Seller under this Purchase and Sale Agreement, from and after the Effective Date, the Seller shall comply with all Applicable Laws with respect to the Transaction Documents to which it is a party and the Counterparty Agreement, the violation of which would reasonably be expected to result in a Material Adverse Change.

d. From and after the Effective Date, the Seller shall not enter into any contract, agreement or other legally binding arrangement (whether written or oral), or grant any right to any other Person, in any case that would (i) reasonably be expected to result in a Material Adverse Change or (ii) reasonably be expected to conflict with the Transaction Documents or serve or operate to limit, circumscribe or alter the Purchaser's rights under the Transaction Documents (or the Purchaser's ability to exercise any such rights) or result in a default of Seller's obligations under the Transaction Documents or the Counterparty Agreement; provided, that the Seller's relationship with Counterparty in respect of the subject matter of this Section 5.3(d) shall be governed by Section 5.5.

Section 5.4 Payments on Account of the Purchased Assets and Payments Generally.

a. Notwithstanding the terms of the Counterparty Instruction, if Counterparty, any Sublicensee or any other Person makes any future payment in respect of the Purchased Assets to the Seller (or any of its Affiliates), then (i) the portion of such payment that represents Vorasidenib Receivables shall be held by the Seller (or such Affiliate) in trust for the benefit of the Purchaser in a segregated account, (ii) the Seller (or such Affiliate) shall have no right, title or interest whatsoever in such portion of such payment and shall not create or suffer to exist any Lien thereon (other than Liens granted in favor of the Purchaser by Section 2.1(f)), and (iii) the Seller (or such Affiliate) promptly, and in any event no later than [**] following the receipt by the Seller (or such Affiliate) of such portion of such payment, shall remit such portion of such payment to the Deposit Account pursuant to Section 5.4(b) in the exact form received with all necessary endorsements. Notwithstanding the terms of the Counterparty Instruction, if Counterparty, any Sublicensee or any other Person makes any future payment in respect of the Retained Receivables to the Purchaser (or any of its Affiliates), including in the event that the Applicable Percentage is reduced to 80.0% for the balance of Net Sales occurring during a particular calendar year because the Purchaser has actually received $150 million in Vorasidenib

Receivables in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring during such calendar year, then (i) the portion of such payment that represents Retained Receivables shall be held by the Purchaser (or such Affiliate) in trust for the benefit of the Seller in a segregated account (provided that the Deposit Account shall constitute a segregated account for this purpose if the Deposit Account only contains payments from the Counterparty), (ii) the Purchaser (or such Affiliate) shall have no right, title or interest whatsoever in such portion of such payment and shall not create or suffer to exist any Lien thereon, and (iii) the Purchaser (or such Affiliate) promptly, and in any event no later than [**] following the receipt by the Purchaser (or such Affiliate) of such portion of such payment, shall remit such portion of such payment to the Seller Account in the exact form received with all necessary endorsements.

b. The Seller shall make all payments required to be made by it to the Purchaser pursuant to this Purchase and Sale Agreement (including (i) any payment of Vorasidenib Receivables, (ii) any payment by the Seller pursuant to Section 5.4(d); (iii) any payment by the Seller of amounts pursuant to Section 5.6, (iv) any payment of amounts to gross up Seller for any Specified Tax Withholding pursuant to Section 5.7, and (v) any payment paid to the Purchaser pursuant to Section 7.1) by wire transfer of immediately available funds, without set-off, off-set, deduction or withholding for or on account of any Taxes (subject to Section 5.7(b)) (provided that the Purchaser has delivered to the Seller a properly executed IRS Form W-8BEN-E, or other applicable IRS withholding form, establishing entitlement to an exemption from withholding under a United States income Tax treaty), to the Deposit Account as set forth on Schedule 1.2 (or to such other account as the Purchaser shall notify the Seller in writing from time to time).

c. The Purchaser shall make all payments required to be made by it to the Seller pursuant to this Purchase and Sale Agreement by wire transfer of immediately available funds, without set-off, off-set, deduction or withholding for or on account of any Taxes (except as otherwise provided in Section 5.7) (provided that the Seller has delivered to the Purchaser a properly executed IRS Form W-9 or other appropriate form in order to avoid Tax withholding), to the Seller Account.

d. If Counterparty, any Affiliate of Counterparty or any Sublicensee takes any Receivables Reduction against Vorasidenib Receivables (other than for Permitted Deductions or for any prior over-payment of Vorasidenib Receivables actually made to the Purchaser or as a result of a Credit Event), then the Seller shall cause the amount of such Receivables Reduction (or portion thereof, as the case may be) to be paid promptly (but in no event later than [**] following such Receivables Reduction) to the Deposit Account. For the avoidance of doubt, nothing herein or in any other Transaction Document shall provide recourse by the Purchaser to the Seller as a result of any failure by a Counterparty to generate Net Sales unless such failure results from the breach by the Seller of a representation, warranty, or covenant hereunder, and no such failure by a Counterparty to generate Net Sales shall be deemed a Receivables Reduction hereunder.

e. Unless and until this Purchase and Sale Agreement is terminated pursuant to Section 8.1, the Seller shall not amend, modify, supplement, restate, waive or change the Counterparty Instruction except as provided in Section 5.11.

f. Following receipt by the Purchaser of a Receivables Report reporting over $1 billion in aggregate Net Sales of the Earn-Out Product (vorasidenib) for a particular calendar year, the Purchaser shall thereafter promptly (and in no event later than [**]) after receipt by the Purchaser of an aggregate of $150 million in Vorasidenib Receivables in respect of such Net Sales occurring during such calendar year provide written notice to the Seller that the Applicable Percentage shall decrease for Net Sales of the Earn-Out Product (vorasidenib) occurring during the remainder of such calendar year in accordance with the terms of this Agreement.

