

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 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 March 31, 2022

OR

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

For the transition period from _____ to _____

Commission File Number: 001-38871

Turning Point Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

10628 Science Center Drive, Ste. 200
San Diego, California
(Address of principal executive offices)

46-3826166
(I.R.S. Employer
Identification No.)

92121
(Zip Code)

Registrant's telephone number, including area code: (858) 926-5251

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.0001 par value per share	TPTX	The Nasdaq Stock Market LLC

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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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

As of May 3, 2022, the registrant had 49,666,288 shares of common stock outstanding.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements

Turning Point Therapeutics, Inc.
Condensed Balance Sheets
(In thousands, except share and par value amounts)

	March 31, 2022	December 31, 2021
	<u>Unaudited</u>	
Assets		
Current assets:		
Cash and cash equivalents	\$ 309,532	\$ 427,879
Marketable securities	608,655	553,703
Prepaid and other current assets	9,244	10,880
Total current assets	927,431	992,462
Property and equipment, net	3,875	3,822
Right-of-use lease assets	5,439	5,158
Other assets	2,041	2,021
Total assets	\$ 938,786	\$ 1,003,463
Liabilities and stockholders' equity		
Liabilities:		
Current liabilities:		
Accounts payable	\$ 7,610	\$ 5,656
Accrued expenses and other current liabilities	27,632	25,300
Accrued compensation	6,363	12,503
Current portion of operating lease liabilities	3,961	3,630
Total current liabilities	45,566	47,089
Operating lease liabilities, long-term	1,873	1,949
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 10,000,000 shares authorized at March 31, 2022 and December 31, 2021, zero shares outstanding at March 31, 2022 and December 31, 2021	—	—
Common stock, \$0.0001 par value; 200,000,000 shares authorized at March 31, 2022 and December 31, 2021; 49,664,473 and 49,582,638 shares issued and outstanding at March 31, 2022 and December 31, 2021, respectively	5	5
Additional paid-in capital	1,487,906	1,472,421
Accumulated other comprehensive loss	(5,392)	(1,274)
Accumulated deficit	(591,172)	(516,727)
Total stockholders' equity	891,347	954,425
Total liabilities and stockholders' equity	\$ 938,786	\$ 1,003,463

See accompanying notes.

Turning Point Therapeutics, Inc.

Condensed Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended March 31,	
	2022	2021
Revenue	\$ 429	\$ 25,205
Operating expenses:		
Research and development	55,050	41,263
General and administrative	20,314	19,991
Total operating expenses	75,364	61,254
Loss from operations	(74,935)	(36,049)
Other income, net	490	545
Net loss	(74,445)	(35,504)
Unrealized loss on marketable securities, net of tax	(4,118)	(186)
Comprehensive loss	\$ (78,563)	\$ (35,690)
Net loss per share, basic and diluted	\$ (1.50)	\$ (0.73)
Weighted-average common shares outstanding, basic and diluted	49,611,492	48,920,403

See accompanying notes.

Turning Point Therapeutics, Inc.

Condensed Statements of Stockholders' Equity
(In thousands, except share amounts)
(Unaudited)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2021	49,582,638	\$ 5	\$ 1,472,421	\$ (1,274)	\$ (516,727)	\$ 954,425
Issuance of common stock under equity incentive plans	81,835	—	396	—	—	396
Stock-based compensation expense	—	—	15,089	—	—	15,089
Net loss	—	—	—	—	(74,445)	(74,445)
Other comprehensive loss	—	—	—	(4,118)	—	(4,118)
Balance at March 31, 2022	49,664,473	\$ 5	\$ 1,487,906	\$ (5,392)	\$ (591,172)	\$ 891,347

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2020	48,678,540	\$ 5	\$ 1,389,860	\$ 209	\$ (280,176)	\$ 1,109,898
Issuance of common stock under equity incentive plans	438,500	—	9,679	—	—	9,679
Stock-based compensation expense	—	—	17,278	—	—	17,278
Net loss	—	—	—	—	(35,504)	(35,504)
Other comprehensive loss	—	—	—	(186)	—	(186)
Balance at March 31, 2021	49,117,040	\$ 5	\$ 1,416,817	\$ 23	\$ (315,680)	\$ 1,101,165

See accompanying notes.

Turning Point Therapeutics, Inc.

Condensed Statements of Cash Flows
(In thousands)
(Unaudited)

	Three Months Ended March 31,	
	2022	2021
Operating activities		
Net loss	\$ (74,445)	\$ (35,504)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	15,089	17,278
Depreciation	393	253
Accretion of premium on marketable securities	893	1,400
Amortization of right-of-use operating lease asset	861	380
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,636	1,036
Other assets	(20)	—
Accounts payable	1,954	1,542
Accrued expenses and other liabilities	1,448	2,690
Accrued compensation	(6,140)	(4,723)
Net cash used in operating activities	(58,331)	(15,648)
Investing activities		
Purchases of marketable securities	(134,783)	(160,650)
Sales and maturities of marketable securities	74,818	81,862
Purchases of property and equipment	(447)	(143)
Net cash used in investing activities	(60,412)	(78,931)
Financing activities		
Proceeds from issuance of common stock under equity incentive plans	396	9,679
Net cash provided by financing activities	396	9,679
Net decrease in cash, cash equivalents and restricted cash	(118,347)	(84,900)
Cash, cash equivalents and restricted cash at the beginning of period	429,755	554,174
Cash, cash equivalents and restricted cash at the end of period	\$ 311,408	\$ 469,274
Supplemental disclosure of cash flow information:		
Cash paid for income taxes	\$ —	\$ 1
Supplemental disclosure of non-cash investing and financing information:		
Purchases of property and equipment in accounts payable	\$ 42	\$ 16
Operating lease liabilities arising from obtaining right-of-use assets	\$ 1,142	\$ —

See accompanying notes.

Notes to Unaudited Condensed Financial Statements

1. Organization

Description of Business

Turning Point Therapeutics, Inc. (the Company) was organized in October 2013 and commenced operations in 2014. The Company is a clinical-stage precision oncology company designing and developing novel targeted therapies for cancer treatment. The Company's principal operations are in the United States and the Company operates in one segment with its headquarters in San Diego, California.

The Company's primary activities since inception have been to build infrastructure, conduct research and development, including clinical trials, perform business and financial planning, and raise capital.

Liquidity

The Company's activities are subject to significant risks and uncertainties, including concentration on the Company's lead development program, which has significant competition from cancer therapies in development by other companies or already approved for sale by the U.S. Food and Drug Administration.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Drug candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The COVID-19 pandemic and ongoing geopolitical events continue to rapidly evolve and have already resulted in a significant disruption of global financial markets. The Company's ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and further disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the pandemic or geopolitical actions. If such further disruption occurs, the Company could experience an inability to access additional capital.

The Company determined that there are no conditions or events that raise substantial doubt about its ability to continue as a going concern for a period of at least twelve months from the date of issuance of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America (U.S. GAAP) for interim financial information and pursuant to Form 10-Q and Article 10 of Regulation S-X of the Securities and Exchange Commission (SEC). Accordingly, since they are interim statements, the accompanying condensed financial statements do not include all of the information and notes required by U.S. GAAP for complete financial statements. These unaudited condensed financial statements should be read in conjunction with the audited financial statements and the notes thereto for the year ended December 31, 2021 included in the Company's Annual Report on Form 10-K filed with the SEC. In the opinion of management, the unaudited condensed financial statements and notes thereto include all adjustments (consisting only of normal recurring adjustments) that are necessary for the fair presentation of the Company's financial position and of the results of operations and cash flows for the periods presented. The operating results presented in these unaudited condensed financial statements are not necessarily indicative of the results that may be expected for any future periods.

Use of Estimates

The preparation of the Company's financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. The most significant estimates in the Company's

financial statements relate to determining the standalone selling prices (SSP) of performance obligations associated with license and collaboration arrangements, accrued research and development expenses and stock-based compensation expenses. The Company bases these estimates on historical experience, knowledge of current events and actions it may undertake in the future, and on various other assumptions that are believed to be reasonable. Actual results may differ materially from these estimates and assumptions. Although the impact of the COVID-19 pandemic to the Company's business and operating results presents additional uncertainty, the Company continues to use the best information available to update its critical accounting estimates.

Cash, Cash Equivalents and Restricted Cash

The following table presents a reconciliation of cash, cash equivalents and restricted cash to the amounts shown in the unaudited condensed statements of cash flows (in thousands):

	March 31, 2022	March 31, 2021
Cash and cash equivalents	\$ 309,532	\$ 469,167
Restricted cash included in other assets	1,876	107
Total cash, cash equivalents and restricted cash	\$ 311,408	\$ 469,274

Concentration of Credit Risk

Substantially all of the Company's cash, cash equivalent and marketable securities are held at two financial institutions. Due to the financial strength of the depository institutions, the Company believes these financial institutions represent minimal credit risk. Cash amounts held at financial institutions are insured by the Federal Deposit Insurance Corporation (FDIC) up to \$250,000. At March 31, 2022, cash, cash equivalents and marketable securities totaling \$917.9 million are either not subject to FDIC insurance, or exceed the FDIC insured limit. The Company's cash, cash equivalents and marketable securities are invested in short term, high credit quality securities, and as a result, the Company believes represent a minimal credit risk.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss available to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share assumes the conversion, exercise or issuance of all potential common stock equivalents, unless the effect of inclusion would be anti-dilutive. For purposes of this calculation, common stock equivalents include the Company's stock options, restricted stock units (RSUs) and performance stock units (PSUs). The Company excluded stock options to purchase common stock, RSUs and PSUs from the number of shares used to calculate diluted shares outstanding because the inclusion of these potentially dilutive securities would have been antidilutive.

Historical outstanding anti-dilutive securities not included in the diluted net loss per share calculation include the following:

	Three Months Ended March 31,	
	2022	2021
Common stock options	6,246,784	5,581,907
RSUs	727,643	162,165
PSUs	275,649	176,675
Total	7,250,076	5,920,747

3. Marketable Securities

The Company invests its excess cash in marketable securities, including debt instruments of financial institutions, corporations with investment grade credit ratings, commercial paper and government agencies.

At March 31, 2022, marketable securities consisted of the following (in thousands):

	Maturity in Years	Amortized Cost	Unrealized		Fair Value
			Gains	Losses	
U.S. Treasuries	2 years or less	\$ 372,647	\$ 4	\$ (4,206)	\$ 368,445
U.S. Government agency securities	2 years or less	125,331	—	(679)	124,652
Non-U.S. Government agency securities	2 years or less	13,709	—	(156)	13,553
Corporate debt securities	2 years or less	88,453	8	(344)	88,117
Commercial paper	Less than 1	13,888	—	—	13,888
Total marketable securities		<u>\$ 614,028</u>	<u>\$ 12</u>	<u>\$ (5,385)</u>	<u>\$ 608,655</u>

At December 31, 2021, marketable securities consisted of the following (in thousands):

	Maturity in Years	Amortized Cost	Unrealized		Fair Value
			Gains	Losses	
U.S. Treasuries	2 years or less	\$ 305,763	\$ 1	\$ (1,006)	\$ 304,758
U.S. Government agency securities	2 years or less	151,047	—	(180)	150,867
Non-U.S. Government agency securities	2 years or less	23,787	—	(49)	23,738
Corporate debt securities	2 years or less	74,391	5	(56)	74,340
Total marketable securities		<u>\$ 554,988</u>	<u>\$ 6</u>	<u>\$ (1,291)</u>	<u>\$ 553,703</u>

The Company segments its portfolio based on the underlying risk profiles of their current securities being held. The Company regularly reviews the securities in an unrealized loss position and evaluates the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, current and expected future economic conditions. As of March 31, 2022 and December 31, 2021, the Company did not record an allowance for credit loss related to its investment portfolio.

4. Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. Fair value should maximize the use of observable inputs and minimize the use of unobservable inputs. The Company determines the fair value of financial assets and liabilities using three levels of inputs as follows:

Level 1 — Observable inputs such as quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2 — Inputs (other than quoted market prices included in Level 1) that are either directly or indirectly observable, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the instrument's anticipated life; and

Level 3 — Unobservable inputs for assets or liabilities and include little or no market activity.

A financial instrument's categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

The Company measures fair value based on the prices that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The carrying amounts of certain of the Company's financial instruments, including cash and cash equivalents, prepaid and other current assets, accounts payable, and accrued liabilities, approximate fair value due to the short-term nature of these items.

The Company's financial assets subject to fair value measurements on a recurring basis and the level of inputs used for such measurements were as follows (in thousands):

	Fair Value Measurements at March 31, 2022 Using:			
	Level 1	Level 2	Level 3	Total
Money market funds	\$ 149,746	\$ —	\$ —	\$ 149,746
U.S. Treasuries	368,445	—	—	368,445
U.S. Government agency securities	—	124,652	—	124,652
Non-U.S. Government securities	—	13,553	—	13,553
Corporate debt securities	—	88,117	—	88,117
Commercial paper	—	172,807	—	172,807
Total cash equivalents and marketable securities	<u>\$ 518,191</u>	<u>\$ 399,129</u>	<u>\$ —</u>	<u>\$ 917,320</u>

	Fair Value Measurements at December 31, 2021 Using:			
	Level 1	Level 2	Level 3	Total
Money market funds	\$ 232,813	\$ —	\$ —	\$ 232,813
U.S. Treasuries	304,758	—	—	304,758
U.S. Government agency securities	—	150,867	—	150,867
Non-U.S. Government securities	—	23,738	—	23,738
Corporate debt securities	—	77,400	—	77,400
Commercial paper	—	191,130	—	191,130
Total cash equivalents and marketable securities	<u>\$ 537,571</u>	<u>\$ 443,135</u>	<u>\$ —</u>	<u>\$ 980,706</u>

5. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	March 31, 2022	December 31, 2021
Laboratory equipment	\$ 3,611	\$ 3,368
Computer equipment and software	1,347	1,283
Tenant improvements	1,557	1,468
Furniture and fixtures	403	358
Property and equipment	6,918	6,477
Less: accumulated depreciation	(3,043)	(2,655)
Property and equipment, net	<u>\$ 3,875</u>	<u>\$ 3,822</u>

Depreciation expense for the three months ended March 31, 2022 and 2021 was \$0.4 million and \$0.3 million, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	March 31, 2022	December 31, 2021
Accrued research and development expenses	\$ 25,454	\$ 23,497
Accrued general and administrative expenses	1,986	1,655
Other current liabilities	192	148
Total	<u>\$ 27,632</u>	<u>\$ 25,300</u>

7. Zai License Agreements

Zai Repotrectinib Agreement

In July 2020, the Company entered into a license agreement (the Zai Repotrectinib Agreement) with Zai Lab (Shanghai) Co., Ltd. (Zai), pursuant to which the Company granted Zai exclusive rights to develop and commercialize products containing the Company's drug candidate, repotrectinib (the Repotrectinib Products), in Mainland China, Hong Kong, Macau and Taiwan (collectively, the Zai Territory or Greater China). The Company retains exclusive rights to, among other things, develop, manufacture

and commercialize the Repotrectinib Products outside the Zai Territory. The Company will supply or have supplied to Zai the Repotrectinib Products for use in the Zai Territory pursuant to a supply agreement for agreed upon consideration, except that Zai has the right, at its election, to package and label the Repotrectinib Products in or outside the Zai Territory for use in the Zai Territory.

Pursuant to the terms of the Zai Repotrectinib Agreement, the Company received an upfront cash payment of \$25.0 million in 2020 and is eligible to receive up to \$151.0 million in development and sales milestone payments, consisting of up to \$46.0 million of development milestones and up to \$105.0 million of sales milestones. In addition, during the term of the Zai Repotrectinib Agreement, Zai is obligated to pay the Company tiered percentage royalties ranging from mid-to-high teens on annual net sales of the Repotrectinib Products in the Zai Territory, subject to adjustments in specified circumstances.

Zai is responsible for conducting the development and commercialization activities in the Zai Territory related to the Repotrectinib Products at Zai's own expense, subject to limited exceptions pursuant to which the Company may be responsible for the cost. The Company is responsible for global clinical studies of the Repotrectinib Products, including the portions that may be conducted in the Zai Territory, at the Company's expense, except that Zai will participate in global clinical studies of the Repotrectinib Products through clinical trial sites in the Zai Territory as agreed as of the effective date of the Zai Repotrectinib Agreement and may, at Zai's election, participate in future global clinical studies of the Repotrectinib Products through clinical trial sites in the Zai Territory, in each case at Zai's expense.

The Zai Repotrectinib Agreement will continue in effect until expiration of the last royalty term for a Repotrectinib Product in any region in the Zai Territory, where the royalty term for a Repotrectinib Product in a region continues until the later of (i) the date of the last-to-expire valid claim within Company's patent rights that covers the Repotrectinib Product in such region in the Zai Territory; (ii) the expiry of the regulatory exclusivity for such Repotrectinib Product in such region; or (iii) the close of business of the day that is exactly 10 years after the date of the first commercial sale of such Repotrectinib Product in such region. Subject to the terms of the Zai Repotrectinib Agreement, Zai may terminate the Zai Repotrectinib Agreement for convenience by providing written notice to the Company, which termination will be effective following a prescribed notice period. In addition, the Company may terminate the Zai Repotrectinib Agreement under specified circumstances if Zai or certain other parties challenge the Company's patent rights. Either party may terminate the Zai Repotrectinib Agreement for the other party's uncured material breach of the Zai Repotrectinib Agreement, with a customary notice and cure period, for the other party's insolvency or if the other party acquires a third party and the acquired party is engaged in activities with a competing product that is not divested or discontinued within a specified period. After termination (but not natural expiration), other than certain terminations by Zai for cause, the Company is entitled to retain a worldwide and perpetual license from Zai to exploit the Repotrectinib Products.

Revenue Recognition

The Company determined that two performance obligations existed: (1) the exclusive license, bundled with the associated know-how and (2) the Company's initial obligation to supply repotrectinib for clinical development in the Zai Territory.

The total transaction price of \$25.7 million was allocated to the performance obligations on the basis of the relative stand-alone selling price estimated for each performance obligation. In estimating the stand-alone selling price for each performance obligation, the Company developed assumptions that require judgment and included forecasted revenues, expected development timelines, discount rates, probabilities of technical and regulatory success and costs for manufacturing clinical supplies.

The Company delivered the license and technical know-how to Zai in the third quarter of 2020 to satisfy this performance obligation, and accordingly the Company recognized license revenue of \$25.0 million in the third quarter of 2020. The \$0.7 million in consideration allocable to the clinical supply performance obligation was recognized when clinical trial material was shipped by the Company and Zai obtained control of the goods upon delivery, over the period of the obligation. In the second quarter of 2021, the Company recognized \$5.0 million of revenue upon the achievement of certain development milestones. The upfront payment received in 2020 and the development milestone payments received in 2021 were subject to foreign tax withholdings, which was recorded as general and administrative expense.

For the three months ended March 31, 2022 and 2021, the Company recognized \$0.4 million and \$0.2 million, respectively, of revenue associated with the clinical supply performance obligation.

The Company assessed and determined that there is no significant financing component associated with the Zai Repotrectinib Agreement.