Section 5.5 Counterparty Agreement.

a. From and after the Effective Date, the Seller shall perform and comply in all material respects with its duties and obligations under the Counterparty Agreement related to or affecting the Purchased Assets and shall otherwise act as reasonably instructed from time to time by the Purchaser under the Counterparty Agreement in respect of the Purchased Assets. From and after the Effective Date, the Seller (i) shall not forgive, release or compromise any amount owed to or becoming owing to it under the Counterparty Agreement related to the Purchased Assets, (ii) shall not assign, cancel or terminate (or consent to any cancellation or termination of) the Counterparty Agreement, or amend, modify, supplement, restate or waive any provision of the Counterparty Agreement related to the Purchased Assets, (iii) shall not enter into any new agreement or legally binding arrangement in respect of the Purchased Assets, (iv) shall not waive any obligation of, or grant any consent to, Counterparty under or in respect of the Purchased Assets and (v) shall not agree to do any of the foregoing, except, in each case, as reasonably instructed by the Purchaser. The Seller shall promptly (and in any case within [**] of receipt thereof) deliver to the Purchaser copies of all fully-executed or definitive writings related to the matters set forth in clauses (i), (ii), (iii), (iv) or (v).

b. From and after the Effective Date, the Seller shall not, except as reasonably instructed by the Purchaser (and at the Purchaser's sole cost and expense), grant or withhold any consent, exercise or waive any right or option, and shall not, in contravention of any instruction by the Purchaser, fail to exercise any right or option or exercise or fail to exercise any action in or under the Counterparty Agreement affecting or relating to the Purchased Assets; provided that the Purchaser shall not issue any instruction to Seller or exercise any action that would be reasonably likely to reduce the Vorasidenib Receivables.

c. If (i) the Seller receives a written notice from Counterparty (A) terminating the Counterparty Agreement (in whole or in part) or any of its obligations thereunder, (B) alleging any breach of or default under the Counterparty Agreement by the Seller, (C) asserting the existence of any facts, circumstances or events that, alone or together with other facts, circumstances or events, would reasonably be expected (with or without the giving of notice or passage of time, or both) to give rise to a breach of or default under the Counterparty Agreement by the Seller or the right to terminate the Counterparty Agreement (in

whole or in part) or any of its obligations thereunder by Counterparty, (D) that would otherwise reasonably be expected to result in a Material Adverse Change or (E) any other material correspondence relating to the foregoing, or (ii) the Seller otherwise obtains Knowledge of any fact, circumstance or event that, alone or together with other facts, circumstances or events, would reasonably be expected (with or without the giving of notice or passage of time, or both) to give rise to a breach of or default under the Counterparty Agreement by the Seller or give rise to the right of Counterparty to terminate the Counterparty Agreement (in whole or in party) or any of its obligation thereunder by Counterparty or would otherwise reasonably be expected to result in a Material Adverse Change, in each case, the Seller shall (A) promptly (and in any event within [**]) give a written notice to the Purchaser describing the material details thereof, including a copy of any written notice received from Counterparty, and, in the case of any such breach or default or alleged breach or default by the Seller, describing in reasonable detail any corrective action the Seller proposes to take, and (B) in the case of any breach or default or alleged breach or default by the Seller, use its commercially reasonable efforts to promptly cure such breach or default.

d. If Seller obtains Knowledge of a breach of or default under, or an alleged breach of or default under, the Counterparty Agreement by Counterparty or of the existence of any facts, circumstances or events that, alone or together with other facts, circumstances or events, would reasonably be expected (with or without the giving of notice or passage of time, or both) to give rise to (x) a breach of or default under the Counterparty Agreement by Counterparty relating to or affecting the Purchased Assets or (y) the right to terminate the Counterparty Agreement (in whole or in part) by the Seller, in each case, the Seller shall (i) promptly (but in any event within [**]) give a written notice to the Purchaser and provide the Purchaser with a written summary of all material details thereof, and (ii) at the sole cost and expense of the Purchaser, act in accordance with the Purchaser's reasonable instructions to take such permissible actions (including commencing legal action against Counterparty and the selection of legal counsel reasonably satisfactory to the Purchaser) to enforce compliance by Counterparty with the relevant provisions of the Counterparty Agreement and to exercise any or all of the Purchaser's or the Seller's rights and remedies, whether under the Counterparty Agreement or by operation of law, with respect thereto, provided that the reasonableness of any such instruction shall take into account the rights of the Seller to the Retained Receivables. The proceeds of any enforcement action taken pursuant to the immediately preceding sentence to the extent compensating for losses arising directly from the Purchased Assets shall be considered to be Vorasidenib Receivables for all purposes hereunder. Notwithstanding anything to the contrary contained in this Article V, nothing herein shall prevent, restrict or limit the Purchaser from directly enforcing, at the Purchaser's sole cost and expense, the Purchaser's entitlement to the Purchased Assets with counsel selected by the Purchaser in its sole discretion, provided that any such enforcement shall reasonably consider the rights of the Seller to the Retained Receivables.

e. Purchaser shall reasonably cooperate with Seller and Seller's counterparties under the Sagard Agreement to minimize any conflicts between Purchaser's rights hereunder and such counterparties' rights under the Sagard Agreement, provided that nothing in this paragraph shall require Purchaser to compromise its rights hereunder.

f. The Seller shall make available its relevant records and personnel to the Purchaser in connection with any prosecution of litigation by the Seller or the Purchaser against Counterparty to enforce any of the Purchaser's rights under the Counterparty Agreement related to or affecting the Purchased Assets, and provide reasonable assistance and authority to file and bring the litigation, including, if required to bring the litigation, being joined as a party plaintiff.

Section 5.6 Mergers, Consolidation and Asset Sales Involving Counterparty. If there occurs a merger or consolidation between the Seller, on the one hand, and Counterparty or any of its Affiliates, on the other hand, a sale of all or substantially all of the Seller's assets to Counterparty or a sale or assignment of the Counterparty Agreement by the Seller to Counterparty, and in any such case the Purchaser's rights to the Purchased Assets or under this Purchase and Sale Agreement are diminished in any material respect, (i) the Seller (or its successor) shall pay to the Purchaser an amount in cash equal to any Vorasidenib Receivables that it does not receive from the Counterparty on the same basis (in both amount and timing) as if the Purchaser's rights to the Purchased Assets or under this Purchase and Sale Agreement were not so diminished and (ii) the Purchaser's rights with respect to the Purchased Assets and the covenants of the Seller under this Purchase and Sale Agreement shall continue to apply on the same basis as if the Purchaser's rights to the Purchased Assets or under this Purchase and Sale Agreement were not diminished in such way.

Section 5.7 Tax Matters.

a. Notwithstanding anything to the contrary in the Transaction Documents, the Seller and the Purchaser shall treat the transactions contemplated by this Purchase and Sale Agreement as a sale of the Purchased Assets for United States federal, state and local Tax purposes.

b. All payments to the Purchaser and the Seller under this Purchase and Sale Agreement shall be made without any deduction or withholding for or on account of any Tax, except as required by Applicable Law; provided, that, if any deduction or withholding of any Tax is required from any such payment under this Purchase and Sale Agreement or from any payment under the Counterparty Agreement by reason of the Seller being a party to the Counterparty Agreement or to the extent resulting from any action by the Seller, including any assignment or transfer by the Seller pursuant to Section 8.4 of this Agreement (a "Specified Tax Withholding"), then the Seller shall, within [**] of the Purchaser receiving any payment subject to such Specified Tax Withholding make a payment to the Purchaser so that, after making all such required deductions and withholdings (including any deductions and withholdings required with respect to any such additional payment), the Purchaser receives an amount equal to the amount that it would have received had no such deductions or withholdings been made. Notwithstanding the above, the parties agree that as long as the Purchaser provides the Seller with IRS withholding forms establishing entitlement to an exemption from withholding in accordance with Section 5.4(b), if applicable, no such deduction or withholding is intended on any payment made to the Purchaser under this Purchase and Sale Agreement. If the Seller determines or becomes aware that any such deduction or withholding is required by Applicable Law with respect to any payment pursuant to the Counterparty Agreement or to be remitted by the Seller on any payment hereunder, (i) the Seller shall notify the Purchaser at least [**] in advance of such payment,

(ii) the Seller shall use its commercially reasonable efforts to make such filings and take such other actions as may be specified by the Purchaser in order to permit an exemption from or reduction of withholding Tax imposed on or with respect to any payments made to the Purchaser under this Purchase and Sale Agreement or the Counterparty Agreement, and (iii) if such Tax is to be remitted by the Seller on any payment hereunder, the Seller shall timely pay to the applicable Governmental Authority the full amount deducted or withheld and provide the Purchaser with proof of payment of such amounts to the applicable Governmental Authority within [**] of making such payment. For the avoidance of doubt, but subject to Article VII of this Purchase and Sale Agreement (to the extent there is any deduction or withholding of Taxes arising out of a breach by Seller of any representations, warranties or covenants that would be reimbursable under Article VII of this Purchase and Sale Agreement), Seller shall not be obligated to pay or otherwise reimburse the Purchaser for any deduction or withholding for or on account of any Tax required in connection with payments made under this Purchase and Sale Agreement or from any payment under the Counterparty Agreement, other than in connection with a Specified Tax Withholding.

c. The parties hereto, severally and not jointly, agree not to take any position that is inconsistent with the provisions of this Section 5.7 on any Tax return or in any audit or other Tax-related administrative or judicial proceeding unless the other parties hereto have consented in writing to such actions. If there is an inquiry by any Governmental Authority of the Seller or the Purchaser related to the treatment described in this Section 5.7, the parties hereto shall cooperate with each other in responding to such inquiry in a reasonable manner which is consistent with this Section 5.7.