Zai Elzovantinib Agreement

On January 10, 2021, the Company entered into a license agreement with Zai, which was amended on March 31, 2021 (the Zai Elzovantinib Agreement), pursuant to which the Company granted Zai exclusive rights to develop and commercialize products containing the Company's drug candidate, Elzovantinib (the Elzovantinib Products), in the Zai Territory. The Company retains exclusive rights to, among other things, develop, manufacture and commercialize the Elzovantinib Products outside the Zai Territory.

Pursuant to the terms of the Zai Elzovantinib Agreement, the Company received an upfront cash payment of \$25.0 million in the first quarter of 2021 and is eligible to receive up to \$336.0 million in development and sales milestone payments, consisting of up to \$121.0 million of development milestones and up to \$215.0 million of sales milestones. In addition, during the term of the Zai Elzovantinib Agreement, Zai is obligated to pay the Company tiered percentage royalties ranging from mid-teens to low twenties on annual net sales of the Elzovantinib Products in the Zai Territory, subject to adjustments in specified circumstances.

Zai is responsible for conducting the development and commercialization activities in the Zai Territory related to the Elzovantinib Products at Zai's own expense, subject to limited exceptions pursuant to which the Company may be responsible for the cost. The Company is responsible for global clinical studies of the Elzovantinib Products, including the portions that may be conducted in the Zai Territory, at the Company's expense, except that Zai will participate in global clinical studies of the Elzovantinib Products through clinical trial sites in the Zai Territory as agreed as of the effective date of the Zai Elzovantinib Agreement and may, at Zai's election subject to specified exceptions, participate in future global clinical studies of the Elzovantinib Products through clinical trial sites in the Zai Territory, in each case at Zai's expense.

The Zai Elzovantinib Agreement will continue in effect until expiration of the last royalty term for a Elzovantinib Product in any region in the Zai Territory, where the royalty term for a Elzovantinib Product in a region continues until the later of (i) the expiry of the last-to-expire valid claim within Company's patent rights that covers the Elzovantinib Product in such region in the Zai Territory; (ii) the expiry of the regulatory exclusivity for such Elzovantinib Product in such region; or (iii) the close of business of the day that is exactly 10 years after the date of the first commercial sale of such Elzovantinib Product in such region. Subject to the terms of the Zai Elzovantinib Agreement, Zai may terminate the Zai Elzovantinib Agreement for convenience by providing written notice to the Company, which termination will be effective following a prescribed notice period. In addition, the Company may terminate the Zai Elzovantinib Agreement under specified circumstances if Zai or certain other parties challenge the Company's patent rights. Either party may terminate the Zai Elzovantinib Agreement for the other party's uncured material breach of the Zai Elzovantinib Agreement, with a customary notice and cure period, for the other party's insolvency or if the other party acquires a third party and the acquired party is engaged in activities with a competing product that is not divested or discontinued within a specified period. After termination (but not natural expiration), other than certain terminations by Zai for cause, the Company is entitled to retain a worldwide and perpetual license from Zai to exploit the Elzovantinib Products.

Revenue Recognition

The Company determined that two performance obligations existed: (1) the exclusive license, bundled with the associated know-how and (2) the Company's initial obligation to supply elzovantinib for clinical development in the Zai Territory.

The total transaction price of \$25.9 million was allocated to the performance obligations on the basis of the relative stand-alone selling price estimated for each performance obligation. In estimating the stand-alone selling price for each performance obligation, the Company developed assumptions that require judgment and included forecasted revenues, expected development timelines, discount rates, probabilities of technical and regulatory success and costs for manufacturing clinical supplies.

The Company delivered the license and technical know-how to Zai in the first quarter of 2021 to satisfy this performance obligation, and accordingly the Company recognized license revenue of \$25.0 million in the first quarter of 2021. The upfront payment received was subject to foreign tax withholdings, which was recorded as general and administrative expense. The \$0.9 million in consideration allocable to the clinical supply performance obligation will be recognized when clinical trial material has been shipped by the Company and Zai obtains control of the goods upon delivery, over the period of the obligation. As of March 31, 2022, the Company has not recognized any revenue associated with the clinical supply performance obligation under the Zai Elzovantinib Agreement.

The Company assessed and determined that there is no significant financing component associated with the Zai Elzovantinib Agreement.

8. Commitments and Contingencies

Operating Leases

The Company leases office and laboratory space under lease agreements with remaining lease terms ranging from 1.4 years to 2 years. One of the leases contains an option to extend the lease for five years, which was not included in the determination of the lease term as it was not reasonably certain that the Company would exercise this option.

As of March 31, 2022, the Company recorded \$5.4 million as right-of-use (ROU) assets, \$4.0 million as current operating lease liabilities, and \$1.9 million as non-current operating lease liabilities on its balance sheet. As of December 31, 2021, the Company recorded \$5.2 million as ROU assets, \$3.6 million as current operating lease liabilities and \$2.0 million as non-current operating lease liabilities on its balance sheet.

Operating lease costs for the three months ended March 31, 2022 and 2021 were \$1.0 million and \$0.4 million, respectively. Variable lease costs representing the Company's share of the operating expenses and utility costs of the leased properties were \$0.4 million and \$0.3 million for the three months ended March 31, 2022 and 2021, respectively. Cash paid for amounts included in the measurement of operating lease liabilities was \$1.0 million and \$0.4 million for the three months ended March 31, 2022 and 2021, respectively.

The Company's operating leases had a weighted-average remaining lease term of 1.5 years as of March 31, 2022 and December 31, 2021, respectively, and a weighted-average discount rate of 5.5% and 7.0% as of March 31, 2022 and December 31, 2021, respectively.

Maturities of operating lease liabilities as of March 31, 2022 were as follows (in thousands):

2022 (remaining)	\$	3,118
2023		2,886
2024		54
Total future minimum lease payments		6,058
Less: amounts representing interest		(224)
Total lease liability	\$	5,834

In May 2021, the Company entered into a lease agreement with HCP Callan Road, LLC for office and laboratory space for the Company's future corporate headquarters, delivered in two phases. The term of the lease is approximately 11 years and nine months with an option by the Company to extend for an additional five years, and is currently expected to commence in May 2023. The lease term has an initial abatement period with respect to each phase and the initial base rent payable upon the Company's occupancy of both phases will be approximately \$1.0 million per month following the end of the abatement period for each phase, which amount will increase by 3% per year over the lease term. The Company is also responsible for the payment of its share of the operating expenses for the building. Pursuant to the terms of the lease agreement, the landlord will provide the Company with a tenant improvement allowance of up to \$220 per square foot. As of March 31, 2022, total aggregate future lease commitments under the lease were approximately \$165.9 million. As of March 31, 2022, the Company had not taken control of the space. Accordingly, no ROU asset or lease liability related to the lease has been recorded.

In connection with the lease, the Company is required to maintain a letter of credit for the benefit of the landlord in the amount of \$1.8 million, which was delivered in May 2021 and is included in other assets in the Company's condensed balance sheets.

9. Stockholders' Equity

At the Market Offering

In August 2020, the Company entered into an Open Market Sale AgreementSM with Jefferies LLC (ATM facility), under which the Company may offer and sell, from time to time, at its sole discretion, up to \$250.0 million shares of the Company's common stock. As of March 31, 2022, the Company had not yet sold any shares of common stock under the ATM facility.

2019 Equity Incentive Plan

The Company's 2019 Equity Incentive Plan (the Plan) provides for the grant of stock options, restricted stock and other equity awards of the Company's common stock to employees, officers, consultants and directors. In addition, the number of shares of common stock available for issuance under the Plan will be automatically increased on the first day of each calendar year through

January 1, 2029, by an amount equal to 4% of the outstanding number of shares of the Company's common stock on December 31 of the preceding calendar year or such lesser amount as determined by the Company's board of directors. On January 1, 2022, the Company added 1,983,306 shares to the Plan. At March 31, 2022, the Plan had 3,848,546 total shares available for issuance.

Stock Options

Stock options expire within a period of not more than ten years from the date of grant. Initial option grants to employees typically vest 25% on the first anniversary of the original vesting date and monthly thereafter over a three-year period and expire three months after employee termination. Subsequent option grants to employees and grants to non-employees typically vest monthly over a four-year period.

The following table summarizes stock option activity under the Plan for the periods presented:

	Outstanding Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Balance as of December 31, 2021	5,418,467	\$ 47.17	7.5	\$ 91,794
Options granted	1,246,164	\$ 37.59		
Options exercised	(51,772)	\$ 7.65		
Options forfeited or cancelled	(366,075)	\$ 64.19		
Balance as of March 31, 2022	<u>6,246,784</u>	\$ 44.59	7.5	\$ 41,881
Options vested and exercisable as of March 31, 2022	<u>3,004,222</u>	\$ 31.98	6.3	\$ 35,898

The weighted-average grant-date fair value of options granted to employees was \$25.13 and \$91.68 for the three months ended March 31, 2022 and 2021, respectively. As of March 31, 2022, total unrecognized compensation expense related to unvested options was \$113.0 million, which is expected to be recognized over a weighted-average term of 2.7 years. The total intrinsic value of stock options exercised during the three months ended March 31, 2022 and 2021 was \$1.2 million and \$44.3 million, respectively.

The fair values of the stock options granted during the three months ended March 31, 2022 and 2021 was estimated at the date of grant using the Black-Scholes option-pricing model using the following assumptions:

	Three Months Ended March 31,	
	2022	2021
Risk-free interest rate	1.85%	0.68%
Volatility	75.7%	80.6%
Expected term (in years)	6.08	6.07
Dividend yield	—	—

Restricted Stock Units

The following table summarizes restricted stock unit activity under the Plan for the periods presented:

	Restricted Stock Units Outstanding	Weighted Average Grant Date Fair Value	Aggregate Intrinsic Value (in thousands)
Balance as of December 31, 2021	358,760	\$ 89.09	\$ 17,113
Granted	465,601	\$ 37.67	
Vested	(30,063)	\$ 135.11	
Forfeited	(66,655)	\$ 67.44	
Outstanding as of March 31, 2022	<u>727,643</u>	\$ 56.27	\$ 19,537

As of March 31, 2022, total unrecognized compensation related to RSUs granted was \$36.5 million, which is expected to be recognized over a weighted-average period of approximately 3.4 years. The total fair value of RSUs vested during the three months ended March 31, 2022 was \$1.1 million. There were no RSUs vested during the three months ended March 31, 2021.

Performance Stock Units

The Company grants PSUs that vest based on the achievement of certain predefined Company-specific performance criteria. The fair value of PSUs is estimated based on the closing price of the Company's common stock on the date of grant. The Company recognizes expense in proportion to the number of PSUs that are deemed probable of vesting, based on the Company's evaluation of the respective performance-based criteria, at each reporting date.

The following table summarizes performance stock unit activity under the Plan for the periods presented:

	Performance Stock Units Outstanding	Weighted Average Grant Date Fair Value	Aggregate Intrinsic Value (in thousands)
Balance as of December 31, 2021	204,759	\$ 120.34	\$ 9,767
Granted	107,747	\$ 37.74	
Vested	—	\$ —	
Forfeited	(36,857)	\$ 111.03	
Outstanding as of March 31, 2022	<u>275,649</u>	\$ 89.30	\$ 7,401

As of March 31, 2022, the Company does not estimate that the achievement of any performance-based criteria is probable. To date, there have been no PSUs that have vested and the Company has not recognized any stock-based compensation expense related to the PSUs.

2019 Employee Stock Purchase Plan

The Company adopted an employee stock purchase plan in 2019 (the ESPP). The ESPP permits eligible employees who elect to participate in an offering under the ESPP to have up to 15% of their eligible earnings withheld, subject to certain limitations, to purchase shares of common stock pursuant to the ESPP. Under the ESPP, eligible employees may purchase shares of the Company's common stock at 85% of the lower of the fair market value of the common stock at the commencement date of each offering period or the date of purchase. Each offering period is 24 months, with new offering periods commencing every six months on the dates of June 11 and December 11 of each year. Each offering period consists of four six month purchase periods (each a Purchase Period) during which payroll deductions of the participants are accumulated under the ESPP. The last business day of each Purchase Period is referred to as the "Purchase Date." Purchase Dates are every six months on the dates of June 10 and December 10 of each year. As of March 31, 2022, a total of 202,046 shares of common stock were available for purchase under the ESPP.

Modifications to Outstanding Equity Awards

On March 30, 2021, Sheila Gujrathi, M.D. and Jacob M. Chacko, M.D. resigned from the Board of Directors (the Board) of the Company, effective immediately, to focus on other endeavors. Dr. Gujrathi also resigned from her position as Chair of the Board and Dr. Chacko resigned from each committee of the Board for which he was a member. In connection with the foregoing, the Board approved an amendment to the option awards held by Drs. Gujrathi and Chacko to provide that (i) all shares subject to such option awards are fully vested and exercisable as of the resignation date and (ii) the post-resignation exercise period shall be extended to September 30, 2022.

The Company determined that the modification to extend the term of vested stock options was a Type I modification pursuant to ASC 718, Compensation – Stock Compensation (ASC 718). The acceleration of the vesting of the unvested stock options was deemed a Type III modification pursuant to ASC 718, because without Board approval, these stock options would have been forfeited on the date of resignation. As a result of these modifications the Company recognized \$5.6 million of stock-based compensation expense in the first quarter of 2021 in general and administrative expenses in the condensed statements of operations and comprehensive loss.

Stock-Based Compensation Expense

Stock-based compensation expense recognized is presented in the condensed statements of operations and comprehensive loss as follows (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development	\$ 7,247	\$ 6,002
General and administrative	7,842	11,276
Total stock-based compensation expense	<u>\$ 15,089</u>	<u>\$ 17,278</u>

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance consisted of the following:

	March 31, 2022
Options to purchase common stock	6,246,784
PSUs outstanding	275,649
RSUs outstanding	727,643
Options to purchase common stock available for issuance under the Plan	3,848,546
Shares available for purchase under ESPP	<u>202,046</u>
Total	<u>11,300,668</u>

10. Subsequent Event

On May 4, 2022, the Company entered into a license agreement (the LaNova License Agreement) with LaNova Medicines Limited (LaNova) for an exclusive, royalty-bearing license to intellectual property related to LM-302, a clinical stage anti-Claudin18.2 antibody drug conjugate (the LaNova Product), on a worldwide basis excluding Greater China and South Korea (the Company Territory). Under the LaNova License Agreement, the Company has the exclusive right to research, develop, use, register, offer for sale, import and otherwise commercialize the LaNova Product in the Company Territory and non-exclusive rights to manufacture the LaNova Product worldwide in support of activities in the Company Territory.

Pursuant to the LaNova License Agreement, the Company will pay LaNova an upfront cash payment of \$25.0 million and may be obligated to pay milestone payments, which include up to \$195.0 million in development and regulatory milestones and up to \$880.0 million in sales milestones, and tiered royalty payments based on percentages (ranging from the mid-single digits to the mid-teens) of net sales (subject to customary deductions).

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited condensed financial statements and related notes included in this Quarterly Report on Form 10-Q (Quarterly Report) and the audited financial statements and notes thereto as of and for the year ended December 31, 2021 and the related Management’s Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 filed with the Securities and Exchange Commission (SEC) on February 28, 2022.

Unless the context requires otherwise, references in this Quarterly Report to “we,” “us,” and “our” refer to Turning Point Therapeutics, Inc.

Forward-Looking Statements

This Quarterly Report includes forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), which are subject to the “safe harbor” created by those sections, that involve a number of risks, uncertainties and assumptions. These forward-looking statements can generally be identified as such because the context of the statement will include words such as “may,” “will,” “intend,” “plan,” “believe,” “anticipate,” “expect,” “estimate,” “predict,” “potential,” “continue,” “likely,” or “opportunity,” the negative of these words or other similar words. Similarly, statements that describe our plans, strategies, intentions, expectations, objectives, goals or prospects and other statements that are not historical facts are also forward-looking statements. For such statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. Readers of this Quarterly Report are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the time this Quarterly Report was filed with the SEC. These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. These risks and uncertainties include, without limitation, the risk factors identified in our SEC reports, including this Quarterly Report. In addition, past financial or operating performance is not necessarily a reliable indicator of future performance, and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to update publicly or revise our forward-looking statements.

Overview

We are a clinical-stage precision oncology company designing and developing novel targeted therapies for cancer treatment. We have developed a macrocycle platform from which we designed our current pipeline of proprietary small, compact tyrosine kinase inhibitors (TKIs) with rigid structures that have the potential to bind to their targets with greater precision and affinity than other kinase inhibitors. Our drug discovery approach integrates tumor biology with structure-based drug design to develop a new generation of orally available proprietary agents that we believe will have the potential to address important unmet medical needs for patients.

Repotrectinib

Our lead drug candidate, repotrectinib, is being evaluated in an ongoing Phase 1/2 clinical trial called TRIDENT-1 for the treatment of patients with *ROS1*+ advanced non-small cell lung cancer (NSCLC) and patients with *NTRK*+ advanced solid tumors. The U.S. Food and Drug Administration (FDA) has granted repotrectinib breakthrough therapy designations (i) for the treatment of patients with *ROS1*+ metastatic NSCLC who have not been treated with a *ROS1* TKI; (ii) for the treatment of patients with *ROS1*+ metastatic NSCLC who have been previously treated with one *ROS1* TKI and who have not received prior platinum-based chemotherapy; and (iii) for the treatment of patients with advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with one or two prior TRK TKIs, with or without prior chemotherapy, and have no satisfactory alternative treatments. In addition, the FDA has granted repotrectinib orphan drug designation for the treatment of advanced NSCLC with adenocarcinoma histology; and four fast track designations for the treatment of patients with: (1) *ROS1*+ advanced NSCLC who have not been previously treated with a *ROS1* TKI; (2) *ROS1*+ advanced NSCLC who have been previously treated with one prior line of platinum-based chemotherapy and one prior line of a *ROS1* TKI; (3) *ROS1*+ advanced NSCLC who have been previously treated with one prior *ROS1* TKI and who have not received prior platinum-based chemotherapy; and (4) *NTRK*+ advanced solid tumors who have been previously treated with one prior line of chemotherapy and one or two prior TRK TKIs.

Our multi-cohort Phase 2 registrational portion of TRIDENT-1 is ongoing at sites in North America, Europe and the Asia-Pacific regions. The Phase 2 portion of TRIDENT-1 is a registrational trial for potential approval in *ROS1*+ advanced NSCLC and *NTRK*+ advanced solid tumors. In the second quarter of 2021 we reached enrollment of 50 patients pooled from the Phase 1 and Phase 2 portions of the TRIDENT-1 study in EXP-1 and in the first quarter of 2022 we reached enrollment of 60 patients from the Phase 2

portion of the TRIDENT-1 study in EXP-4 and 40 patients from the Phase 2 portion of the TRIDENT-1 study in EXP-6. Enrollment is ongoing in all cohorts in the study. We reported topline blinded independent central review (BICR) data from all of the *ROS1*+ NSCLC cohorts from the Phase 1/2 TRIDENT-1 study in April 2022. The primary objective of the TRIDENT-1 study is to determine the confirmed objective response rate (cORR) based on BICR as assessed by RECIST 1.1, and the key secondary objectives include duration of response (DOR), progression free survival (PFS) and intracranial activity.