Section 5.8 Existence. From and after the Effective Date, the Seller shall (a) preserve and maintain its existence (provided, however, that, subject in all respects to Section 8.4, nothing in this Section 5.8(a) shall prohibit the Seller from entering into any merger, consolidation or amalgamation with, or selling or otherwise transferring all or substantially all of its assets to, and other Person if the Seller is the continuing or surviving entity or if the surviving or continuing or acquiring entity assumes (whether expressly or by operation of law) all of the obligations of the Seller), (b) preserve and maintain its rights, franchises and privileges unless failure to do any of the foregoing would not be a Material Adverse Change, (c) qualify and remain qualified in good standing in each jurisdiction where the failure to preserve and maintain such qualifications would be a Material Adverse Change, including appointing and employing such agents or attorneys in each jurisdiction where it shall be necessary to take action under this Purchase and Sale Agreement, and (d) comply with its organizational documents unless failure to do so would not be a Material Adverse Change.

Section 5.9 Audits; Underpayment of Vorasidenib Receivables; Overpayment of Vorasidenib Receivables.

a. From and after the Effective Date, the Seller shall not, without the prior written consent of the Purchaser (such consent not to be unreasonably withheld, conditioned or delayed if such inspection or audit has been requested by the Purchaser's Representative (as defined in the Sagard Agreement)), and the Seller shall, upon the written request of the Purchaser (and at the sole cost and expense of the Purchaser), cause an inspection or audit of

Counterparty's books and records to be conducted pursuant to, and in accordance with, Section 2.13(e) of the Counterparty Agreement related to the Purchased Assets. In furtherance of the foregoing, the Seller shall provide the Purchaser (i) written notice if the Purchaser (as defined in the Sagard Agreement) exercises its right to cause an inspection or audit of Counterparty's books and records pursuant to Section 5.9(a) of the Sagard Agreement and (ii) a reasonable advanced opportunity to join in such inspection or audit. For the purposes of exercising the Purchaser's rights pursuant to this Section 5.9, the Seller shall select such Independent Accounting Firm as the Purchaser shall recommend for such purpose. The Seller shall provide to the Purchaser all Audit Reports, including without limitation (i) a copy of the summary of the preliminary conclusions of the Independent Accounting Firm), which Purchaser shall have the exclusive right to provide comments thereon pursuant to Section 2.13(e) of the Counterparty Agreement related to the Purchased Assets and (ii) copies of any Audit Reports summarizing the results of any audit of the records of Counterparty in respect of the payment of Vorasidenib Receivables pursuant to Section 2.13(e) of the Counterparty Agreement. The Seller and the Purchaser agree that all of the out-of-pocket expenses of any inspection or audit carried out with the consent or at the request of the Purchaser that would otherwise be borne by the Seller pursuant to the Counterparty Agreement shall, to the extent such inspection or audit relates to the Purchased Assets, instead be borne by the Purchaser, including such fees and expenses of such Independent Accounting Firm as are to be borne by the Seller pursuant to Section 2.13(e) of the Counterparty Agreement together with the Seller's reasonable and documented out-of-pocket costs and expenses incurred in connection with such inspection or audit to the extent such inspection or audit relates to the Purchased Assets. The Seller will furnish to the Purchaser any inspection or audit report prepared in connection with such inspection or audit. The Purchaser shall have the right to require the Seller, in writing, at the sole cost and expense of the Purchaser, to exercise the Seller's rights under the Counterparty Agreement to cause Counterparty to cure any discrepancy identified in the relevant audit report in accordance with the Counterparty Agreement. If the Applicable Percentage is reduced to 80.0% for the balance of Net Sales occurring during a particular calendar year because the Purchaser has actually received $150 million in Vorasidenib Receivables in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring during such calendar year, the Purchaser and the Seller shall reasonably cooperate with one another regarding any audit request to the Counterparty with respect to Net Sales of the Earn-Out Product (vorasidenib) occurring during the remaining portion of such calendar year when the Applicable Percentage is 80.0%.

b. In the event of an underpayment of Vorasidenib Receivables under the Counterparty Agreement in respect of aggregate annual Net Sales of the Earn-Out Product (vorasidenib) made in the US Territory, the Seller shall, upon the request of the Purchaser, furnish to Counterparty an invoice created by the Purchaser for the amount of such underpayment within [**] after the final determination thereof, and shall instruct Counterparty to pay or cause to be paid to the Deposit Account an amount in cash equal to such underpayment. If the Applicable Percentage is reduced to 80.0% for the balance of Net Sales occurring during a particular calendar year because the Purchaser has actually received $150 million in Vorasidenib Receivables in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring during such calendar year, the Purchaser and the Seller shall reasonably cooperate with one another regarding any underpayment of Vorasidenib Receivables and/or Retained Receivables by the Counterparty

with respect to Net Sales of the Earn-Out Product (vorasidenib) occurring during the remaining portion of such calendar year when the Applicable Percentage is 80.0%.

c. In the event of an overpayment of Vorasidenib Receivables under the Counterparty Agreement received by the Purchaser in respect of aggregate annual Net Sales of the Earn-Out Product (vorasidenib) made in the US Territory, the Purchaser shall (x) if the Counterparty chooses cash repayment of such overpayment pursuant to clause (A) in the second sentence of 2.13(a)(iv) or 2.13(e)(A) of the Counterparty Agreement, pay or cause to be paid to Counterparty the amount in cash equal to such overpayment within [**] following receipt of an invoice from Counterparty after the after the final determination thereof, or (y) if the Counterparty chooses to offset such overpayment pursuant to clause (B) in the second sentence of 2.13(a)(iv) or 2.13(e)(B) of the Counterparty Agreement, such offset shall be deemed to be a "Permitted Deduction" hereunder for which the Seller shall not be obligated to reimburse the Purchaser under this Purchase and Sale Agreement. If the Applicable Percentage is reduced to 80.0% for the balance of Net Sales occurring during a particular calendar year because the Purchaser has actually received $150 million in Vorasidenib Receivables in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring during such calendar year, the Purchaser and the Seller shall reasonably cooperate with one another regarding any overpayment of Vorasidenib Receivables and/or Retained Receivables by the Counterparty with respect to Net Sales of the Earn-Out Product (vorasidenib) occurring during the remaining portion of such calendar year when the Applicable Percentage is 80.0%.

Section 5.10 Confidentiality. The Purchaser agrees to keep confidential the Counterparty Agreement, the Quarterly Net Sales Statements produced by Counterparty pursuant to Section 2.13(a)(iii) of the Counterparty Agreement, the Annual Net Sales Statements produced by Counterparty pursuant to Section 2.13(a)(iv) of the Counterparty Agreement, and any Audit Reports received pursuant to Section 2.13(e) of the Counterparty Agreement, in each case in accordance with or on terms no less restrictive than those set forth in Section 5.5 of the Counterparty Agreement.

Section 5.11 Deposit Account. The Purchaser shall establish the Deposit Account prior to the Closing. The parties hereto agree to act reasonably in amending the Counterparty Instruction to reflect the Seller's irrevocable instruction to the Counterparty to pay the Vorasidenib Receivables to any deposit account designated by the Purchaser (which shall initially be the Deposit Account), and the Seller shall promptly deliver such amended Counterparty Instruction to the Counterparty. If the Applicable Percentage is reduced to 80.0% for the balance of Net Sales occuring during a particular calendar year because the Purchaser has actually received $150 million in Vorasidenib Receivables in respect of Net Sales of the Earn-Out Product (vorasidenib) occurring during such calendar year, the parties hereto shall promptly cooperate regarding a mechanism to divide and distribute the Vorasidenib Receivables to the Purchaser and the Retained Receivables to the Seller, including, as appropriate, through the continued use of the Deposit Account from which Purchaser will divide and distribute the applicable amounts to the Seller for the remainder of such calendar year, or, if the Purchaser is in material breach of this Purchase and Sale Agreement and the Seller so elects, through a revised Counterparty Instruction by which Seller instructs the Counterparty to make payments on account of the Retained Receivables directly to the Seller; provided that, in all events, payments received by the

Purchaser on account of Retained Receivables shall be paid to the Seller within [**] following receipt by the Purchaser.

ARTICLE VI
CONDITIONS TO CLOSING; CLOSING DATE DELIVERIES

Section 6.1 Purchaser Conditions to Closing. The Purchaser's obligation to purchase, acquire and accept all of the Seller's rights, title and interest in and to the Purchased Assets at the Closing and to pay the Purchase Price at the Closing is subject to the fulfillment as of the Closing Date of the following conditions (unless waived in writing by the Purchaser):

a. FDA Approval shall have occurred on or prior to October 31, 2024;

b. all representations and warranties of Seller contained herein and in the other Transaction Documents shall be true and correct in all material respects as of the Closing Date (except that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof), as though made on and as of such dates (except to the extent that such representations and warranties relate solely to an earlier date, in which case such representations and warranties shall be true and correct in all material respects (except that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof) as of such earlier date);

c. the Seller shall have delivered to the Purchaser a certificate of an officer of the Seller, dated the Closing Date, (i) certifying as to the Seller's organizational documents and the attached resolutions adopted by the board of directors of the Seller authorizing the transactions contemplated by the Transaction Documents and (ii) setting forth the incumbency of the officer or officers of the Seller who have executed and delivered the Transaction Documents, including therein a signature specimen of each such officer;

d. the Seller shall have delivered to the Purchaser the Bill of Sale executed by the Seller;

e. the Seller shall have delivered to the Purchaser the Counterparty Instruction executed by the Seller and shall have completed the Seller information in Schedule 1.2;

f. the Seller shall have delivered or caused to be delivered to the Purchaser an opinion of WilmerHale, special counsel to the Seller, dated the Effective Date and in form and substance satisfactory to the Purchaser and its counsel;

g. the Seller shall have delivered to the Purchaser a valid, properly executed IRS Form W-9 certifying that the Seller is exempt from U.S. federal "backup" withholding tax; and

h. the Seller shall have delivered to the Purchaser financing statements naming the Purchaser as the "Buyer" of the Purchased Assets and the Secured Party, to create, evidence and perfect the sale, contribution, assignment, transfer, conveyance and grant of the Purchased Assets pursuant to Section 2.1(b) and the back-up security interest granted pursuant to Section 2.1(f).