As of the February 11, 2022 data cutoff date, the data include the following findings:

- In the *ROS1*+ TKI-naïve advanced NSCLC patients (EXP-1: n=71), the cORR was 79%, with four patients achieving a complete response (CR) and 52 patients achieving a partial response (PR). The cORR does not include one patient in an unconfirmed partial response (uPR) with tumor regression of -38% on the last scan, who remained on treatment awaiting the next scan as of the data cutoff date. DOR ranged from 1.4+ to 35.1+ months and PFS ranged from 0+ to 40.4+ months.
- In the *ROS1*+ advanced NSCLC population pretreated with one prior TKI and prior platinum-based chemotherapy (EXP-2: n=26), the cORR was 42%, with 1 patient achieving a CR and 10 patients achieving a PR. DOR ranged from 3.6 to 18.3+ months.
- In the *ROS1*+ advanced NSCLC population pretreated with two prior TKIs without prior chemotherapy (EXP-3: n=18), the cORR was 28%, with 1 patient achieving a CR and 4 patients achieving a PR. DOR ranged from 1.9+ to 20.3+ months.
- In the *ROS1*+ advanced NSCLC population pretreated with one prior TKI without prior chemotherapy (EXP-4: n=56), the cORR was 36%, with 4 patients achieving a CR and 16 patients achieving a PR. The cORR does not include two patients with an uPR who both had tumor regressions of -47% on their last scans, both of whom remained on treatment awaiting their next scans as of the data cutoff date. DOR ranged from 1.9+ to 17.8 months.
- Across the *ROS1*+ TKI-pretreated advanced NSCLC population (EXP-2, EXP-3 and EXP-4), 17 patients had an identified *ROS1* G2032R solvent front mutation detected, of which the cORR was 59%, with 1 patient achieving a CR and 9 patients achieving a PR. DOR ranged from 1.9+ to 20.3+ months.
- Repotrectinib was generally well tolerated in a total of 380 patients with a safety and tolerability profile that was consistent with previously reported findings. The most commonly reported treatment emergent adverse event was dizziness, of which 76% of patients who reported dizziness had a maximum severity of grade 1.

We anticipate discussing the BICR data with the FDA at a pre-new drug application (NDA) meeting in the second quarter of 2022, and we plan on providing a detailed update, including intracranial activity, from the *ROS1*+ advanced NSCLC cohorts of the TRIDENT-1 study at an upcoming medical conference in the second half of 2022. We also anticipate reporting additional data from patients with *NTRK*+ advanced solid tumors in the second half of 2022. We plan to conduct a pre-NDA meeting with the FDA in the first quarter of 2023 to discuss topline BICR results from 40 patients from the *NTRK*+ TKI pre-treated patient cohort (EXP-6) and at least 30 patients from the *NTRK*+ TKI-naïve patient cohort (EXP-5) with responders having at least six months of follow-up.

In addition to the TRIDENT-1 study, we are also conducting our Phase 1/2 CARE study of repotrectinib in pediatric and young adult patients with *ALK*+, *ROS1*+ or *NTRK*+ advanced solid tumors and our Phase 1b/2 TRIDENT-2 study of repotrectinib in combination with trametinib in *KRAS* mutant *G12D* advanced solid tumors.

Elzovantinib (TPX-0022)

Elzovantinib, our MET/SRC/CSF1R inhibitor, is currently being evaluated in our ongoing Phase 1 SHIELD-1 clinical trial, in patients with advanced solid tumors harboring genetic alterations in MET. The FDA has granted elzovantinib orphan drug designation for the treatment of gastric cancer, including gastroesophageal junction adenocarcinoma and fast track designation for the treatment of patients with MET amplified advanced or metastatic gastric cancer or gastroesophageal junction (GEJ) adenocarcinoma after prior chemotherapy. Our Phase 1 SHIELD-1 clinical trial is designed to evaluate the overall safety profile, pharmacokinetics and preliminary efficacy of elzovantinib and includes a dose-finding portion followed by dose expansion in multiple cohorts of MET alterations and tumor types.

We have completed enrollment into the 60 mg QD to 60 mg BID intermediate dose level cohort within the dose escalation portion of SHIELD-1. In parallel, we continue to enroll patients in the Phase 1 dose expansion portion of the study at 40 mg QD to 40 mg BID. We anticipate providing a clinical data update from the Phase 1 SHIELD-1 study in the second half of 2022. We also

anticipate initiating the planned Phase 2 portion of SHIELD-1 in the second half of 2022 pending feedback from the FDA on data from the intermediate dose level.

In October 2021 we entered into a clinical trial collaboration agreement with EQRx, Inc. (EQRx) to evaluate elzovantinib in combination with aumolertinib (EQ143), EQRx's drug candidate targeting EGFR, in patients with EGFR mutant MET-amplified advanced NSCLC. Our investigational new drug (IND) submission for our planned Phase 1b/2 SHIELD-2 combination study of elzovantinib and aumolertinib was cleared by the FDA in January 2022 and we anticipate initiating the study in mid-2022. Preclinical data suggest the combination of MET and EGFR inhibition has the potential to increase anti-tumor activity based on complementary mechanisms. It is estimated that 15% to 20% of patients who progress on a first-line EGFR inhibitor develop MET amplification as the basis of acquired resistance.

TPX-0046

The Phase 1 dose-finding portion of our Phase 1/2 SWORD-1 clinical trial of our RET inhibitor, TPX-0046, in patients with advanced solid tumors harboring RET genetic alterations is ongoing at sites in North America and the Asia-Pacific regions. The trial is designed to enroll TKI-naïve and TKI-pretreated patients with RET-altered non-small-cell lung, thyroid, and other advanced cancers in multiple cohorts to assess safety, tolerability, pharmacokinetics and preliminary clinical activity of TPX-0046, in a Phase 1 dose-finding portion, followed by multiple Phase 1 dose expansion cohorts after determination of the recommended Phase 2 dose. We are continuing to further characterize the pharmacokinetics, safety, and efficacy profile of TPX-0046 before determining the recommended Phase 2 dose.

TPX-0131

Our fourth drug candidate, TPX-0131, is a next-generation ALK inhibitor. TPX-0131 has been designed with a compact macrocyclic structure and in preclinical studies has been shown to potently inhibit wildtype ALK and numerous ALK mutations, in particular the clinically observed G1202R solvent front mutation, L1196M gatekeeper mutation and G1202R/L1196M compound mutation. Additionally, preclinical in vivo studies have shown that TPX-0131 has significant brain tissue penetration after repeat oral dosing supporting the potential to cross the blood-brain barrier.

We initiated our Phase 1/2 FORGE-1 study of TPX-0131 in patients with locally advanced or metastatic TKI-pretreated ALK-positive NSCLC in the second quarter of 2021. The study endpoints include safety and tolerability, determination of the maximum tolerated dose and/or the recommended Phase 2 dose, and objective response rate by RECIST 1.1. The dose-finding portion of the Phase 1/2 FORGE-1 study is ongoing. We anticipate providing early interim data from initial patients treated in the dose-finding portion of the FORGE-1 study in the fourth quarter of 2022 or early 2023.

TPX-4589 (LM-302)

On May 4, 2022, we entered into a license agreement (the LaNova License Agreement) with LaNova Medicines Limited (LaNova) for an exclusive, royalty-bearing license to intellectual property related to LM-302, a clinical stage anti-Claudin18.2 antibody drug conjugate (the LaNova Product), on a worldwide basis excluding Greater China and South Korea (the Company Territory). Under the LaNova License Agreement, we have the exclusive right to research, develop, use, register, offer for sale, import and otherwise commercialize the LaNova Product in the Company Territory and non-exclusive rights to manufacture the LaNova Product worldwide in support of activities in the Company Territory.

Pursuant to the LaNova License Agreement, we will pay LaNova an upfront cash payment of \$25.0 million and may be obligated to pay milestone payments, which include up to \$195.0 million in development and regulatory milestones and up to \$880.0 million in sales milestones, and tiered royalty payments based on percentages (ranging from the mid-single digits to the mid-teens) of net sales (subject to customary deductions).

As part of the LaNova License Agreement, we also obtained the right of first negotiation for an exclusive license to develop, use, manufacture and commercialize other products containing components of the LaNova Product. In addition, we have the option to collaborate with LaNova on up to three additional antibody drug conjugate programs, initiated or proposed by either us or LaNova.

LM-302, now designated TPX-4589, is a potentially first-in-class anti-Claudin18.2 ADC that suppresses cell proliferation of gastric and pancreatic cell lines with nanomolar potency in preclinical models. It also has demonstrated efficacy in gastric and pancreatic cancer xenograft models. TPX-4589 is currently in Phase 1 clinical trials in both the U.S. and China, and the FDA has granted TPX-4589 two orphan drug designations for the treatment of pancreatic cancer and for the treatment of gastric cancer, including cancer of the gastroesophageal junction. The Phase 1 clinical trial in the U.S. is designed to evaluate the overall safety profile, pharmacokinetics, and preliminary efficacy and immunogenicity of TPX-4589 and includes a dose-finding portion followed

by dose expansion in subjects with *Claudin18.2+* advanced solid tumors who have progressed or are intolerant to standard therapy or for whom standard therapy is not available. We anticipate providing additional guidance on the clinical development plan for TPX-4589 by early 2023, as well as presenting preclinical data at an upcoming medical conference by early 2023.

Business Development and Pipeline Expansion

We will continue to engage in business development efforts to expand our portfolio where we can leverage our deep expertise in drug development and clinical trial execution in oncology. Our focus is to actively explore opportunities for acquisitions, partnerships, collaborations and license agreements for targeted therapy product candidates that would complement our strategic goals and R&D pipeline. We have evaluated a number of preclinical and clinical assets and platforms and continue to actively review opportunities.

Discovery Platform

Our approach to the discovery of new and potentially differentiated small-molecule drug candidates is to use a methodology anchored by our significant structure-based drug design expertise that exploits innovative protein-ligand interactions, coupled with a disciplined chemistry approach and deep enabling biology. We anticipate our internal and external exploration of oncology candidates will continue to include kinase targets and other oncogenic signaling proteins and pathways that address high unmet medical need. We currently have four internal discovery programs targeting aberrant GTPase signaling known to drive genomically defined cancers with significant unmet medical need. The most advanced programs target KRAS G12D and the p21 activated kinase, or “PAK” family. We are targeting the identification of two development candidates in the second half of 2022 with a goal to achieve at least one new IND per year beginning in 2023. We anticipate providing details on our other two GTPase signaling discovery programs in the second half of 2022.

COVID-19 Pandemic

We have experienced disruptions to our business operations as a result of the COVID-19 pandemic. Due to the continued evolving and uncertain global impacts of the COVID-19 pandemic, including the omicron variant and future potential variants, we cannot precisely determine or quantify the impact this pandemic will have on our ongoing business, operations and financial performance. For our ongoing and planned clinical trials, while we anticipate and have experienced some temporary delays or disruptions due to the COVID-19 pandemic, in particular with respect to activation of additional clinical trial sites and patient enrollment, we continue to work closely with our contract research organizations (CROs) and clinical sites as we navigate and seek to mitigate the impact of COVID-19 on our clinical studies and current timelines. Measures we have taken in response to COVID-19, include where feasible, conducting remote clinical trial site activations and data monitoring, enabling patients to have routine tests conducted closer to home, allowing trial sites to evaluate certain patients remotely, in compliance with their local procedures, and direct-to-patient study drug shipping. In addition, we believe our current supply and plans for supply will be sufficient to meet our anticipated clinical development needs for our drug candidates through 2022. However, depending on the length and ultimate impact of the COVID-19 pandemic, and available manufacturing capacity at our suppliers, our suppliers could be adversely impacted, which may result in delays or disruptions in our current or future supply chain.

We will continue to assess the duration, scope and severity of the COVID-19 pandemic and the existing and potential impacts on our business, operations and financial performance, and we will continue to work closely with our third-party vendors, CROs, collaborators and other parties in order to seek to advance our drug candidates as quickly as possible, while making the health and safety of our employees and their families, healthcare providers, patients and communities a top priority. Please refer to our Risk Factors in Part II, Item IA of this Quarterly Report for further discussion of risks related to the COVID-19 pandemic.

Liquidity Overview

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our drug candidates. As of March 31, 2022, we had an accumulated deficit of \$591.2 million. For the three months ended March 31, 2022 and for the year ended December 31, 2021, we incurred net losses of approximately \$74.4 million and \$236.6 million, respectively. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years.

To date, our operations have been financed primarily through the sale of common stock and convertible preferred stock. At March 31, 2022, we had \$918.2 million of cash, cash equivalents and marketable securities.

In August 2020, we entered into an Open Market Sale AgreementSM with Jefferies LLC (ATM facility) under which we may offer and sell, from time to time, at our sole discretion, up to \$250.0 million shares of our common stock. As of March 31, 2022, we had not yet sold any shares of our common stock under the ATM facility.

We will not generate revenue from product sales until we successfully complete clinical development and obtain regulatory approval for our drug candidates. If we obtain regulatory approval for any of our drug candidates and do not enter into a commercialization partnership, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. The COVID-19 pandemic and ongoing geopolitical events continue to rapidly evolve and have already resulted in a significant disruption of global financial markets. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and further disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the pandemic or geopolitical actions. If such further disruption occurs, we could experience an inability to access additional capital. If we fail to raise capital or enter into such agreements we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our drug candidates.

Components of Our Results of Operations

Revenue

To date, we have not generated any revenue from product sales. If our development efforts for our drug candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales. If we enter into license or collaboration agreements for any of our drug candidates or intellectual property, such as our license agreements with Zai Lab (Shanghai) Co., Ltd. (Zai) that we executed in July 2020 (the Zai Repotrectinib Agreement) and January 2021, which was amended in March 2021 (the Zai Elzovantinib Agreement, and together with the Zai Repotrectinib Agreement, the Zai License Agreements), we may generate revenue in the future from payments as a result of such license or collaboration agreements. Under the Zai Repotrectinib Agreement, we recognized revenue of \$0.4 million and \$0.2 million for the three months ended March 31, 2022 and 2021, respectively. Under the Zai Elzovantinib Agreement, we recognized revenue of \$25.0 million for the three months ended March 31, 2021. Unless and until we are able to generate revenue from future product sales, we expect that our revenue, if any, will be derived primarily from the Zai License Agreements, as well as any collaborations or additional license agreements that we may enter into in the future. We cannot provide assurance as to the timing of future milestone or royalty payments or that we will receive any of these payments at all. We cannot predict if, when, or to what extent we will generate revenue from the commercialization and sale of our drug candidates. We may never succeed in obtaining regulatory approval for any of our drug candidates.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of:

- employee-related expenses, including salaries, related benefits, travel and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our drug candidates, including expenses incurred under the agreements with the CROs;
- the cost of consultants and contract manufacturing organizations (CMOs) that manufacture drug products for use in our preclinical studies and clinical trials; and
- facilities, depreciation and other expenses, which include allocated expenses for rent and maintenance of facilities, insurance and supplies.

We expense research and development costs to operations as incurred. Nonrefundable advance payments for services in advance of the performance of the related research and development activities are recorded as prepaid assets and recognized as expense in the period when the services are performed.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, such as fees paid to consultants, central laboratories, contractors, CMOs and CROs in connection with our preclinical and clinical development activities. We allocate indirect expenses, such as employee salaries, fringe benefits, facilities, travel and other miscellaneous expenses, based on an estimated percentage of time worked on programs.

The table below summarizes our research and development expenses incurred by development program for the periods presented (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development expenses		
Repotrectinib	\$ 31,055	\$ 23,690
Elzovantinib	7,397	5,808
TPX-0046	1,694	3,761
TPX-0131	3,442	3,032
Other research programs	11,462	4,972
Total research and development expenses	\$ 55,050	\$ 41,263

Drug 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 that our research and development expenses will increase substantially in connection with our ongoing and planned clinical and preclinical development activities in the near term and in the future. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our drug candidates.

The successful development of our drug candidates is highly uncertain. This is due to the numerous risks and uncertainties, including the following:

- successful completion of preclinical studies and clinical trials;
- the impact of the COVID-19 pandemic and ongoing geopolitical events on our business, operations and financial condition;
- delays in regulators or institutional review boards authorizing us or our investigators to commence our clinical trials or in our ability to negotiate agreements with clinical trial sites or CROs;
- the number and location of clinical sites included in the trials;
- raising additional funds necessary to complete clinical development of our drug candidates;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity for our drug candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for clinical supplies of our drug candidates;
- the ability to obtain clearance or approval of companion diagnostic tests, if required, on a timely basis, or at all;
- the results of our clinical trials;
- protecting and enforcing our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development of our drug candidates may significantly impact the costs and timing associated with the development of our drug candidates. We may never succeed in obtaining regulatory approval for any of our drug candidates.

Research and development activities are central to our business model. There are numerous factors associated with the successful commercialization of any of our drug candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. In addition, future regulatory factors beyond our control may impact our clinical development programs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and employee-related costs, including stock-based compensation expense, for personnel in executive, finance, legal, commercial and other administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting and tax-related services, insurance costs, recruiting costs, travel expenses and facility-related costs.

We anticipate that our general and administrative expenses will continue to increase as a result of increased payroll, expanded infrastructure and higher consulting, legal, accounting and investor relations costs, and director and officer insurance premiums associated with being a public company.

Other Income, net

Other income, net consists of interest earned on cash, cash equivalents and our marketable securities.

Critical Accounting Policies, Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. We evaluate these estimates and assumptions on an ongoing basis. We base our estimates on historical experience, knowledge of current events and actions we may undertake in the future, and on various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ materially from these estimates and assumptions.

There have been no significant changes to our critical accounting policies and use of estimates from our disclosure reported in "Critical Accounting Policies, Significant Judgements and Estimates" in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, except as described in Note 2 to the interim unaudited condensed financial statements included elsewhere in this Quarterly Report on Form 10-Q.

Results of Operations

Comparison of the Three Months Ended March 31, 2022 and 2021

The following table summarizes our results of operations for the three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,		Change
	2022	2021	
Revenue	\$ 429	\$ 25,205	\$ (24,776)
Operating expenses:			
Research and development	55,050	41,263	13,787
General and administrative	20,314	19,991	323
Total operating expenses	75,364	61,254	14,110
Loss from operations	(74,935)	(36,049)	(38,886)
Other income, net	490	545	(55)
Net loss	\$ (74,445)	\$ (35,504)	\$ (38,941)

Revenue

Revenue recognized during the three months ended March 31, 2022 was \$0.4 million from the sale of clinical supply to Zai for supporting the TRIDENT-1 Phase 2 clinical trials in the Zai Territory. Revenue recognized during the three months ended March 31, 2021 was \$25.2 million, consisting of \$25.0 million related to an upfront payment received under the Zai Elzovantinib Agreement and \$0.2 million from the sale of clinical supply to Zai for supporting the TRIDENT-1 Phase 2 clinical trials in the Zai Territory. We recognized the upfront payment as license revenue upon the delivery to Zai of the license and the associated technical know-how under the Zai Elzovantinib Agreement.

Research and Development Expenses

Research and development expenses increased \$13.8 million to \$55.1 million during the three months ended March 31, 2022 compared to \$41.3 million during the three months ended March 31, 2021. The increase was primarily attributable to increased activities related to the ongoing clinical trials for the Phase 2 registrational portion of TRIDENT-1, the Phase 1 clinical trial for elzovantinib, discovery efforts and higher personnel-related expenses due to an increase in headcount. We expect that our research and

development expenses will continue to increase in future periods with the advancement of our clinical programs and additional future clinical trials and discovery efforts.

General and Administrative Expenses

General and administrative expenses increased \$0.3 million to \$20.3 million during the three months ended March 31, 2022 compared to \$20.0 million during the three months ended March 31, 2021. The increase was primarily attributable to higher personnel-related expenses as a result of increased employee headcount, facility-related costs and professional fees, including those associated with product launch readiness, partially offset by a decrease in stock-based compensation expense of \$3.4 million. In the first quarter of 2021, we recorded a one-time charge of \$5.6 million as stock-based compensation expense associated with the resignations of two board members and a \$1.3 million foreign tax withholding expense related to the upfront payment received from Zai under the Zai Elzovantiniib Agreement.

We anticipate that our general and administrative expenses will continue to increase as a result of increased payroll, expanded infrastructure and higher consulting, legal, accounting and investor relations costs, and director and officer insurance premiums associated with being a public company.

Other Income, net

Other income, net was \$0.5 million during each of the three months ended March 31, 2022 and 2021, consisting of interest earned on our marketable securities and money market funds.

Liquidity and Capital Resources

At March 31, 2022, we had \$918.2 million of cash, cash equivalents and marketable securities. Based on our current and anticipated level of operations, we believe that our cash, cash equivalents and marketable securities as of March 31, 2022 will be sufficient to fund current operations through the first half of 2024. Our cash, cash equivalents and marketable securities include money market funds, government agency securities, corporate debt, commercial paper and U.S. treasuries. We maintain established guidelines relating to diversification and maturities of our investments to preserve principal and maintain liquidity.

Since inception, our operations have been financed primarily through the sale of common stock and convertible preferred stock. Through March 31, 2022, we received net proceeds of approximately \$1.3 billion from the issuance of common stock and convertible preferred stock and through stock option exercises.

In August 2020, we entered into the ATM facility, under which we may offer and sell, from time to time, at our sole discretion, up to \$250.0 million shares of our common stock. As of March 31, 2022, we had not yet sold any shares of our common stock under the ATM facility.

On May 4, 2022, we entered into the LaNova License Agreement with LaNova. Pursuant to the LaNova License Agreement, we will pay LaNova an upfront cash payment of \$25.0 million and may be obligated to pay milestone payments, which include up to \$195.0 million in development and regulatory milestones and up to \$880.0 million in sales milestones, and tiered royalty payments based on percentages (ranging from the mid-single digits to the mid-teens) of net sales (subject to customary deductions).

Since inception, we have primarily devoted our resources to build infrastructure, conduct research and development, including clinical trials, perform business and financial planning, and raise capital. To fund future operations, we will need to raise significant additional capital. The amount and timing of future funding requirements will depend on many factors, including the timing and results of our ongoing development activities, the potential expansion of our current development programs, potential new development programs and related general and administrative support. We may seek to obtain additional financing in the future through equity or debt financings or other sources, such as potential collaboration agreements. We cannot make assurances that anticipated additional financing will be available to us on favorable terms, or at all. The COVID-19 pandemic and ongoing geopolitical events continue to rapidly evolve and have already resulted in a significant disruption of global financial markets. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and further disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the pandemic or geopolitical actions. If such further disruption occurs, we could experience an inability to access additional capital, which could in the future negatively affect our capacity to fund research and development programs, including discovery research, preclinical and clinical development activities and activities to support commercialization. Although we have previously been successful in obtaining financing through our equity securities offerings, there can be no assurance that we will be able to do so in the future.

Cash Flows

The following table summarizes our sources and uses of cash and cash equivalents for each of the periods presented (in thousands):

	Three Months Ended March 31,	
	2022	2021
Statement of Cash Flows Data:		
Net cash used in operating activities	(58,331)	(15,648)
Net cash used in investing activities	(60,412)	(78,931)
Net cash provided by financing activities	396	9,679

Operating Activities

Net cash used in operating activities was approximately \$58.3 million in the first quarter of 2022, primarily due to spending on ongoing research and development activities related to the Phase 2 registrational portion of TRIDENT-1, the Phase 1 clinical trial for elzovantinib, the Phase 1/2 clinical trial for TPX-0046, the Phase 1/2 clinical trial for TPX-0131, discovery efforts and general and administrative activities.

Net cash used in operating activities in the first quarter of 2021 was approximately \$15.6 million, primarily due to spending on the Phase 2 registrational portion of TRIDENT-1, the Phase 1 clinical trial for elzovantinib, the Phase 1/2 clinical trial for TPX-0046 and the Phase 1/2 clinical trial for TPX-0131. Cash used to fund operations was partially offset by a \$25.0 million upfront payment received under the Zai Elzovantinib Agreement.

Investing Activities

Net cash used in investing activities was approximately \$60.4 million in the first quarter of 2022, consisting of approximately \$60.0 million for the purchases (net of maturities) of marketable securities and approximately \$0.4 million for the purchases of property and equipment. Net cash used in investing activities was approximately \$78.9 million in the first quarter of 2021, primarily for the purchases (net of maturities) of marketable securities.

Financing Activities

Net cash provided by financing activities was approximately \$0.4 million and \$9.7 million in the first quarter of 2022 and 2021, respectively, from the sale of common stock to employees under our equity compensation plans.

Contractual Obligations and Commitments

During the three months ended March 31, 2022, there were no material changes to our contractual obligations and commitments as set forth in Part II, Item 7 “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, 2021.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risks in the ordinary course of our business. These risks primarily relate to equity price risk and interest rate fluctuations. Substantially all of our cash, cash equivalents and marketable securities are held at two financial institutions. Due to the financial strength of the depository institutions, we believe these financial institutions represent a minimal credit risk. Cash amounts held at financial institutions are insured by the Federal Deposit Insurance Corporation (FDIC) up to \$250,000. At March 31, 2022, cash, cash equivalents and marketable securities totaling \$917.9 million are either not subject to FDIC insurance, or exceed the FDIC insured limit. Our cash, cash equivalents and marketable securities are invested in short term, high grade securities, and as a result, we believe represent a minimal credit risk. If a 10% change in interest rates were to have occurred on March 31, 2022, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized, and reported within the time periods

specified in the SEC’s rules and forms, and that such information is accumulated and communicated to our management, including our President and Chief Executive Officer (our principal executive officer) and Executive Vice President and Chief Financial Officer (our principal financial officer), as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of March 31, 2022, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on this evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2022.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. In addition, we have not experienced any material impact to our internal controls over financial reporting as a result of the COVID-19 pandemic, including from employees working remotely. We are continually monitoring and assessing the impact of the COVID-19 pandemic on our internal controls over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

We are not currently subject to any material legal proceedings. From time to time, we may be involved in legal proceedings or subject to claims incident to the ordinary course of business. Regardless of the outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 1A. Risk Factors.

RISK FACTORS SUMMARY

We face many risks and uncertainties, as more fully described in this section under the heading “Risk Factors.” Some of these risks and uncertainties are summarized below. The summary below does not contain all of the information that may be important to you, and you should read this summary together with the more detailed discussion of these risks and uncertainties contained in “Risk Factors.”

- We are highly dependent on the success of our lead drug candidate, repotrectinib, which is currently in a Phase 2 potentially registrational clinical trial, and our other drug candidates which are in early clinical development. We have not successfully completed late-stage clinical trials or obtained regulatory approval for any drug candidate. We may never obtain approval for any of our drug candidates or achieve or sustain profitability.
- Drug development involves a lengthy and expensive process. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of repotrectinib or our other drug candidates.
- If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, our receipt of necessary regulatory approval could be delayed or prevented.
- The COVID-19 pandemic has and could adversely impact our business in the future, including our ongoing and planned clinical trials.
- Adverse side effects or other safety risks associated with repotrectinib, elzovantinib or our other drug candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials or abandon further development, limit the

commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

- The development and commercialization of pharmaceutical products are subject to extensive regulation, and we may not obtain regulatory approvals for repotrectinib or any other drug candidates, on a timely basis or at all.
- We have incurred significant operating losses since our inception and have not generated any revenue from product sales. We expect to incur continued losses for the foreseeable future and may never achieve or maintain profitability.
- The incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue potential and ability to achieve profitability will be adversely affected.
- If we are unable to obtain and maintain sufficient patent protection for our drug candidates, or if the scope of the patent protection is not sufficiently broad, third parties, including our competitors, could develop and commercialize products similar or identical to ours, and our ability to commercialize our drug candidates successfully may be adversely affected.
- The trading price of our common stock has been and may in the future be volatile and fluctuate substantially, which could result in substantial losses.

RISK FACTORS

Investing in our common stock involves a high degree of risk. In addition to the information included or incorporated by reference in this Quarterly Report and in our other public filings, you should carefully consider the risks described below in evaluating our company. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not currently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations. We have marked with an asterisk () those risk factors that reflect changes from the risk factors previously disclosed in Item 1A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on February 28, 2022.*

Risks Related to the Discovery and Development of Our Drug Candidates and Regulatory Approval

We are highly dependent on the success of our lead drug candidate, repotrectinib, which is currently in a Phase 2 potentially registrational clinical trial, and our other drug candidates which are in early clinical development. We have not successfully completed late-stage clinical trials or obtained regulatory approval for any drug candidate. We may never obtain approval for any of our drug candidates or achieve or sustain profitability.*

Our future success is highly dependent on our ability to obtain regulatory approval for, and then successfully commercialize, our lead product candidate, repotrectinib, and our other drug candidates which are in earlier stages of development. We currently have no products that are approved for sale. Our Phase 2 registrational portion of our TRIDENT-1 clinical trial for our lead drug candidate, repotrectinib, is ongoing and our other drug candidates currently in clinical trials are only in Phase 1 studies. There can be no assurance that repotrectinib or our other drug candidates in development will achieve success in their clinical trials or obtain regulatory approval.

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of repotrectinib or other drug candidates in development. The success of our drug candidates, including repotrectinib, will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials;
- acceptance of IND submissions by the FDA or other clinical trial or similar applications from foreign regulatory authorities for future clinical trials for our current or any future pipeline drug candidates;
- timely and successful enrollment of patients in, and completion of, clinical trials with favorable results;
- demonstration of safety, efficacy and acceptable risk-benefit profiles of our drug candidates to the satisfaction of the FDA and foreign regulatory agencies;
- our ability, or that of our collaborators, to develop and obtain clearance or approval of companion diagnostics, on a timely basis, or at all;

- receipt and related terms of marketing approvals from applicable regulatory authorities, including the completion of any required post-marketing studies or trials;
- raising additional funds necessary to complete clinical development of and commercialize our drug candidates;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity for our drug candidates;
- making arrangements with third-party manufacturers and establishing manufacturing capabilities or scaling up manufacturing processes for both clinical and commercial supplies of our drug candidates;
- developing and implementing marketing and reimbursement strategies;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others such as Zai, our licensee for repotrectinib and elzovantinib in Mainland China, Hong Kong, Macau and Taiwan (collectively, Greater China);
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining third-party payor coverage and adequate reimbursement;
- protecting and enforcing our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the products following approval.

Many of these factors are beyond our control, and it is possible that none of our drug candidates will ever obtain regulatory approval even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates, which would materially harm our business. For example, our business could be harmed if results of our clinical trials of repotrectinib or our other drug candidates vary adversely from our expectations.

Our assumptions about the EXP-1 cohort to support a potential NDA for the treatment of patients with *ROS1*+ metastatic NSCLC who have not been treated with a *ROS1* TKI may not be accurate. We held a Type B meeting with the FDA in April 2021 during which we received feedback on next steps toward a potential NDA submission for repotrectinib for the treatment of *ROS1*+ metastatic NSCLC that has not been treated with a *ROS1* TKI. The FDA's guidance at that meeting may be subject to change, including on the basis of the topline results from this cohort. A change in the assumptions or FDA requirements for NDA acceptance for filing and approval may delay our development timelines.

Drug development involves a lengthy and expensive process. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of repotrectinib or our other drug candidates.*

We currently have five drug candidates in clinical development, and the risk of failure is high. We are unable to predict when or if our drug candidates will prove effective or safe in humans or will obtain marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim or preliminary results of a clinical trial do not necessarily predict final results. In particular, the small number of patients and limited geographies in our early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. Although we have observed encouraging preliminary objective response rates (ORRs) in the Phase 1 portion of our ongoing TRIDENT-1 clinical trial of repotrectinib, the primary objectives were to determine the safety, tolerability and maximum tolerated dose of repotrectinib and to determine a recommended Phase 2 dose and not to demonstrate efficacy. The assessments of efficacy from this portion of the clinical trial were not designed to demonstrate statistical significance and may not be predictive of the results of further clinical trials of repotrectinib. Additionally, the early interim data we reported from the Phase 2 portion of TRIDENT-1 in August 2020, January 2021 and October 2021 was only physician assessed data from subsets of patients and may not be predictive of the final results of the trial. Furthermore, the topline data we reported in April 2022 from the Phase 1 and Phase 2 portions of the TRIDENT-1 study may be subject to change following a more comprehensive review of the data and results, and as

patient enrollment and treatment continues and more patient data become available. The preliminary interim data we reported from both our elzovantinib Phase 1 SHIELD-1 clinical trial in October 2020 and October 2021 and our TPX-0046 Phase 1 SWORD-1 clinical trial in April 2021, were only physician assessed data from patients enrolled in the dose escalation portions of each trial and may not be predictive of the final results of the trials or of any further trials of elzovantinib or TPX-0046.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to obtain marketing approval or commercialize our drug candidates, including:

- regulators or Institutional Review Boards (IRB)/Ethics Committees (EC) may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials for our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials, delay clinical trials or abandon product development programs;
- the number of patients required for clinical trials for our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or the duration of these clinical trials may be longer than we anticipate;
- competition for clinical trial participants from investigational and approved therapies may make it more difficult to enroll patients in our clinical trials;
- we or third-party collaborators may fail to obtain the clearance or approval of companion diagnostic tests, if required, on a timely basis, or at all;
- our third-party contractors may fail to meet their contractual obligations to us in a timely manner, or at all, or may fail to comply with regulatory requirements;
- we may have to suspend or terminate clinical trials for our drug candidates for various reasons, including a finding by us or by a Data Monitoring Committee for a trial that the participants are being exposed to unacceptable health risks;
- our drug candidates may have undesirable or unexpected side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs/ECs to suspend or terminate the trials;
- the cost of clinical trials for our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials for our drug candidates may be insufficient or inadequate and result in delays or suspension of our clinical trials; and
- we or a diagnostic development partner may fail to receive regulatory approval of a companion diagnostic for use with a marketed product.

Our product development costs will increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know if any of our planned preclinical studies or clinical trials will begin in a timely basis or at all. We do not know whether any of our ongoing clinical trials will need to be restructured or will be completed on schedule, or at all. For example, the FDA may place a partial or full clinical hold on any of our clinical trials for a variety of reasons. In February 2018, we received a Deficiency–Potential Hold Issues letter from the FDA stating that the number of patients treated in the Phase 1 portion of TRIDENT-1 exceeded the protocol-specified dose escalation enrollment plan. Additionally, the Development Safety Update Report (DSUR) and the Investigator’s Brochure (IB) had not been updated with available clinical safety information. Following discussion with the FDA, our IND was placed on partial clinical hold pending the submission of an amended protocol, an updated DSUR and updated IB. The partial clinical hold was removed on June 29, 2018 after the requested documents were revised and TRIDENT-1 resumed patient enrollment.

Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations.

Any delays in the commencement or completion, or termination or suspension, of our ongoing, planned or future clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.*

Before we can initiate clinical trials of a drug candidate in any indication, we must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities along with other information, including information about the drug candidate's chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND or similar regulatory filing.

Before obtaining marketing approval from the FDA or comparable foreign regulatory authorities, for the sale of repotrectinib or any other drug candidate in any indication, we must conduct extensive clinical studies to demonstrate safety and efficacy. Clinical testing is expensive, time consuming and uncertain as to outcome. In addition, we expect to rely in part on preclinical, clinical and quality data generated by our CROs and other third parties for regulatory submissions for our drug candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase. We will require the acceptance by the FDA of an IND prior to initiating any clinical trials in the United States for any future combination studies of any of our drug candidates, or for any of our future potential drug candidates. The FDA may require us to conduct additional preclinical studies for any drug candidate before it allows us to initiate clinical trials under any IND, which may lead to additional delays and increase the costs of our preclinical development programs.

Any delays in the commencement or completion of our ongoing, planned or future clinical trials could significantly affect our product development costs. We do not know whether our planned trials will begin on time or at all, or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials or with our recommended dose for any of our pipeline programs;
- obtaining FDA or comparable foreign regulatory authorities' authorization to commence a trial or reaching a consensus with regulatory authorities on trial design;
- failing to obtain regulatory clearance or approval of companion diagnostics we may use to identify patients for enrollment in our clinical trials;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval from one or more IRBs/ECs;
- IRBs/ECs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- failing to manufacture or obtain sufficient quantities of drug candidate or, if applicable, combination therapies for use in clinical trials;
- patients failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-up, including patients failing to remain in our trials due to movement restrictions, health reasons or otherwise resulting from the COVID-19 pandemic;
- patients choosing an alternative treatment, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- patients experiencing severe or unexpected drug-related adverse effects;

- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- selecting or being required to use clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our drug candidates or any of their components being ordered by the FDA to temporarily or permanently shut down due to violations of the FDA's Current Good Manufacturing Practices (cGMP) regulations or other applicable requirements, or infections or cross-contaminations of drug candidates in the manufacturing process;
- interruptions to operations of clinical sites, manufacturers, suppliers, or other vendors from a health epidemic or pandemic such as COVID-19 or from geopolitical actions;
- any changes to our manufacturing process that may be necessary or desired, including any changes necessary to scale-up the manufacturing process;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practices (GCP) or other regulatory requirements;
- us, or our third-party contractors not performing data collection or analysis in a timely or accurate manner or improperly disclosing data prematurely or otherwise in violation of a clinical trial protocol; or
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs/ECs of the institutions in which such trials are being conducted, by a Data Monitoring Committee for such trial or by the FDA. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a pharmaceutical, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs/ECs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Certain of our scientific advisors or consultants who have received compensation from us are investigators for our clinical trials. Under certain circumstances, we may be required to report some of these relationships to the FDA. Although we believe our existing relationships are within the FDA's guidelines, the FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of repotrectinib or other drug candidates. If we experience delays in the completion of, or termination of, any clinical trial of repotrectinib or any other drug candidate, the commercial prospects of such drug candidate will be harmed, and our ability to generate product revenues will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues, which may harm our business, financial condition, results of operations and prospects significantly.

If we experience delays or difficulties in enrolling patients in our ongoing or planned clinical trials, our receipt of necessary regulatory approval could be delayed or prevented.