Section 6.2 Seller Conditions to Closing. The Seller's obligation to sell, contribute, assign, transfer, convey and grant to the Purchaser all of the Seller's rights, title and interests in and to the Purchased Assets at the Closing is subject to the fulfillment as of the Closing Date of the following conditions (unless waived in writing by the Seller):

a. all representations and warranties of the Purchaser contained herein and in the other Transaction Documents shall be true and correct in all material respects as of the Closing Date (except that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof), as though made on and as of such dates (except to the extent that such representations and warranties relate solely to an earlier date, in which case such representations and warranties shall be true and correct in all material respects (except that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof) as of such earlier date);

b. the Purchaser shall have delivered to the Seller a certificate of an officer of the Purchaser, dated the Closing Date, setting forth the incumbency of the officer or officers of the Purchaser who have executed and delivered the Transaction Documents, including therein a signature specimen of each such officer; and

c. the Purchaser shall have completed the Purchaser information in Schedule 1.2, shall have established the Deposit Account, and shall have delivered to the Seller a valid, properly executed IRS Form W-8BEN-E, or other applicable IRS withholding form, certifying that the Purchaser is (or payments to the Purchaser are) exempt from U.S. federal withholding tax with respect to any and all payments pursuant to this Purchase and Sale Agreement.

ARTICLE VII
INDEMNIFICATION

Section 7.1 Indemnification by the Seller. From and after the Effective Date, the Seller agrees to indemnify and hold the Purchaser and its Affiliates and any and all of its respective officers, directors, employees, consultants, representatives and advisers (each, a "Purchaser Indemnified Party") harmless from and against, and will pay to each Purchaser Indemnified Party the amount of, any and all Losses (including attorneys' fees) awarded against or incurred or suffered by such Purchaser Indemnified Party whether or not involving a third party claim, demand, action or proceeding, in each case of the foregoing arising out of (i) any breach of any representation, warranty or verification made by the Seller in any of the Transaction Documents to which the Seller is party or certificates given by the Seller to the Purchaser in writing pursuant to this Agreement, (ii) any breach of any covenant or agreement by the Seller under (A) any Transaction Document to which the Seller is party or (B) the

Counterparty Agreement, (iii) any Excluded Liabilities and Obligations, and (iv) any fees, expenses, costs, liabilities or other amounts incurred or owed by the Seller to any brokers, financial advisors or comparable other Persons retained or employed by it in connection with the transactions contemplated by this Purchase and Sale Agreement; provided, however, that Seller shall not be liable for the payment to any Purchaser Indemnified Party for any portion of such Losses resulting from such Purchaser Indemnified Party's gross negligence or willful misconduct as determined in a final, non-appealable judgment of a court of competent jurisdiction or resulting from any Permitted Deduction or Credit Event. Any amounts due to any Purchaser Indemnified Party hereunder shall be payable to the Seller to such Purchaser Indemnified Party within [**] of written demand.

Section 7.2 Indemnification by the Purchaser. The Purchaser agrees to indemnify and hold each of the Seller and its Affiliates and any and all of their respective officers, directors, employees, consultants, representatives and advisers (each, a "Seller Indemnified Party") harmless from and against, and will pay to each Seller Indemnified Party the amount of, any and all Losses (including attorneys' fees) awarded against or incurred or suffered by such Seller Indemnified Party whether or not involving a third party claim, demand, action or proceeding, arising out of (i) any breach of any representation, warranty or certification made by the Purchaser in any of the Transaction Documents to which the Purchaser is party or certificates given by the Purchaser in any of the Transaction Documents to which the Purchaser is party or certificates given by the Purchaser in writing pursuant hereto or thereto, (ii) any breach of or default under any covenant or agreement by the Purchaser pursuant to any Transaction Document to which the Purchaser is party and (iii) any fees, expenses, costs, liabilities or other amounts incurred or owed by the Purchaser to any brokers, financial advisors or comparable other Persons retained or employed by it in connection with the transaction contemplated by this Purchase and Sale Agreement; provided, however, that the Purchaser shall not be liable for the payment to any Seller Indemnified Party for any portion of such Losses resulting from such Seller Indemnified Party's gross negligence or willful misconduct as determined in a final, non-appealable judgment of a court of competent jurisdiction. Any amounts due to any Seller Indemnified Party hereunder shall be payable by the Purchaser to such Seller Indemnified Party within [**] of written demand.

Section 7.3 Procedures. If any claim, demand, action or proceeding (including any investigation by any Governmental Authority) 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 7.1 or Section 7.2, the indemnified party shall, promptly after receipt of notice of the commencement of any such claim, demand, action or proceeding, notify the indemnifying party in writing of the commencement of such claim, demand, action or proceeding, 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 7.1 or Section 7.2 unless, and only to the extent that, the indemnifying party is actually prejudiced by such omission. In the event that any such action is brought against an indemnified party and it notifies the indemnifying party of the commencement thereof in accordance with this Section 7.3, the indemnifying party will be entitled, at the indemnifying party's sole cost and expense, to participate therein and, to the extent that it may wish, to assume the defense thereof, with counsel reasonably satisfactory to such indemnified party (who shall not, except with the consent of the indemnified party, be counsel to the indemnifying party), and, after notice from the indemnifying party to such indemnified party of its election so to assume the defense thereof, the indemnifying party will not be liable to such indemnified party under this Article

VII for any legal expenses subsequently incurred by such indemnified party in connection with the defense thereof other than reasonable costs of investigation. In any such proceeding, 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 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 assumed the defense of such proceeding and has failed within a reasonable time to retain counsel reasonably satisfactory to such indemnified party or (c) the named parties to any such proceeding (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 indemnified party, in which case the reasonable fees and expenses of such counsel shall be at the expense of the indemnifying party. It is agreed that the indemnifying party shall not, in connection with any proceeding 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 proceeding effected without its written consent (such consent not to be unreasonably withheld), 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 (such consent not to be unreasonably withheld), effect any settlement, compromise or discharge of any claim or pending or threatened proceeding in respect of which any indemnified party is or could have been a party and indemnity could 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 obligation or restrictions on any indemnified party.