We may not be able to initiate or continue our ongoing or planned clinical trials for our drug candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA. In addition, some of our competitors may have planned or ongoing clinical trials or expanded access programs for approved and/or investigational drugs that would treat the same patients as repotrectinib or our other drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in our competitors' clinical trials or expanded access programs. This is relevant for our development of repotrectinib for the treatment of patients with *ROS1*+ advanced NSCLC, *NTRK*+ advanced solid tumors and *KRAS* mutant *G12D* advanced solid tumors; development of elzovantinib for the treatment of patients with *MET*+ advanced solid tumors and EGFR mutant *MET*-amplified advanced NSCLC; development of TPX-0046 for the treatment of patients with *RET*+ advanced solid tumors;

development of TPX-0131 for the treatment of patients with *ALK*+ NSCLC; and development of TPX-4589 for the treatment of patients with Claudin18.2+ advanced solid tumors, indications for which approved and/or investigational drugs are competing for clinical trial participants. Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- our ability to recruit clinical trial investigators of appropriate competencies and experience;
- the incidence and prevalence of our target indications;
- clinicians' and patients' awareness of, and perceptions as to the potential advantages and risks of our drug candidates in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- invasive procedures required to enroll patients and to obtain evidence of the drug candidate's performance during the clinical trial;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria defined in the protocol for the trial in question;
- the ability of our companion diagnostics to identify patients;
- the size of the patient population required for analysis of the trial's primary endpoints;
- efforts to facilitate timely enrollment in clinical trials;
- whether we are subject to a partial or full clinical hold on any of our clinical trials;
- reluctance of physicians to encourage patient participation in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- our ability to obtain and maintain patient consents;
- proximity and availability of clinical trial sites for prospective patients, and
- our ability to timely activate clinical trial sites during the ongoing COVID-19 pandemic.

Our inability to enroll and retain a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs, which would cause the value of our company to decline and limit our ability to obtain additional financing.

The COVID-19 pandemic has and could adversely impact our business in the future, including our ongoing and planned clinical trials.*

Our business could be materially adversely affected by the effects of health epidemics. Health epidemics, such as the ongoing COVID-19 pandemic in the United States and in other countries in which we have planned or active clinical trial sites and where our third party manufacturers operate, has impacted and could impact our business and clinical trials in the future, including:

- delays or difficulties in conducting research activities, including preclinical studies such as synthetic chemistry and toxicology studies, some of which are or could be conducted in geographic areas that have experienced rising rates of COVID-19;
- delays or difficulties in screening and enrolling and retaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;

- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- inability or unwillingness of subjects to travel to the clinical trial sites;
- delays or difficulties in data collection and analysis and other related activities;
- decreased implementation of protocol required clinical trial activities and quality of source data verification at clinical trial sites;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials and our other research and development activities, including because of sickness of employees or their families or mitigation measures such as lock-downs and social distancing;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product used in our clinical trials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, delays, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- refusal of regulatory authorities such as FDA or European Medicines Agency (EMA) to accept data from clinical trials in affected geographies; and
- adverse impacts on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed.

Such disruptions could impede, delay, limit or prevent completion of our ongoing clinical trials and preclinical studies or commencement of new clinical trials and ultimately lead to the delay or denial of regulatory approval of our product candidates, which would seriously harm our operations and financial condition and increase our costs and expenses. Measures we have taken in response to COVID-19, include where feasible, conducting remote clinical trial site activations and data monitoring, enabling patients to have routine tests conducted closer to home, allowing trial sites to evaluate certain patients remotely, in compliance with their local procedures and direct-to-patient study drug shipping. Such greater dependency on electronic monitoring could prove to be less reliable and could increase data privacy and cybersecurity risks. However, despite these efforts, we have experienced some temporary delays or disruptions due to the COVID-19 pandemic, in particular with respect to activation of additional clinical trial sites and patient screening and enrollment. We may also experience delays or disruptions in trial data collection and analysis. These delays could have an adverse impact on our timelines and our business. If patients drop out of our trials, miss scheduled doses or follow-up visits or otherwise fail to follow trial protocols, or if our trials are otherwise disrupted due to COVID-19 or actions taken to slow its spread, the integrity of data from our trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program and could have an adverse impact on our business. The COVID-19 pandemic could also affect the business of the FDA, EMA or other health authorities, which could result in delays in meetings related to planned or completed clinical trials and ultimately of reviews and approvals of our product candidates. The global COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 pandemic may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Additionally, although we are currently not aware of any material impacts on our supply chain of our current or potential product candidates as a result of the COVID-19 pandemic, some of our third-party manufacturers which we use for the supply of materials for product candidates or other materials necessary to manufacture product to conduct preclinical tests and clinical

trials and CROs that we may utilize may be impacted by COVID-19, and should they experience continued disruptions, such as temporary closures or suspension of services, we would likely experience delays in advancing clinical trials. Accordingly, while we have not yet experienced material adverse effects to our business as a result of the COVID-19 pandemic, the ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and could have negative impact our business, financial condition and operating results.

Adverse side effects or other safety risks associated with repotrectinib, elzovantinib or our other drug candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials or abandon further development, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Results of clinical trials of our drug candidates could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our drug candidates could result in the delay, suspension or termination of clinical trials by us or the FDA for a number of reasons. Additionally, due to the high mortality rates of the cancers for which we are initially pursuing development and the pretreated nature of many patients in our clinical trials of our drug candidates, a material percentage of patients in these clinical trials may die during a trial, which could impact development of our drug candidates. If we elect or are required to delay, suspend or terminate any clinical trial, the commercial prospects of our drug candidates will be harmed and our ability to generate product revenues from this drug candidate will be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of our drug candidates. Any of these occurrences may harm our business, prospects, financial condition and results of operations significantly.

Moreover, if our drug candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon or limit their development to more narrow 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, which may limit the commercial expectations for our drug candidates, if approved. We may also be required to modify our study plans based on findings in clinical trials of our drug candidates. Many drugs that initially showed promise in early stage testing have later been found to cause side effects that prevented further development. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations. Zai has rights to develop and commercialize products containing repotrectinib and products containing elzovantinib within Greater China. If serious adverse events occur during any clinical trials Zai conducts with respect to repotrectinib or elzovantinib, the FDA and other regulatory authorities may delay, limit or deny approval of repotrectinib or elzovantinib or require us to conduct additional clinical trials as a condition to marketing approval, which would increase our costs.

It is possible that as we test our drug candidates in larger, longer and more extensive clinical trials, including with different dosing regimens, or as the use of our drug candidates becomes more widespread following any regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly.

In addition, if any of our drug candidates receive marketing approval, and we or others later identify undesirable side effects caused by treatment with such drug, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approval of the drug;
- we may be required to recall a product or change the way the drug is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or a contraindication, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to implement a Risk Evaluation and Mitigation Strategy (REMS) or create a medication guide outlining the risks of such side effects for distribution to patients;
- additional restrictions may be imposed on the marketing or promotion of the particular product or the manufacturing processes for the product or any component thereof;
- we could be sued and held liable for harm caused to patients;
- the drug could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our drug candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

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

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials, such as the preliminary interim and topline data from the Phase 1 and Phase 2 portions of our repotrectinib TRIDENT-1 clinical trial, and the preliminary interim data from our elzovantiniib Phase 1 SHIELD-1 clinical trial and from the Phase 1 portion of our TPX-0046 Phase 1/2 SWORD-1 clinical trial. The interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. For our TRIDENT-1 data updates in August 2020, January 2021 and October 2021, we reported preliminary safety and efficacy data as assessed by trial investigators, or physician assessment, using standard RECIST 1.1 criteria. We also reported topline BICR data from all of the ROS1+NSCLC cohorts from the Phase 1/2 TRIDENT-1 study in April 2022. The topline data from TRIDENT-1, including related findings and conclusions, are subject to change following a more comprehensive review of the data related to the trial, and as the trial continues to enroll, treatment continues and more patient data becomes available.

We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, preliminary and topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, repotrectinib or any other drug candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

If we are unable to successfully develop companion diagnostic tests for our drug candidates that require such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these drug candidates.*

We are developing or plan to develop, either by ourselves or with collaborators, companion diagnostic tests for our drug candidates for certain indications. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA approval for companion diagnostic tests on our own, we will require additional personnel. We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our therapeutic drug candidates that require such tests. If these parties are unable to successfully develop companion diagnostics for these therapeutic drug candidates, or experience delays in doing so, we may be unable to enroll enough patients for our current and planned clinical trials, the development of these therapeutic drug candidates may be adversely affected, these therapeutic drug candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that obtain marketing approval. We have developed a prototype companion diagnostic that is being used as a clinical trial assay to confirm the presence of ROS1+ or NTRK+ gene fusions in patients in the Phase 2 portion of TRIDENT-1. We are also enrolling patients into the Phase 2 portion of TRIDENT-1 based on the results of select laboratory developed tests (LDTs) and other tests used by the clinical sites. There is no guarantee that the results obtained from such LDTs or other tests will be consistent with the results obtained from our prototype companion diagnostic. Any inconsistency may result in inclusion of patients with false positive test results that could adversely impact the results of the clinical trial and adversely impact the development and approval of a companion diagnostic. We have selected a diagnostic partner to support development of the companion diagnostic and submission of a pre-market approval application to the FDA. In May 2019, the FDA

approved an Investigational Device Exemption (IDE) for use of this clinical trial assay in the Phase 2 portion of TRIDENT-1 and the assay was CE-marked under the In-Vitro Diagnostic Medical Device Directive in Europe (A CE Mark is a mandatory conformity marking for certain products sold within the European Economic Area). An approved companion diagnostic may be required in order to obtain marketing approval of repotrectinib in patients with *ROS1*+ advanced NSCLC and patients with *NTRK*+ advanced solid tumors. Any failure to successfully develop this companion diagnostic may prevent us from ultimately seeking approval for repotrectinib in patients with *ROS1*+ advanced NSCLC and patients with *NTRK*+ advanced solid tumors. As a result, our business, results of operations and financial condition could be materially harmed.

The failure to obtain required regulatory clearances or approvals for any companion diagnostic tests that we may pursue may prevent or delay approval of any of our drug candidates. Moreover, the commercial success of any of our drug candidates that require a companion diagnostic will be tied to the receipt of any required regulatory clearances or approvals and the continued availability of such tests.

In connection with the clinical development of our drug candidates for certain indications, we may work with collaborators to develop or obtain access to companion diagnostic tests to identify appropriate patients for our drug candidates. We may rely on third parties for the development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory clearances or approvals, and the commercial supply of these companion diagnostics. The FDA and foreign regulatory authorities regulate companion diagnostics as medical devices that will likely be subject to analytical and clinical validation studies in conjunction with the clinical trials for drug candidates, and which will require separate regulatory clearance or approval prior to commercialization. This process could include additional meetings with health authorities, such as a pre-submission meeting and the requirement to submit an IDE. In the case of a companion diagnostic that is designated as “significant risk device,” such as the clinical trial assay we are using in the Phase 2 portion of TRIDENT-1, approval of an IDE by the FDA and IRB is required before such diagnostic is used in conjunction with the clinical trials for a corresponding drug candidate. In May 2019, the FDA approved an IDE for the clinical trial assay we are using in the Phase 2 portion of TRIDENT-1. We or our third-party collaborators may fail to obtain the required regulatory clearances or approvals in the United States or in relevant geographies outside the United States, which could prevent or delay approval of our drug candidates in such geographies. In addition, the commercial success of any of our drug candidates that require a companion diagnostic will be tied to and dependent upon the receipt of required regulatory clearances or approvals and the continued ability of such third parties to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies.

We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug 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 drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug 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 drug candidate.

We may not be successful in our efforts to design additional potential drug candidates.

A key element of our strategy is to apply our knowledge and our understanding of the structure, biology and activity of kinase inhibitors to design drug candidates. The therapeutic design and development activities that we are conducting may not be successful in developing drug candidates that are useful in treating cancer or other diseases. Our research programs may initially show promise in identifying potential drug candidates, yet fail to yield drug candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential drug candidates;
- potential drug candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will obtain marketing approval or achieve market acceptance; or
- potential drug candidates may not be effective in treating their targeted diseases.

Research programs to identify and design new drug candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a drug discovery program or potential drug candidate that ultimately proves to be unsuccessful. We may also pursue opportunities to acquire or in-license additional businesses, technologies or drug candidates to

complement or augment our existing drug discovery and development pipeline. If we are unable to identify or design suitable drug candidates for preclinical and clinical development, we will not be able to obtain revenues from the sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

The development and commercialization of pharmaceutical products are subject to extensive regulation, and we may not obtain regulatory approvals for repotrectinib or any other drug candidates, on a timely basis or at all.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing, distribution, adverse event reporting, including the submission of safety and other post-marketing information and reports, and other possible activities relating to our drug candidates are subject to extensive regulation. Marketing approval of drugs in the United States requires the submission of an NDA to the FDA and we are not permitted to market any drug candidate in the United States until we obtain approval from the FDA of the NDA for that product. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing and controls.

FDA approval of an NDA is not guaranteed, and the review and approval process is an expensive and uncertain process that may take several years. The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for NDA approval varies depending on the drug candidate, the disease or the condition that the drug candidate is designed to treat and the regulations applicable to any particular drug candidate. For example, if successful, we believe that the Phase 2 portion of TRIDENT-1 may be sufficient to support FDA approval of an NDA for repotrectinib, but the FDA may disagree with the sufficiency of our data and require additional clinical trials. Additionally, depending upon the results of the Phase 2 portion of TRIDENT-1, we may choose to seek Subpart H Accelerated Approval for repotrectinib, which would require completion of a confirmatory trial or trials to validate the clinical benefit of the drug. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage. The results of preclinical and early clinical trials of repotrectinib or any other drug candidate may not be predictive of the results of our later-stage clinical trials.

Clinical trial failure may result from a multitude of factors including flaws in trial design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits, and failure in clinical trials can occur at any stage. Companies in the pharmaceutical industry frequently suffer setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from clinical trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may further delay, limit or prevent marketing approval.

The FDA could delay, limit or deny approval of a drug candidate for many reasons, including because they:

- may not deem our drug candidate to be adequately safe and effective as compared to available therapies;
- may not agree that the data collected from preclinical studies and clinical trials are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval, and may impose requirements for additional preclinical studies or clinical trials;
- may determine that adverse events experienced by participants in clinical trials of our drug candidates represent an unacceptable level of risk;
- may determine that population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- may not accept clinical data from trials, which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- may disagree regarding the formulation, labeling and/or the specifications;
- may not approve the manufacturing processes or facilities associated with our drug candidate;
- may change approval policies or adopt new regulations; or
- may not accept a submission due to, among other reasons, the content or formatting of the submission.

Generally, public concern regarding the safety of pharmaceutical products could delay or limit our ability to obtain regulatory approval, result in the inclusion of unfavorable information in our labeling, or require us to undertake other activities that may entail additional costs. We have not obtained FDA approval for any product. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for repotrectinib or any of our other drug candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of repotrectinib or our other drug candidates, our commercial prospects will be harmed and our ability to generate revenues will be materially impaired which would adversely affect our business, prospects, financial condition and results of operations.

A breakthrough therapy designation by the FDA for repotrectinib may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that repotrectinib will receive marketing approval.*

The FDA has granted breakthrough therapy designations to repotrectinib (i) for the treatment of patients with *ROS1*+ metastatic NSCLC who have not been treated with a *ROS1* TKI; (ii) for the treatment of patients with *ROS1*+ metastatic NSCLC who have been previously treated with one *ROS1* TKI and who have not received prior platinum-based chemotherapy; and (iii) for the treatment of patients with advanced solid tumors that have an *NTRK* gene fusion who have progressed following treatment with one or two prior *TRK* TKIs, with or without prior chemotherapy, and have no satisfactory alternative treatments. We may also seek breakthrough therapy designation for other indications or for some of our other drug candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our drug candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a drug candidate may not result in a faster development process, review or approval compared to other drugs and does not assure ultimate approval by the FDA. In addition, even though we received breakthrough therapy designation for certain indications for repotrectinib and even if one or more of our other drug candidates qualify as breakthrough therapies, the FDA may later decide that the drugs no longer meet the conditions for qualification or may decide that the time period for FDA review or approval will not be shortened.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process for our drug candidates.

The FDA has granted fast track designations to repotrectinib for the treatment of patients with (i) *ROS1*+ advanced NSCLC who have not been previously treated with a *ROS1* TKI; (ii) *ROS1*+ advanced NSCLC who have been previously treated with one prior line of platinum-based chemotherapy and one prior line of a *ROS1* TKI; (iii) *ROS1*+ advanced NSCLC who have been previously treated with one prior *ROS1* TKI and who have not received prior platinum-based chemotherapy; and (iv) *NTRK*+ advanced solid tumors who have been previously treated with one prior line of chemotherapy and one or two prior *TRK* TKIs. The FDA has also granted fast track designation to elzovantinib for the treatment of patients with *MET* amplified advanced or metastatic gastric cancer or *GEJ* adenocarcinoma after prior chemotherapy. We may also seek fast track designation for other indications or for some of our other drug candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even though we have received four fast track designations for repotrectinib, and one fast track designation for elzovantinib, or even if we receive fast track designation for other indications or for our other drug candidates, we may not experience a faster development process, review or approval. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed abroad, and any approval we are granted for our drug candidates in the United States would not assure approval of drug candidates in foreign jurisdictions.

In order to market and sell our products in the European Union (EU) or other jurisdictions outside the United States, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Zai is responsible for obtaining marketing approval for repotrectinib and elzovantinib in Greater China. The approval procedure varies among countries and jurisdictions 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. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. 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. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not be able to submit for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Even if we obtain marketing approval for repotrectinib or any of our other drug candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if marketing approval of a drug candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, which may include the requirement to implement a REMS or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We must also comply with requirements concerning advertising and promotion for any of our drug candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to ensure that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

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

We may not be able to obtain or maintain orphan drug designation or exclusivity for our drug candidates.*

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as "orphan drugs." Under the Orphan Drug Act, the FDA may designate a drug candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or if the disease or condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making a drug product available in the United States for the type of disease or condition will be recovered from sales of the product.

Orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Additionally, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity. This means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in certain circumstances, including proving clinical superiority (*i.e.*, another product is safer, more effective or makes a major contribution to patient care) to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity, or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

We have obtained orphan drug designations in the United States for use of repotrectinib in treatment of NSCLC with adenocarcinoma histology and for use of elzovantinib in treatment of gastric cancer, including gastroesophageal junction adenocarcinoma. We may apply for similar designations in other geographies or for our other drug candidates in the future. Orphan drug status does not ensure that we will receive marketing exclusivity in a particular market, and we cannot assure you that any future application for orphan drug designation in any other geography or with respect to any other drug candidate will be granted. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant operating losses since our inception and have not generated any revenue from product sales. We expect to incur continued losses for the foreseeable future and may never achieve or maintain profitability.*

Investment in drug discovery and development is a highly speculative undertaking and involves a substantial degree of risk. We are a clinical-stage precision oncology company that was formed in 2013 and commenced operations in 2014. We have no approved products for commercial sale and have not generated any revenue from product sales. We continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we have never been profitable and have incurred losses in each year since inception. For the three months ended March 31, 2022 and for the year ended December 31, 2021, we reported net losses of approximately \$74.4 million and \$236.6 million, respectively. As of March 31, 2022, we had an accumulated deficit of \$591.2 million.

Since our inception, we have focused substantially all of our efforts and financial resources on the research and development of our lead drug candidate, repotrectinib, and our other drug candidates. To date, we have funded our operations primarily with proceeds from sales of shares of our common stock and convertible preferred stock. From inception through March 31, 2022, we received an aggregate of \$1.3 billion in net proceeds from such sales. As of March 31, 2022, our cash, cash equivalents and marketable securities were \$918.2 million.

We expect to incur increasing levels of operating losses for the foreseeable future, particularly as we advance repotrectinib, and our other drug candidates through clinical development. Our prior losses, combined with expected future losses, have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase in connection with our drug discovery activities and our ongoing and planned clinical trials, and any other clinical trials or development activities we may choose to pursue. In addition, if we obtain marketing approval for repotrectinib or any of our other drug candidates, we will incur significant sales, marketing and outsourced manufacturing expenses in connection with the commercialization of these drug candidates. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from product sales and we do not know when, or if, we will generate any such revenue. If we enter into license or collaboration agreements for any of our drug candidates or intellectual property, such as the Zai License Agreements, we may generate revenue in the future from payments as a result of such license or collaboration agreements. Unless and until we are able to generate revenue from future product sales, we expect that our revenue, if any, will be derived primarily from the Zai License Agreements, as well as any collaborations or additional license agreements that we may enter into in the future. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and begin to sell, repotrectinib or another drug candidate. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete the Phase 2 portion of TRIDENT-1;
- initiate and successfully complete all safety, pharmacokinetic and other studies required to obtain U.S. and foreign marketing approval for repotrectinib as a treatment for patients with *ROS1*+ advanced NSCLC and patients with *NTRK*+ advanced solid tumors;
- initiate and successfully complete other later-stage clinical trials that meet their clinical endpoints, including our planned Phase 2 clinical trial of elzovantinib;
- obtain favorable results from our clinical trials and apply for and obtain marketing approval for repotrectinib or another drug candidate;
- establish licenses, collaborations or strategic partnerships that may expand our pipeline or increase the value of our programs;
- successfully manufacture or contract with others to manufacture repotrectinib and our other drug candidates;
- establish and maintain a sales, marketing, market access, patient services and distribution infrastructure to commercialize any products for which we may obtain marketing approval, including, assisting our licensee Zai in its efforts to develop and, if approved, commercialize repotrectinib and elzovantinib in Greater China, and/or entering into additional licenses and/or collaborations with third parties;

- obtain, maintain, protect and defend our intellectual property portfolio; and
- achieve market acceptance of repotrectinib and our other drug candidates in the medical community and with third-party payors.

To become and remain profitable, we must succeed in designing, developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials for our drug candidates, designing additional drug candidates, establishing arrangements with third parties for the manufacture of clinical supplies of our drug candidates, obtaining marketing approval for our drug candidates and manufacturing, marketing and selling any products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

In cases where we are successful in obtaining regulatory approval to market one or more of our drug candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, or if, we will be able to achieve profitability. If we decide to or are required by the FDA or other regulatory authorities to perform studies or clinical trials in addition to those currently expected, or if there are any delays in establishing appropriate manufacturing arrangements for, in initiating or completing our current and planned clinical trials for, or in the development of, any of our drug candidates, our expenses could increase materially and profitability could be further delayed.

Even 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will require substantial additional funding. If we are unable to raise capital on favorable terms when needed, we could be forced to delay, reduce or eliminate our research or drug development programs or any future commercialization efforts.*

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our lead drug candidate, repotrectinib, elzovantini, and our other drug candidates through clinical development and further develop our pipeline. We expect increased expenses as we continue our research and development, initiate additional clinical trials, and seek marketing approval for repotrectinib and our other drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to continue to incur significant costs associated with operating as a public company.

In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for sale for at least the next several years, if ever, and such funds, if raised, may not be sufficient to enable us to continue to implement our business strategy. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on favorable terms, or at all. In addition, the COVID-19 pandemic and ongoing geopolitical events continue to rapidly evolve and have already resulted in a significant disruption of global financial markets. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and further disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the pandemic or geopolitical actions. If such further disruption deepens, we could experience an inability to access additional capital. Further, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on favorable terms, we could be forced to delay, reduce or eliminate our research and development programs, our commercialization plans or other operations. We believe that our existing cash and cash equivalents and marketable securities as of March 31, 2022, will be sufficient to enable us to fund our operating expenses through the first half of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Changes beyond our control may occur that would cause us to use our available capital before that time, including changes in and progress of our drug development activities and changes in regulation. Our future capital requirements will depend on many factors, including:

- the progress and results of our Phase 2 portion of TRIDENT-1, our Phase 1/2 pediatric study of repotrectinib and any other additional clinical trials evaluating repotrectinib;
- the scope, rate of progress, results and costs of drug design, preclinical development, and clinical trials for the other drug candidates in our pipeline, including elzovantinib, TPX-0046, TPX-0131 and TPX-4589;
- the extent to which we develop, in-license or acquire other pipeline drug candidates or technologies and associated intellectual property rights;
- the number and development requirements of other drug candidates that we may pursue, and other indications for our current drug candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our drug candidates and any companion diagnostics we may pursue;
- the scope and costs of making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our drug candidates;
- the cost associated with commercializing any approved drug candidates, including to establish sales and marketing capabilities;
- the cost associated with completing any post-marketing studies or trials required by the FDA or other regulatory authorities;
- the revenue, if any, received from commercial sales of repotrectinib, if approved, or our other pipeline drug candidates that receive marketing approval;
- the achievement of milestones or occurrence of other developments that trigger payments, including, without limitation, milestone or royalty payments, to us under our Zai License Agreements or any collaboration or other license agreements that we may enter into in the future, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims that we may become subject to; and
- to the extent we pursue strategic collaborations, including additional collaborations to commercialize repotrectinib or any of our other drug candidates, our ability to establish and maintain collaborations on favorable terms, if at all.

We will require additional capital to complete our planned clinical development programs for our current drug candidates to obtain regulatory approval. Any additional capital-raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future drug candidates, if approved.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not currently have any committed external source of funds. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. In August 2020, we entered into an Open Market Sale AgreementSM with Jefferies LLC (ATM facility), under which we may offer and sell, from time to time, at our sole discretion, up to \$250.0 million shares of our common stock. As of March 31, 2022, we had not yet sold any shares of our common stock under the ATM facility.

If we raise additional funds through additional collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug 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 or other arrangements when needed, we may be required to delay, limit, reduce or terminate our

research, product development or future commercialization efforts or grant rights to third parties to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

We rely, and intend to continue to rely, on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties, fail to comply with applicable regulatory requirements or do not meet expected deadlines, our development programs may be delayed or subject to increased costs or we may be unable to obtain regulatory approval, each of which may have an adverse effect on our business, financial condition, results of operations and prospects.

We do not have the ability to independently conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are dependent on third parties to conduct our ongoing and planned clinical trials and other studies of repotrectinib and our other drug candidates. The timing of the initiation and completion of these studies and trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Specifically, our CROs, clinical investigators and consultants play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each clinical trial is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA for drug candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA, EMA and comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that our clinical trials comply with GCPs. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure or the failure of third parties on whom we rely to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise perform in a substandard manner, or terminate their engagements with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If our clinical trial site terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trial unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, certain of our scientific advisors or consultants who receive compensation from us are clinical trial investigators for our clinical trial. Although we believe our existing relationships are within the FDA's guidelines, if these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA. Any such delay or rejection could prevent us from commercializing repotrectinib or any other drug candidates.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors for whom they may also be conducting clinical trials or other pharmaceutical product development activities that could harm our competitive position. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for repotrectinib or any other drug candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

Manufacturing pharmaceutical products is complex and subject to product loss for a variety of reasons. We contract with third parties for the manufacture of our drug candidates for preclinical testing and clinical trials and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.*

We do not have any manufacturing facilities. We produce in our laboratory very small quantities of small molecules for evaluation in our research programs. We rely, and expect to continue to rely, on third parties for the manufacture of our drug candidates for preclinical and clinical testing, for the supply of third-party drug product for our planned and ongoing combination clinical trials, as well as for commercial manufacture if any of our drug candidates obtain marketing approval. This reliance on third

parties increases the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We rely heavily on manufacturers in China for starting materials for our drug candidates. Any delays or interruptions in the supply of starting materials for the manufacture of any of our drug candidates could delay, prevent or impair our development or commercialization efforts. We believe we currently have sufficient supply or plans for supply to meet our anticipated clinical development needs for repotrectinib, elzovantinib, TPX-0046, TPX-0131 and TPX-4589 through 2022. However, depending on the length and ultimate impact of the COVID-19 pandemic, and available manufacturing capacity at our supplier, our supply could be adversely impacted, which may result in delays or disruptions in our current or future supply chain.

We may be unable to establish any agreements with third-party manufacturers or to do so on favorable 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 and quality assurance;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or the issuance of an FDA Form 483 notice or warning letter;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know how;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our drugs under specified storage conditions and in a timely manner.

We have only limited supply arrangements in place with respect to our drug candidates, and these arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long-term committed arrangements with respect to our drug candidates and other materials. If we obtain marketing approval for any of our drug candidates, we will need to have established an agreement for commercial manufacture with a third party.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers and suppliers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. In addition, our third-party manufacturers and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of regulatory actions that may be brought against these third parties in the future, our clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

Our drug candidates and any products that we may develop may compete with other drug candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority or timely basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

For later-stage clinical trials and potential commercialization, we need to take steps to increase the scale of production of our drug candidates. In scaling up the manufacturing process for our drug candidates, even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our drug candidates or in the manufacturing facilities in which our drug candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply. If our current contract manufacturers for preclinical and clinical materials cannot perform as agreed, we may suffer delays or disruptions in our current or future supply chain and our clinical trials may be adversely impacted as a result. If our current third-party manufacturers cannot perform as agreed, we may also be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Although we believe that

there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement manufacturer or be able to reach agreement with any alternative manufacturer. Further, our third-party manufacturers may experience manufacturing or shipping difficulties due to resource constraints or as a result of natural disasters, labor disputes, unstable political environments, or public health epidemics such as the COVID-19 outbreak.

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

We may enter into collaborations with third parties for the development and commercialization of our drug candidates. If those collaborations, including, without limitation, our license arrangements with Zai for the development and commercialization of repotrectinib and elzovantinib in Greater China, are not successful, we may not be able to capitalize on the market potential of these drug candidates.*

We currently have and may in the future seek third-party collaborators for the development and commercialization of some of our drug candidates on a selected basis. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. For example, we have granted to Zai, a China and U.S.-based commercial stage biopharmaceutical company, rights to develop and commercialize products containing repotrectinib and products containing elzovantinib, in Greater China. Consequently, our ability to generate any revenues from repotrectinib or elzovantinib in Greater China depends on our ability to maintain our collaborations with Zai. We have limited control over the amount and timing of resources that Zai will dedicate to these efforts. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for any future collaboration we may seek, 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.

To the extent we have, and if we do enter into any further such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our drug candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our drug candidates, such as our collaborations with Zai, pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may de-emphasize or not pursue development and commercialization of our drug candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a sale or disposition of a business unit or development function, 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 drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or drug candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or drug candidates or that result in costly litigation or arbitration that diverts management attention and resources;

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates;
- collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner or at all; and
- if a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If our collaborations, such as our license arrangements with Zai, our clinical collaboration with EQRx, Inc., our license arrangements with LaNova, or any future license or collaboration we may enter into, if any, are not successful, our business, financial condition, results of operations, prospects and development and commercialization efforts may be adversely affected. Any termination or expiration of either of the Zai License Agreements, or any other license or collaboration we may enter into, if any, could adversely affect us financially or harm our business reputation, development and commercialization efforts.

We may explore new licensing arrangements, strategic collaborations and acquisitions that may never materialize or may fail.*

We have been continuously exploring a variety of potential business development opportunities in an effort to expand our product candidate portfolio. At the current time, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and these strategic collaborations can be complicated and time-consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic collaborations because of the numerous risks and uncertainties associated with establishing strategic collaborations.

Risks Related to the Commercialization of Our Drug Candidates

The incidence and prevalence for target patient populations of our drug candidates have not been established with precision. If the market opportunities for our drug candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue potential and ability to achieve profitability will be adversely affected.

The total addressable market opportunity for repotrectinib and our other drug candidates will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each such drug candidate if our drug candidates are approved for sale for these indications, acceptance by the medical community and patient access, drug and any related companion diagnostic pricing and their reimbursement. The number of patients in our targeted commercial markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Even if any of our drug candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our drug candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments, such as existing targeted therapies, chemotherapy, and radiation therapy, are well established in the medical community, and doctors may continue to rely on these treatments. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- limitations or warnings contained in the labeling approved for our drug candidates by the FDA;
- the size of the target patient population;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- our ability to offer our products for sale at competitive prices;

- the convenience and ease of administration compared to alternative treatments;
- the strength of marketing and distribution support;
- publicity for our drug candidates and competing products and treatments;
- incorporation into clinical treatment guidelines such as the National Comprehensive Cancer Network Guidelines;
- the existence of distribution and/or use restrictions, such as through a REMS;
- the availability of third-party payor coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on the use of our products together with other medications.

We have no experience as a company in commercializing products and we may have to invest significant resources to develop these capabilities. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate revenue.*

We do not have a sales infrastructure and are only in the very early stages of building a marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either ourselves or through collaboration or other arrangements with third parties.

We plan to build our own focused, specialized sales and marketing organization in the United States. Outside of the United States, in addition to our existing repotrectinib and elzovantinib licenses to Zai for Greater China, we plan to selectively establish partnerships in markets outside the United States to support the commercialization of drug candidates for which we obtain marketing approval and that can be commercialized with such capabilities.

There are risks involved with establishing our own sales and marketing capabilities. 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 drug 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. These efforts are expected to 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 products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our inability to raise financing necessary to build our commercialization infrastructure;
- the inability of sales personnel to obtain access to physicians or educate an adequate number of physicians as to the benefits of our products;
- unfavorable third-party payor coverage and reimbursement in any geography;
- the lack of complementary products 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.

As a result of any potential partnerships in markets outside of the United States, including our license arrangements with Zai, and LaNova, or if we are unable to establish our own sales and marketing capabilities in the United States and instead enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into

arrangements with third parties to market and sell our drug candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell and market our products 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 any of our drug candidates for which we receive marketing approval.

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

The development and commercialization of pharmaceutical products is highly competitive. We face competition with respect to our current drug candidates, and will face competition with respect to any drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. 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 disease indications for which we are developing our drug candidates. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches. Potential competitors also include 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 large number of pharmaceutical and biotechnology companies developing or marketing targeted treatments for cancer that would be competitive with the drug candidates we are developing, if our drug candidates are approved. Many of these companies are developing cancer therapeutics that are also kinase inhibitors.

If we are successful in developing repotrectinib, we expect that repotrectinib will compete against approved drugs, including: crizotinib, which is marketed by Pfizer Inc. under the name Xalkori for the treatment of *ROS1*+ and *ALK*+ NSCLC; entrectinib, which is marketed by F. Hoffman La Roche AG under the name Rozlytrek, for the treatment of *ROS1*+ NSCLC and *TRK*+ solid tumors; and larotrectinib, which is marketed by Bayer AG under the trade name Vitravki, for the treatment of *TRK*+ solid tumors. We also expect that repotrectinib will compete against other compounds which are currently in late-stage clinical development, including TKIs in Phase 2 or later clinical development for the treatment of *ROS1*+ NSCLC at companies including against Pfizer Inc. (lorlatinib), Novartis Pharmaceuticals Corporation (ceritinib), Betta Pharmaceuticals Co., Ltd. (ensartinib), Exelixis, Inc. (cabozantinib) and AnHeart Therapeutics Company (taletrectinib) and TKIs in Phase 2 or later clinical development for the treatment of *TRK*+ solid tumors at companies including Bayer AG (selitrectinib), Exelixis, Inc. (cabozantinib) and AnHeart Therapeutics Company (taletrectinib).

If we are successful in developing elzovantinib, we expect that elzovantinib will compete against capmatinib, which is marketed by Novartis Pharmaceutical Corporation under the name Tabrecta; tepotinib, which is marketed by Merck KGaA under the name Tepmetko; savolitinib, which is marketed in China by AstraZeneca PLC and Hutchison China MediTech Limited under the name Orpathys; and amivantamab, which is marketed by Johnson & Johnson under the name Rybrevant. Capmatinib, tepotinib and savolitinib are indicated for the treatment of adult patients with metastatic NSCLC harboring *MET* exon 14 skipping alterations. We also expect that elzovantinib will compete against Xalkori (crizotinib) and other compounds which are in Phase 2 or later clinical development for the treatment of *MET*+ tumors at companies including Exelixis, Inc. (cabozantinib), Apollomics, Inc. (APL-101), Haihe Biopharma Co., Ltd (glumetinib), Servier (Sym015), AbbVie Inc. (telisotuzumab vedotin) and Aveo Oncology (ficlatuzumab).

If we are successful in developing TPX-0046, we expect that TPX-0046 will compete against selpercatinib, which is marketed by Eli Lilly and Company under the names Retevmo and Retsevmo for the treatment of NSCLC, medullary thyroid cancer and other types of thyroid cancer in patients with *RET* gene alterations; and pralsetinib, which is marketed by F. Hoffman La Roche AG and Blueprint Medicines Corporation under the name Gavreto for the treatment of NSCLC, medullary thyroid cancer and other types of thyroid cancer in patients with *RET* gene alterations, and are both in development for the treatment of other *RET*+ cancers, and other approved multi-kinase inhibitors with *RET* activity that are being evaluated in clinical trials including cabozantinib (Exelixis, Inc.), lenvatinib (Eisai Inc.), sorafenib (Bayer AG), sunitinib (Pfizer Inc.) and vandetinib (Sanofi Genzyme). We also expect TPX-0046 will compete against compounds which are in Phase 2 or later clinical development for the treatment of *RET*+ tumors at companies including Helsinn Group (HM06).

If we are successful in developing TPX-0131, we expect that TPX-0131 will compete against approved drugs, including: alectinib, which is marketed by F. Hoffman La Roche AG under the name Alecensa for the treatment of *ALK*+ NSCLC; brigatinib, which is marketed by Takeda Pharmaceutical Company Limited under the name Alunbrig for the treatment of *ALK*+ NSCLC; ceritinib, which is marketed by Novartis Pharmaceuticals Corporation under the name Zykadia for the treatment of *ALK*+ NSCLC; crizotinib, which is marketed by Pfizer Inc. under the name Xalkori for the treatment of *ROS1*+ and *ALK*+ NSCLC; and lorlatinib, which is marketed by Pfizer Inc. under the names Lorbreina and Lorviqua for the treatment of *ALK*+ NSCLC. We also expect that

TPX-0131 will compete against other compounds which are currently in late-stage clinical development, including TKIs in Phase 2 or later clinical development for the treatment of ALK+ NSCLC at companies including against Betta Pharmaceuticals Co., Ltd. (ensartinib).

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing and selling 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 other early-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, management and sales and marketing personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are approved for broader indications or patient populations, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other marketing approval for their products more rapidly than any approval we may obtain for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. Generic products are currently on the market for some of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our drug candidates achieve marketing approval, we expect that they will be priced at a significant premium over any competitive generic products. The key competitive factors affecting the success of our drug candidates are likely to be their efficacy, safety, scope and limitations of marketing approval, and availability of reimbursement.

Even if we are able to commercialize any drug candidates, the products may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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. 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 drug candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if such drug candidates obtain marketing approval.