Section 7.4 Exclusive Remedy. Except in the case of fraud or intentional breach, following the Effective Date, the indemnification afforded by this Article VII shall be the sole and exclusive remedy for any and all Losses awarded against or incurred or suffered by a party hereto in connection with the transactions contemplated by the Transaction Documents, including with respect to any breach of any representation, warranty or certification made by a party hereto in any of the Transaction Documents or certificates given by a party hereto in writing pursuant hereto or thereto or any breach of or default under any covenant or agreement by a party hereto pursuant to any Transaction Document. Notwithstanding anything in this Purchase and Sale Agreement to the contrary, in the event of any breach or failure in performance of any covenant or agreement contained in any Transaction Document, the non-breaching party shall be entitled to specific performance, injunctive or other equitable relief pursuant to Section 8.2.

Section 7.5 Limitation of Liability. Notwithstanding anything in this Agreement to the contrary, (a) the Seller shall not have any liability under Section 7.1(i) in excess of [**], provided, that the foregoing limitation shall not apply to breach of any of the representations, covenants or agreements set forth in Sections 3.8 and 5.7, and (b) the Purchaser shall have no liability under Section 7.2(i) in excess of [**].

Section 7.6 Tax Treatment for Indemnification Payments. Any indemnification payments made pursuant to this Article 7 will be treated as an adjustment to the Purchase Price for U.S. federal income tax to the fullest extent permitted by Applicable Law.

ARTICLE VIII
MISCELLANEOUS

Section 8.1 Termination; Survival.

a. [Reserved].

b. This Purchase and Sale Agreement shall commence on the Effective Date, and, so long as the Closing occurs, this Purchase and Sale Agreement shall continue in full force and effect until there are no longer Vorasidenib Receivables from the Earn-Out Product (vorasidenib), at which point this Purchase and Sale Agreement shall terminate, except for any rights, obligations or claims of either party hereto that have accrued prior to such termination; provided, however, that the provisions of Article II, Section 5.2, Section 5.4(d), Section 5.7, Section 5.9, Article VII and Article VIII shall survive such termination. Unless and until this Purchase and Sale Agreement shall have terminated in accordance with the prior sentence, all representations, warranties and covenants made herein and in any other Transaction Document or any certificate delivered pursuant to this Purchase and Sale Agreement shall survive the execution and delivery of this Purchase and Sale Agreement, the Effective Date and the Closing Date; provided that, on and after the Closing Date, all representations and warranties shall be deemed made only as of the Closing Date (except to the extent that such representations and warranties relate solely to an earlier date, in which case such representations and warranties shall be deemed made as of such earlier date). The rights hereunder to indemnification, payment of Losses or other remedies 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 Purchase and Sale Agreement or the Effective Date) in respect of the accuracy or inaccuracy of or compliance with, any such representation, warranty or covenant. The waiver of any condition based on the accuracy of any representation or warranty, or on the performance of or compliance with any covenant, shall not affect the rights hereunder to indemnification, payment of Losses or other remedies based on such representations, warranties and covenants. This Agreement shall automatically terminate in all respects if the FDA Approval has not occurred by October 31, 2024, unless otherwise agreed in writing prior to such date by Seller and Purchaser.

Section 8.2 Specific Performance. Each of the parties hereto acknowledges that the other party hereto will have no adequate remedy at law if it 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 specific performance of this Purchase and Sale Agreement.

Section 8.3 Notices. All notices and other communications under this Purchase and Sale Agreement shall be in writing and shall be by email with PDF attachment, facsimile, courier service or

personal delivery to the following addresses, or to such other addresses as shall be designated from time to time by a party hereto in accordance with this Section 8.3:

If to the Seller, to it at:

Agios Pharmaceuticals, Inc.
88 Sidney St.
Cambridge, MA 02139
Attention: [**]
Email: [**]

with a copy to:

WilmerHale
60 State Street
Boston, MA 02109
Attention: George W. Shuster Jr.
Email: george.shuster@wilmerhale.com

If to the Purchaser, to it at:

Royalty Pharma Investments 2019 ICAV
110 E. 59th Street, Suite 3300
New York, New York 10022
Attention: [**]
Email: [**]

with a copy to:

Goodwin Procter LLP
100 Northern Avenue
Boston, Massachusetts 02210
Attention: Robert M. Crawford and Jacqueline Mercier
Email: [**]