Our ability to commercialize any drug candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government healthcare programs, private health insurers and other organizations. Third-party payors decide which medications they will pay for and establish reimbursement levels.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any drug candidate for which we obtain marketing approval. Obtaining and maintaining coverage and adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval.

Additionally, we are developing or plan to develop, either by ourselves or with collaborators, in vitro companion diagnostic tests for our drug candidates for certain indications. We, or our collaborators, will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. While we have not yet developed any companion diagnostic test for our product candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates.

There may also be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare determinations. Our inability to promptly obtain coverage and adequate reimbursement rates from third-party payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and will face an even greater risk if we commercialize any products that we may develop. If we cannot successfully defend ourselves against any claims that our drug candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any drug candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Our current product liability insurance coverage for the United States and certain other jurisdictions may not be adequate to cover all liabilities that we may incur. We likely will need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our drug candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Marketing of Our Drug Candidates and Other Legal Compliance Matters

Any drug candidate for which we obtain marketing approval will be subject to ongoing enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any drug candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding drug distribution and the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. For example, the FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Although physicians may prescribe products for off-label uses as the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. Companies may only share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. Violations of such requirements may lead to investigations alleging violations of the FDCA and other statutes, including the False Claims Act and other federal and state healthcare fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us, our licensee Zai or any other collaborator with regulatory requirements, including safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population can also result in significant financial penalties.

Our relationships with customers, healthcare providers, and third-party payors may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil and administrative penalties, contractual damages, reputational harm and diminished profits and future earnings.*

Healthcare providers, including physicians, and third-party payors will play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors and customers 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 research, market, sell and

distribute any products 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 and entities 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 of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the False Claims Act, which can be enforced by civil whistleblower or qui tam actions on behalf of the government, and the civil monetary penalties law, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal government 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;
- HIPAA, which, among other things, imposes criminal and civil liability for executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and their implementing regulations, which impose requirements on certain healthcare providers, health plans and healthcare clearinghouses, known as “covered entities,” and persons or entities that perform functions or activities that involve individually identifiable health information on behalf of a covered entity, known as “business associates,” and their covered subcontractors, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively the ACA), requires certain manufacturers of certain drugs, devices, biologics and medical supplies to report to the Centers for Medicare & Medicaid Services (CMS) information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals and ownership and investment interests held by physicians and their immediate family members; and
- analogous state laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, 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 regulations 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, and some state laws require the reporting of information related to drug pricing. Some state and local laws require the registration of pharmaceutical sales representatives. Some state and non-U.S. laws that 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, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional integrity reporting and oversight obligations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our drug candidates and decrease the prices we may obtain.

In the United States and some 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 drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any drug candidates for which we obtain marketing approval.

For example, the ACA was passed in March 2010 and substantially changed the way healthcare is financed by both governmental and private insurers, and continues to significantly impact the U.S. pharmaceutical industry.

With regard to pharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs and a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

There have been executive, judicial and Congressional challenges to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance and eliminating the implementation of certain ACA-mandated fees. Additionally, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction, triggering the legislation's automatic reduction to several government programs. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013, and due to subsequent legislative amendments to the statute, will remain in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the fiscal year of this sequester. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, 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.

Further, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. However, several lawsuits have been brought against the U.S. Department of Health and Human Services (HHS) challenging various aspects of the rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies. In addition, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of the other reform initiatives. In addition, at the state level, individual states have increasingly passed legislation and implemented 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.

We expect that the ACA, 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 receive for any approved product. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly some countries in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. 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 drug candidate 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 business could be harmed. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries. In the EU the regulation of pricing and reimbursement varies widely between individual member states. Some member states prohibit the marketing of products prior to a reimbursement price being agreed, some member states may require the completion of additional studies to assess cost-effectiveness against currently available therapies. Price controls or profit controls are in place in a number of member states.

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

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

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

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

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

We are subject to stringent and changing obligations related to data protection and privacy. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; a disruption of our business operations; reputational harm; loss of revenue or profits; loss of sales; and other adverse business consequences.*

In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (commonly known as processing) personal data and other confidential information, including proprietary business information, trade secrets, intellectual property, and data we collect about trial participants in connection with clinical trials, and sensitive third-party data. Our data processing activities may subject us and potential collaborators to federal, state and foreign data protection and privacy laws and regulations. In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal data could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the HIPAA, as amended by HITECH. We could be subject to penalties if we obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

In addition, the California Consumer Privacy Act of 2018 (CCPA) imposes obligations on covered businesses. These obligations include, but are not limited to, providing specific disclosures in privacy notices and affording California residents certain rights related to their personal data. The CCPA allows for statutory fines for noncompliance (up to \$7,500 per violation) and a private right of action for certain data breaches. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data we maintain about California residents. In addition, it is anticipated that the California Privacy Rights Act of 2020 (CPRA), effective January 1, 2023, will expand the CCPA. Additionally, the CPRA establishes a new California Privacy Protection Agency to implement and enforce the CPRA, which could increase the risk of enforcement. Other states have also enacted data privacy laws. For example, Virginia passed the Consumer Data Protection Act (CDPA), Colorado passed the Colorado Privacy Act (CPA) and Utah passed the Utah Consumer Privacy Act (UCPA), all of which differ from the CPRA and become effective in 2023. If we become subject to new data privacy laws, at the state level, the risk of enforcement action against us could increase because we may become subject to additional obligations, and the number of individuals or entities that can initiate actions against us may increase (including individuals, via a private right of action, and state actors). The CCPA, CPRA, CDPA, CPA and UCPA may impact our business activities and exemplify the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to data protection and privacy. For example, the European Union's General Data Protection Regulation (EU GDPR) and the United Kingdom's GDPR (UK GDPR) impose strict requirements for processing personal data. For example, under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros or 4% of annual global revenue, whichever is greater. Further, individuals may initiate litigation related to processing of their personal data. Additionally, certain jurisdictions have enacted data localization laws and cross-border personal data transfer laws, which could make it more difficult to transfer information across jurisdictions (such as transferring or receiving personal data that originates in the EU or in other foreign jurisdictions). For example, the EU GDPR increases our responsibility and liability in relation to personal data that we process. In addition, the GDPR prohibits the transfer of personal data to countries outside of the EEA, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Switzerland and the United Kingdom have adopted similar restrictions. U.S. companies had been able to rely on the Privacy Shield and the standard contractual clauses for compliantly transferring personal data, both of which were struck down by the Court of Justice of the European Union in July 2020. In June 2021, the European Commission released a set of "Standard Contractual Clauses" that are designed to be a valid mechanism by which entities can transfer personal data out of the EEA to jurisdictions that the European Commission has not found to provide an adequate level of protection. Currently, these Standard Contractual Clauses are a valid mechanism to transfer personal data outside of the EEA. The Standard Contractual Clauses, however, require parties that rely upon that legal mechanism to comply with additional obligations, such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. Moreover, due to potential legal challenges, there exists some uncertainty regarding whether the Standard Contractual Clauses will remain a valid mechanism for transfers of personal data out of the EEA. If we cannot implement a valid compliance mechanism for cross-border data transfers, we may face increased exposure to regulatory actions, substantial fines, and injunctions against processing or transferring personal data from Europe or other foreign jurisdictions. The inability to import personal data to the United States could significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties that are subject to such cross-border data transfer or localization laws; or requiring us to increase our personal data processing capabilities and infrastructure in foreign jurisdictions at significant expense.

Compliance with U.S. and international data protection and privacy laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U.S. and international data protection and privacy laws and regulations could result in government enforcement actions (which could include civil, criminal, and administrative penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our

potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection and privacy laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

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 harm our business.

We are subject to numerous foreign, federal, state and local 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 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, including any available insurance.

In addition, our leasing and operation of real property may subject us to liability pursuant to certain of these laws or regulations. Under existing U.S. environmental laws and regulations, current or previous owners or operators of real property and entities that disposed or arranged for the disposal of hazardous substances may be held strictly, jointly and severally liable for the cost of investigating or remediating contamination caused by hazardous substance releases, even if they did not know of and were not responsible for the releases.

We could incur significant costs and liabilities which may adversely affect our financial condition and operating results for failure to comply with such laws and regulations, including, among other things, civil or criminal fines and penalties, property damage and personal injury claims, costs associated with upgrades to our facilities or changes to our operating procedures, or injunctions limiting or altering our operations.

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.

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, which are becoming increasingly more stringent, may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to certain U.S. and certain foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations prohibit, among other things, companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of these laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase over time. We expect to rely on third parties for research, preclinical studies and clinical trials and/or to obtain necessary permits, licenses, patent registrations and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Our business may be adversely impacted by the consequences of Russia's invasion of Ukraine.*

Economic, political and social conditions resulting from Russia's invasion of Ukraine could materially disrupt our clinical trials, increase our costs and may disrupt planned clinical development activities. To the extent the conflict between Ukraine and Russia adversely impacts our ability to enroll patients or complete enrollments in process or adversely impacts the ability of our suppliers to

produce and distribute supplies that we need for our clinical trials, the timing for completing our clinical trials may be adversely impacted. In addition, the United States, United Kingdom and European Union governments, among others, have instituted various sanctions and export-control measures in response to the invasion, including comprehensive financial sanctions, targeted at Russia or designated individuals and entities with business interests and/or government connections to Russia or those involved in Russian military activities. Governments have also enhanced export controls and trade sanctions targeting Russia's imports of goods. The duration and intensity of this conflict and its economic impact on our European operations is uncertain at this time, but it is possible that our business, results of operations and financial condition could be materially and adversely affected.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our drug candidates, or if the scope of the patent protection is not sufficiently broad, third parties, including our competitors, could develop and commercialize products similar or identical to ours, and our ability to commercialize our drug candidates successfully may be adversely affected.

Our success depends in large part on our ability to protect our proprietary technologies that we believe are important to our business, including pursuing, obtaining and maintaining patent protection in the United States and other countries intended to cover the composition of matter of our drug candidates, the methods of use, related technologies and other inventions that are important to our business. Although we own patents in the United States and foreign countries, we cannot be certain that the claims in our other U.S. pending patent applications, corresponding international patent applications and patent applications in certain foreign countries will be considered patentable by the USPTO, courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our patents will not be found invalid or unenforceable if challenged. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. If we do not adequately pursue, obtain, maintain, protect or enforce our intellectual property, third parties, including our competitors, may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

To protect our proprietary position, we file patent applications in the United States and abroad related to our drug candidates that we consider important to our business. The patent application and approval process is expensive, time-consuming and complex. We may not be able to file, prosecute and maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, depending on the terms of any future license agreements to which we may become a party, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the patents, covering technology licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Furthermore, the patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. In addition, the determination of patent rights with respect to biological and pharmaceutical products commonly involves complex legal and factual questions, which have 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. Thus, we cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents, whether any patents will be found invalid and unenforceable or will be threatened by third parties or whether any patents will effectively prevent others from commercializing competing technologies and drug candidates.

Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until at least one patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. 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. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file for patent protection for the inventions covered by pending patent applications. In addition, we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, collaborators, CROs, contract manufacturers, hospitals, independent treatment centers, consultants, independent contractors, suppliers, advisors and other third parties; however, 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. Furthermore, if third parties have filed patent applications related to our drug candidates or technology, we may not be able to obtain our own patent rights to those drug candidates or technology.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in post-grant review procedures, oppositions, derivations, revocation, reexaminations, inter partes review or interference proceedings, in the United States or elsewhere, 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 products without infringing third-party rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of exclusivity or in our patent claims being narrowed, invalidated or held unenforceable, in whole or in part, 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 products. Such challenges also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, given the amount of time required for the development, testing and regulatory review of new drug candidates, our patents protecting such drug candidates might expire before or shortly after such drug 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. Moreover, some of our patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our pending and future patent applications may not result in patents being issued that protect our drug candidates, in whole or in part, or which effectively prevent others from commercializing competitive products. 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. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does.

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. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our drug candidates will be protectable or remain protected by valid and enforceable patents. Our competitors and other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors and other third parties may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors or other third parties may seek to market generic versions of any approved products by submitting abbreviated NDAs to the FDA during which process they may claim that patents owned by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, future patents may be subject to a reservation of rights by one or more third parties. For example, to the extent the research resulting in future patent rights or technologies is funded in the future in part by the U.S. government, the government could have certain rights in any resulting patents and technology, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf for non-commercial purposes. If the U.S. government then decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. These rights may also permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government may also exercise its march-in rights if it determines that action is necessary because we failed to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such government-funded inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States.

Any exercise by the government of aforementioned proprietary rights could harm our competitive position, business, financial condition, results of operations, and prospects.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Patent reform legislation in the United States and other countries could increase those uncertainties and costs. For example, the Leahy-Smith America Invents Act (the Leahy-Smith Act) signed into law in September 2011, includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. For example, the Leahy-Smith Act allows third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. In addition, the Leahy-Smith Act has transformed the U.S. patent system from a “first-to-invent” system to a “first-to-file” system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The Leahy-Smith Act could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our or our collaboration partners’ patent applications and the enforcement or defense of our or our collaboration partners’ issued patents, all of which could harm our business, results of operations, financial condition and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Competitors and other third parties may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights, trade secrets or other intellectual property. To counter infringement, misappropriation or other violations, we may be required to file infringement, misappropriation or other violation claims, which can be expensive and time consuming and divert the time and attention of our management and business and scientific personnel. In addition, many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can.

Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their patents or their other intellectual property, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In patent litigation in the United States, counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. Similarly, third parties may initiate legal proceedings against us seeking a declaration that certain of our intellectual property is non-infringed, invalid or unenforceable. The outcome of any such proceeding is generally unpredictable.

In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent’s claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our patents covering one of our drug candidates, we could lose at least a part, and perhaps all, of the patent protection covering such a drug candidate. Competing drugs may also be sold in other countries in which our patent coverage might not exist or be as strong. If we lose a foreign patent lawsuit,

alleging our infringement of a competitor's patents, we could be prevented from marketing our drugs in one or more foreign countries. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. 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 litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Furthermore, third parties may also raise invalidity or unenforceability claims before administrative bodies in the United States or foreign authorities, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post-grant review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation, cancellation or amendment to our patents in such a way that they no longer cover and protect our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or written description. Grounds for an unenforceability assertion could be an allegation that someone connected with the prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution of the patent. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our licensors, our patent counsel and the patent examiner were unaware during prosecution. Moreover, it is possible that prior art may exist that we are aware of but do not believe is relevant to our current or future patents, but that could nevertheless be determined to render our patents invalid. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our drug candidates. Any such loss of patent protection could have a material adverse impact on our business, financial condition, results of operations and prospects.

We may not be able to effectively enforce our intellectual property and proprietary rights throughout the world.*

Filing, prosecuting and defending patents with respect to our drug candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. The requirements for patentability may differ in certain countries, particularly in developing countries. In addition, any future intellectual property license agreements may not always include worldwide rights. Consequently, competitors and other third parties may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States and where our ability to enforce our patents to stop infringing activities may be inadequate. These products may compete with our products in such territories and in jurisdictions where we do not have any patent rights or where any future patent claims or other intellectual property or proprietary rights may not be effective or sufficient to prevent them from competing with us, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Moreover, our ability to protect and enforce our intellectual property and proprietary rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property and proprietary rights in certain foreign jurisdictions. The legal systems of some countries, including, for example, India, China and other developing countries, do not favor the enforcement of patents and other intellectual property or proprietary rights, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violation of our patents or other intellectual property or proprietary rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions, whether or not successful,

could result in substantial costs and divert our efforts and resources from other aspects of our business, could put our patents, trademarks or other intellectual property and proprietary rights at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property and proprietary rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property and proprietary rights in such countries may be inadequate.

Geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could potentially have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

If we are sued for infringing, misappropriating or otherwise violating intellectual property or proprietary rights of third parties, such litigation or disputes could be costly and time consuming and could prevent or delay us from developing or commercializing our drug candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties. If any third-party patents, patent applications or other proprietary rights are found to cover our drug candidates or any related companion diagnostics or their compositions, methods of use or manufacturing, we may be required to pay damages, which could be substantial, and we would not be free to manufacture or market our drug candidates or to do so without obtaining a license, which may not be available on commercially reasonable terms, or at all.

We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property or proprietary rights with respect to our drug candidates and technologies we use in our business. Our competitors or other third parties may assert infringement claims against us, alleging that our drug candidates are covered by their patents. We cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our drug candidates. If a patent holder believes our drug candidate infringes its patent rights, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property or proprietary rights with respect to our drug candidates, including post-grant proceedings before the USPTO. Third parties may assert infringement, misappropriation or other claims against us based on existing or future intellectual property or proprietary rights. The outcome of intellectual property litigation and other disputes is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of using or manufacturing products. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our drug candidates, products or methods of use, manufacturing or other applicable activities either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be successful in doing so. However, proving invalidity or unenforceability is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by patents. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, or enforceability. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and business and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property or proprietary rights and we are unsuccessful in demonstrating that such intellectual property or proprietary rights are invalid or unenforceable, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing drug candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing drug candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby giving our competitors and other third parties access to the same technologies licensed to us. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed such third-party patent rights. A finding of infringement could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees or consultants or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Some of our employees and consultants are currently or have been previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. These employees and consultants may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such other current or previous employment. Although we try to ensure that our employees and consultants 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 third parties. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property or personnel or sustain damages. Such intellectual property could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to our management. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. In addition, such agreements may not be self-executing such that the intellectual property subject to such agreements may not be assigned to us without additional assignments being executed, and we may fail to obtain such assignments. In addition, such agreements may be breached. Accordingly, we may be forced to bring claims against third parties, or defend claims that they may bring against us to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

Rights to improvements to our drug candidates may be held by third parties.

In the course of testing our drug candidates, we have entered into agreements with third parties to conduct clinical testing, which provide that improvements to our drug candidates may be owned solely by a party or jointly between the parties. If we determine that rights to such improvements owned solely by a third party are necessary to commercialize our drug candidates or maintain our competitive advantage, we may need to obtain a license from such third party in order to use the improvements and continue developing, manufacturing or marketing the drug candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain such a license, it could be granted on non-exclusive terms, thereby giving our competitors and other third parties access to the same technologies licensed to us. Failure to obtain a license on commercially reasonable terms or at all, or to obtain an exclusive license, could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business. If we determine that rights to improvements jointly owned between us and a third party are necessary to commercialize our drug candidates or maintain our competitive advantage, we may need to obtain an exclusive license from such third party. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such improvements, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our intellectual property in order to enforce such intellectual property against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

The term of our patents may be inadequate to protect our competitive position on our products.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Depending upon the timing, duration and other factors relating to any FDA marketing approval we receive for any of our drug candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments). We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Hatch-Waxman Amendments permit a patent term extension of up to five years beyond the normal expiration of the patent, limited to the approved indication (or any additional indications approved during the period of extension), as compensation for patent term lost during the regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug is eligible for the extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, and the application for the extension must be submitted prior to the expiration of the patent. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available for our patents, may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors and other third parties may be able to obtain approval of competing products following our patent expiration and take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. In the future, we may rely on licensing partners to pay these fees due to U.S. and non-U.S. patent agencies and to comply with these other requirements with respect to any future licensed patents and patent applications. While an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors and other third parties might be able to enter the market with similar or identical products of technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

While we have filed patent applications or obtained patents with respect to our four drug candidates, we also rely on proprietary know-how and trade secret protection and confidentiality agreements to protect proprietary know-how or trade secrets that are not patentable or that we elect not to patent. We seek to protect our trade secrets and proprietary know-how in part by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, consultants, independent contractors, advisors, contract manufacturers, CROs, hospitals, independent treatment centers, suppliers, collaborators and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary know-how. Additionally, our confidentiality agreements and other contractual protections may not be adequate to protect our intellectual property from unauthorized disclosure, third-party infringement or misappropriation. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or

information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our business, financial condition, results of operations and prospects our business and competitive position could be materially harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products similar to any drug candidates we may develop or utilize similarly related technologies that are not covered by the claims of the patents that we may license or may own in the future;
- we, or any future license partners or current or future collaborators, might not have been the first to make the inventions covered by the patent or pending patent application that we license or may own in the future;
- we, or any future license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating any of our owned or licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to patents;
- patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

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

We are highly dependent on the development and managerial expertise of Athena Countouriotis, M.D., our President and Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time.