Section 8.4 Successors and Assigns. The provisions of this Purchase and Sale Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns. The Seller shall not be entitled to assign or otherwise transfer any Transaction Document or any of its obligations, rights or interests under any of the Transaction Documents, in whole or in part, by operation of law, merger, change of control or otherwise, without the prior written consent of the Purchaser (such consent not to be unreasonably withheld, conditioned or delayed provided that such assignment is an assignment of all of Seller's rights and obligations under this Agreement and meets the provisions of Section 8.04(a)(ii), Section 8.4(a)(iii) and Section 8.4(b) below), and any purported assignment or transfer without such consent shall be void and of no effect; provided, however, that the Seller may, without the prior written consent of the Purchaser, assign all of its obligations and rights under this Purchase and Sale Agreement (in whole, and not in part) to any other Person with

which it may merge or consolidate or to which it may sell all or substantially all of its assets (including the Counterparty Agreement), provided that (a) the assignee under such assignment (i) is a Qualified Assignee, (ii) has also been assigned the Counterparty Agreement in connection with such transaction, and (iii) agrees to be bound by the terms of the Transaction Documents and the Counterparty Agreement and furnishes a written agreement to the Purchaser in form and substance reasonably satisfactory to the Purchaser to that effect, and (b) such transaction does not require either Counterparty to deduct or withhold from payments of the Vorasidenib Receivables any additional taxes pursuant to the Counterparty Agreement or under Applicable Law that would not be reimbursable to the Purchaser under this Purchase and Sale Agreement. The Purchaser may assign any of its obligations and rights hereunder without restriction and without the consent of the Seller: (i) to any of its Affiliates, its limited partners and any feeder vehicles, managed funds and alternative investment vehicles each of them may establish, and (ii) to any other Person with the prior written consent of the Counterparties. The Purchaser shall give notice of any assignment to the Seller promptly after the occurrence thereof.

Section 8.5 Independent Nature of Relationship. The relationship between the Seller and the Purchaser is solely that of seller and purchaser, and neither the Seller nor the Purchaser has any fiduciary or other special relationship with the other party hereto or any of its Affiliates. This Purchase and Sale Agreement is not a partnership, joint venture agreement or similar agreement, and nothing contained herein or in any other Transaction Document shall be deemed to constitute the Seller and the Purchaser, and/or Counterparty, any Sublicensee or Affiliate thereof, as a partnership, an association, a joint venture or any other kind of entity or legal form for any purposes, including any Tax purposes. The parties hereto agree that they shall not take any inconsistent position with respect to such treatment in a filing with any Governmental Authority.

Section 8.6 Entire Agreement. This Purchase and Sale Agreement, together with the Bill of Sale, the Counterparty Instruction, the financing statements and 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 Purchase and Sale 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. Neither this Purchase and Sale Agreement nor any provision hereof is intended to confer upon any Person other than the parties hereto any rights or remedies hereunder, except that (a) Counterparty shall be a third-party beneficiary of the second to last sentence of Section 8.4, (b) Purchaser Indemnified Parties (other than the Purchaser) shall be a third-party beneficiary of Section 7.1, and (c) Seller Indemnified Parties (other than the Seller) shall be a third-party beneficiary of Section 7.2.

Section 8.7 Governing Law.

a. THIS PURCHASE AND SALE 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 OTHER THAN SECTION 5-1401 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 non-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 Purchase and Sale Agreement or any other Transaction Document, 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 Purchase and Sale Agreement in any court referred to in Section 8.7(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 8.3. Nothing in this Purchase and Sale 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 8.8 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 PURCHASE AND SALE 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 PURCHASE AND SALE AGREEMENT BY, AMONG OTHER THINGS, THE MUTUAL WAIVERS AND CERTIFICATIONS IN THIS SECTION 8.8.

Section 8.9 Severability. If one or more provisions of this Purchase and Sale Agreement are held to be invalid or unenforceable by a court of competent jurisdiction, such provision shall be excluded from this Purchase and Sale Agreement and the balance of this Purchase and Sale Agreement shall be interpreted as if such provision were so excluded and shall remain in full force and effect and be

enforceable in accordance with its terms. Any provision of this Purchase and Sale Agreement held invalid 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 or unenforceable.

Section 8.10 Counterparts. This Purchase and Sale 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 Purchase and Sale 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 other similar means of electronic transmission, including "PDF", and such facsimile or other electronic transmission shall be deemed an original.

Section 8.11 Amendments; No Waivers. Neither this Purchase and Sale Agreement nor any term or provision hereof may be amended, supplemented, restated, waived, changed or modified except with the written consent of the Seller and the Purchaser. 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 8.12 Table of Contents and Headings. The Table of Contents and headings of the Articles and Sections of this Purchase and Sale 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 Purchase and Sale Agreement as of the day and year first written above.

AGIOS PHARMACEUTICALS, INC.

By: /s/ Cecilia Jones
Name: Cecilia Jones
Title: Chief Financial Officer

ROYALTY PHARMA INVESTMENTS 2019 ICAV

By: RP Management, LLC, its Manager and lawfully-appointed attorney

By: /s/ Arthur McGivern
Name: Arthur McGivern
Title: EVP & General Counsel

Exhibit D

Counterparty Agreement

Incorporated by reference to Exhibit 2.1 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023 filed with the Securities and Exchange Commission

ACTIVE/129522328.13

Exhibit 31.1

CERTIFICATION

I, Brian Goff, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Agios 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 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 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 1, 2024

/s/ Brian Goff

Brian Goff
Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Cecilia Jones, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Agios 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 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 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 1, 2024

/s/ Cecilia Jones

Cecilia Jones
Chief Financial Officer
(principal financial officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended June 30, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Brian Goff, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 1, 2024

/s/ Brian Goff
Brian Goff
Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended June 30, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Cecilia Jones, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to her knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 1, 2024

/s/ Cecilia Jones
Cecilia Jones
Chief Financial Officer
(principal financial officer)