Our industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive pharmaceuticals industry depends upon our ability to attract, retain and motivate highly skilled and experienced personnel with scientific, clinical, regulatory, manufacturing and management skills and experience. We conduct our operations in the greater San Diego area, a region that is home to many other pharmaceutical companies as well as many academic and research institutions, resulting in fierce competition for qualified personnel. We may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among pharmaceutical companies. Many of the other pharmaceutical companies against which we compete have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Our competitors may provide higher compensation, more diverse opportunities and/or better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high

quality personnel, which could negatively affect our ability to successfully develop and commercialize our drug candidates and to grow our business and operations as currently contemplated.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.*

As of March 31, 2022, we had 248 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, clinical operations, manufacturing, regulatory affairs, commercial and, if any of our drug candidates receives marketing approval, sales, marketing and distribution. To manage our 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. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth and with developing sales, marketing and distribution infrastructure, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources.

If we are not able to effectively manage growth and expand our organization, we may not be able to successfully implement the tasks necessary to further develop and commercialize repotrectinib, our other pipeline drug candidates or any future drug candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our internal information technology systems, or those of our third-party CROs or other vendors, contractors or consultants, may fail or suffer security breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.*

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect and otherwise process personal data and other confidential information, including proprietary business information, trade secrets, intellectual property, and data we collect about trial participants in connection with clinical trials, and sensitive third-party data. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party CROs, vendors, and other contractors and consultants who have access to our confidential information. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third-party CROs, vendors and other contractors and consultants are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security incidents or breaches from inadvertent or intentional actions by our employees, third-party CROs, vendors, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, supply chain attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure, or that of our third-party CROs, vendors and other contractors and consultants, or lead to data leakage. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We may not be able to anticipate all types of security threats, nor may we 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. Changes in how our employees work and access our systems during the current COVID-19 pandemic could lead to additional opportunities for bad actors to launch cyber-attacks or for employees to cause inadvertent security risks or incidents. To the extent that any accidental or intentional disruption or security breach were to result in a material loss of, or damage to, our data or applications, or those of our third-party CROs, vendors and other contractors and consultants, or inappropriate disclosure of confidential or proprietary information, we could incur liability and reputational damage and the further development and commercialization of repotrectinib or any other drug candidates could be delayed. The costs related to significant security breaches or disruptions could be material and exceed the limits of the cybersecurity insurance we maintain against such risks. The effects of a security breach or disruption could be further amplified during the current COVID-19 pandemic. If the information technology systems of our third-party CROs, vendors and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature

from occurring. Ransomware attacks, including by organized criminal threat actors, nation-states, and nation-state-supported actors, are becoming increasingly prevalent and severe – particularly for companies like ours that are engaged in critical infrastructure or manufacturing – and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Similarly, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain or our third-party partners' supply chains have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third-party information technology systems that support us.

While we have not experienced any such system failure, accident or security breach to date, we cannot guarantee that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems, or those of our third-party CROs, vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, or those of our third-party CROs, vendors and other contractors and consultants, it could result in a material disruption of our programs and the development of our drug candidates could be delayed. In addition, the loss of clinical trial data for repotrectinib or any other drug candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or those of our third-party CROs, vendors and other contractors and consultants, or security breaches could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the inability to access, confidential information (including trade secrets or other intellectual property, proprietary business information and personal data), which could result in government enforcement actions (for example, investigations, fines, penalties, audits, and inspections) and financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal data, including personal data regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal data, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our company is located in San Diego, California, an area prone to wildfires and earthquakes. These and other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. Any disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Unused U.S. federal net operating losses for the tax years beginning before January 1, 2018, will carry forward to offset future taxable income, if any, until such unused losses expire. Under current law, unused U.S. federal net operating losses generated in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely but the deductibility of such federal net operating losses in taxable years beginning after December 31, 2020, is limited to 80% of taxable income. In addition, both our current and our future unused losses and other tax attributes may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in our equity ownership by certain stockholders over a three-year period. We have experienced ownership changes in the past and we may also experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of net operating losses or other tax attributes is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use all or a material portion of our net operating losses and other tax attributes, which could adversely affect our future cash flows.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, businesses or assets and out-licensing or in-licensing of products, drug candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near term or long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, drug candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations, systems and personnel of any acquired businesses with our operations, systems and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Our portfolio of marketable securities is subject to market, interest and credit risk that may reduce its value.*

The value of our investments may decline due to increases in interest rates, downgrades of the bonds and other securities included in our portfolio and instability in the global financial markets that reduces the liquidity of securities included in our portfolio. In addition, the COVID-19 pandemic and ongoing geopolitical events have and may continue to adversely affect the financial markets in some or all countries worldwide. Each of these events may cause us to record charges to reduce the carrying value of our investment portfolio or sell investments for less than our acquisition cost. Although we attempt to mitigate these risks through diversification of our investments and continuous monitoring of our portfolio's overall risk profile, the value of our investments may nevertheless decline.

Our employees, clinical trial investigators, CROs, consultants, vendors and any potential commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, clinical trial investigators, CROs, consultants, vendors and any potential commercial partners. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA regulations or those of comparable foreign regulatory authorities, including those laws that require the reporting of true, complete and accurate information, (ii) manufacturing standards, (iii) federal and state health and data privacy, security, fraud and abuse, government price reporting, transparency reporting requirements, and other healthcare laws and regulations in the United States and abroad, (iv) sexual harassment and other workplace misconduct, or (v) laws that require the true, complete and accurate reporting of financial information or data. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We maintain a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or person performing similar functions, as well as a disclosure program and other applicable policies and procedures, 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 comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional integrity reporting and oversight obligations, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Common Stock

*The trading price of our common stock has been and may in the future be volatile and fluctuate substantially, which could result in substantial losses.**

Our stock price is volatile. For example, the closing price of our common stock since April 17, 2019 through March 31, 2022, has ranged from a low of \$24.73 to a high of \$141.30. The stock market in general and the market for smaller pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- the degree of success of competitive products or technologies;
- the commencement, enrollment or results of clinical trials and preclinical studies of our drug candidates or those of our competitors;
- adverse results from, delays in or termination of clinical trials;
- unanticipated serious safety concerns related to the use of our product candidates;
- regulatory or legal developments in the United States and other countries;
- any delay in our regulatory filings for our drug candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- receipt of, or failure to obtain, regulatory approvals;
- lower than expected market acceptance of our product candidates following approval, if any, for commercialization;
- 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 drug candidates or clinical development programs;
- the results of our efforts to design, develop, acquire or in-license additional technologies or drug candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- variations in our financial results or those of companies that are perceived to be similar to us;
- rumors or announcements regarding transactions involving our company or drug candidates;

- proposed changes to healthcare laws in the United States or foreign jurisdictions, or speculation regarding such changes, such as changes in the structure of healthcare payment systems;
- market conditions or trends in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, other events or factors, many of which are beyond our control, such as the COVID-19 outbreak and ongoing geopolitical events; and
- the other events or factors, including those described in this “Risk Factors” section.

Delaware law and provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in our control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that our board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least 66-2/3% of the voting power of all of our then-outstanding common stock;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder’s notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the chair of our board of directors, our Chief Executive Officer or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court’s having personal jurisdiction over the indispensable parties named as defendants. These provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and

state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims.

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 66-2/3% of our then-outstanding common stock.

In addition, as a Delaware corporation, we are subject to Section 203 of the Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer or proxy contest involving our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value in a corporate transaction.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants, the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf, (ii) any action or proceeding asserting a breach of fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders, (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees arising out of or pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware and (vi) any action asserting a claim against us or any of our directors, officers or other employees that is governed by the internal affairs doctrine. These provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims.

These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees and may discourage these types of lawsuits. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could seriously harm our business.

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

As a public company we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global 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. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain and maintain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.

We are required to comply with certain aspects of Section 404 of the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to, among other things, conduct an annual review and evaluation of their internal controls over financial reporting. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that requires frequent evaluation. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

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

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. In addition, the terms of any future debt agreements we may enter into may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Biden administration and Congress have proposed various changes, which if enacted could have a material impact on our business, cash flow, financial condition, or results of operations. In addition, it is uncertain if and to what extent various states will conform to federal tax laws. Future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

General Risk Factors

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our common stock price and trading volume to decline.

Our business could be negatively affected as a result of actions of activist stockholders, and such activism could impact the trading value of our securities.

Stockholders may, from time to time, engage in proxy solicitations or advance stockholder proposals, or otherwise attempt to effect changes and assert influence on our board of directors and management. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition. A proxy contest would require us to incur significant legal and advisory fees, proxy solicitation expenses and administrative and associated costs and require significant time and attention by our board of directors and management, diverting their attention from the pursuit of our business strategy. Any perceived uncertainties as to our future direction and control, our ability to execute on our strategy, or changes to the composition of our board of directors or senior management team arising from a proxy

contest could lead to the perception of a change in the direction of our business or instability which may result in the loss of potential business opportunities, make it more difficult to pursue our strategic initiatives, or limit our ability to attract and retain qualified personnel and business partners, any of which could adversely affect our business and operating results. If individuals are ultimately elected to our board of directors with a specific agenda, it may adversely affect our ability to effectively implement our business strategy and create additional value for our stockholders. We may choose to initiate, or may become subject to, litigation as a result of the proxy contest or matters arising from the proxy contest, which would serve as a further distraction to our board of directors and management and would require us to incur significant additional costs. In addition, actions such as those described above could cause significant fluctuations in our stock price based upon temporary or speculative market perceptions or other factors that do not necessarily reflect the underlying fundamentals and prospects of our business.

We could be subject to securities class action litigation.

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

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

None

Item 3. Defaults Upon Senior Securities.

None

Item 4. Mine Safety Disclosures.

Not applicable

Item 5. Other Information.

None

Item 6. Exhibits.

Furnish the exhibits required by Item 601 of Regulation S-K (§ 229.601 of this chapter).

Exhibit Number	Description
3.1	<u>Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38871), filed with the SEC on April 22, 2019).</u>
3.2	<u>Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-38871), filed with the SEC on April 22, 2019).</u>
4.1	<u>Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-230428), filed with the SEC on April 8, 2019).</u>
10.1†	<u>Transition Consulting Agreement, dated February 16, 2022, by and between the Registrant and Annette North (incorporated by reference to Exhibit 10.28 to the Registrant's Annual Report on Form 10-K (File No. 001-38871), filed with the SEC on February 28, 2022).</u>
10.2†	<u>Executive Employment Agreement, dated March 25, 2022, by and between the Registrant and Brian Sun, M.S., J.D.</u>
10.3†	<u>Non-Employee Director Compensation Policy, as amended</u>
10.4	<u>First Amendment to Lease, dated October 28, 2021, by and between the Registrant and HCP Callan Road, LLC.</u>
31.1	<u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
31.2	<u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
32.1*	<u>Certification of Principal Executive Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2*	<u>Certification of Principal Financial Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
101.INS	XBRL Instance Document - The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)
†	Indicates management contract or compensatory plan.
*	This certification shall not be deemed filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that Section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

SIGNATURES

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

TURNING POINT THERAPEUTICS, INC.

Date: May 10, 2022

By: _____
/s/ Athena Countouriotis
Athena Countouriotis, M.D.
President & Chief Executive Officer
(Principal Executive Officer)

Date: May 10, 2022

By: _____
/s/ Paolo Tombesi
Paolo Tombesi
Executive Vice President & Chief Financial Officer (Principal
Financial Officer)

TURNING POINT THERAPEUTICS, INC.
EXECUTIVE EMPLOYMENT AGREEMENT
for
Brian Sun

This Executive Employment Agreement (this “**Agreement**”), is made and entered into as of 25-March-2022, by and between Brian Sun (“**Executive**”) and Turning Point Therapeutics, Inc. (the “**Company**”).

WHEREAS, the Company desires for Executive to provide services to the Company, and wishes to provide Executive with certain compensation and benefits in return for such employment services; and

WHEREAS, Executive wishes to be employed by the Company and to provide personal services to the Company in return for certain compensation and benefits.

NOW, THEREFORE, in consideration of the mutual promises and covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree as follows:

1. Employment by the Company.

1.1 Position. Executive shall serve as the Company’s Senior Vice President & General Counsel, reporting to Athena Countouriotis, M.D., the Company’s President & CEO (the “**CEO**”). Executive’s commencement of employment with the Company will be on or before April 11, 2022 (such actual date of commencement of employment with the Company, the “**Start Date**”). During the term of Executive’s employment with the Company, Executive will devote Executive’s best efforts and substantially all of Executive’s business time and attention to the business of the Company, except for approved vacation periods and reasonable periods of illness or other incapacities permitted by the Company’s general employment policies.

1.2 Duties and Location. Executive shall perform such duties as are customarily associated with the position of Senior Vice President & General Counsel and such other duties as are assigned to Executive by the CEO. Executive’s primary office location shall be the Company’s headquarters located in San Diego, California. Subject to the terms of this Agreement, the Company reserves the right to reasonably require Executive to perform Executive’s duties at places other than Executive’s primary office location from time to time and to require reasonable business travel.

1.3 Policies and Procedures. The employment relationship between the parties shall be governed by the general employment policies and practices of the Company, except that when the terms of this Agreement differ from or are in conflict with the Company’s general employment policies or practices, this Agreement shall control.

2. Compensation.

2.1 Base Salary. For services to be rendered hereunder, Executive shall receive a base salary at the rate of \$445,000 per year (the “**Base Salary**”), less standard payroll deductions and withholdings and payable in accordance with the Company’s regular payroll schedule.

2.2 Annual Bonus. Executive will be eligible for an annual discretionary bonus (the “**Annual Bonus**”) of up to 40% of Executive’s then current annual Base Salary (the “**Target Bonus Amount**”). Whether Executive receives an Annual Bonus for any given year, and the amount of any such Annual Bonus, will be determined in the good faith discretion of the Company’s Board of Directors (the “**Board**”) (or the Compensation Committee thereof) and the CEO, based upon the Company’s and Executive’s achievement of corporate and individual objectives and milestones to be determined on an annual basis by the Board (or Compensation Committee thereof). No Annual Bonus is guaranteed and, in addition to the other conditions for earning such compensation, Executive must remain an employee in good standing of the Company on the scheduled Annual Bonus payment date in order to be eligible for any Annual Bonus. Executive’s Annual Bonus for 2022, if any, will be pro-rated based upon the portion of 2022 that Executive is employed by the Company.

3. Standard Company Benefits. Executive shall, in accordance with Company policy and the terms and conditions of the applicable Company benefit plan documents, be eligible to participate in the benefit and fringe benefit programs provided by the Company to its executive officers and other employees from time to time. Any such benefits shall be subject to the terms and conditions of the governing benefit plans and policies and may be changed by the Company in its discretion. As an executive at the Company, Executive will be eligible to take paid time off (“**PTO**”) under the Company’s Discretionary PTO Policy (the “**Discretionary PTO Policy**”). Under the Discretionary PTO Policy, Executive does not accrue PTO. Rather, Executive is permitted to use discretion in achieving an appropriate work/life balance by taking time off as needed and consistent with job demands. There is no set minimum or maximum amount of time off that may be taken in a given year, however Executive must obtain prior approval from the CEO before taking PTO, except for absences that qualify under state and local paid sick leave laws. Although there is no limit on the amount of time that may be taken under the Discretionary PTO Policy, Executive is expected to exercise this right responsibly and continue to satisfy all professional obligations. Neglect of professional obligations may result in disciplinary action, up to and including termination of employment.

4. Expenses. The Company will reimburse Executive for reasonable travel, entertainment or other expenses incurred by Executive in furtherance or in connection with the performance of Executive’s duties hereunder, in accordance with the Company’s expense reimbursement policy as in effect from time to time.

5. Equity Awards. Subject to approval by the Board, Executive shall be granted (i) an option to purchase 195,000 shares of Common Stock of the Company at the fair market value on the date of grant (the “**Option**”) and (ii) a restricted stock unit award for 45,000 shares of Common Stock of the Company (the “**RSU**”). The Option shall be governed in all respects by the terms of the governing equity plan documents and option agreement between Executive and the Company and shall be subject to a vesting schedule whereby 25% of the shares subject to the Option shall vest on the first anniversary of the Start Date, with the remaining shares vesting in equal monthly

installments over the following three years thereafter, subject to Executive's continuous service through such vesting date. The RSU shall be governed in all respects by the terms of the governing equity plan documents and restricted stock unit agreements between Executive and the Company. The RSU shall vest in four equal annual installments, subject to Executive's continuous service through such vesting date.

6. Proprietary Information Obligations.

6.1 Proprietary Information Agreement. Executive shall execute, and will abide by, the Company's standard Invention Disclosure and Confidentiality and Proprietary Rights Agreement ("**Proprietary Agreement**").

6.2 Third-Party Agreements and Information. Executive represents and warrants that Executive's employment by the Company does not conflict with any prior employment or consulting agreement or other agreement with any third party, and that Executive will perform Executive's duties to the Company without violating any such agreement. Executive represents and warrants that Executive does not possess confidential information arising out of prior employment, consulting, or other third-party relationships, that would be used in connection with Executive's employment by the Company, except as expressly authorized by that third party. During Executive's employment by the Company, Executive will use in the performance of Executive's duties only information that is generally known and used by persons with training and experience comparable to Executive's own, common knowledge in the industry, otherwise legally in the public domain, or obtained or developed by the Company or by Executive in the course of Executive's work for the Company.

7. Outside Activities and Non-Competition During Employment.

7.1 Outside Activities. Throughout Executive's employment with the Company, Executive may engage in civic and not-for-profit activities so long as such activities do not interfere with the performance of Executive's duties hereunder or present a conflict of interest with the Company or its affiliates. Subject to the restrictions set forth herein, and only with prior written disclosure to and consent of the Board, Executive may engage in other types of business or public activities. The Board may rescind such consent, if the Board determines, in its sole discretion, that such activities compromise or threaten to compromise the Company's or its affiliates' business interests or conflict with Executive's duties to the Company or its affiliates.

7.2 Non-Competition During Employment. Except as otherwise provided in this Agreement and except for any Board position held by Executive as of the date of this Agreement, during Executive's employment by the Company, Executive will not, without the express written consent of the Board, directly or indirectly serve as an officer, director, stockholder, employee, partner, proprietor, investor, joint ventures, associate, representative or consultant of any person or entity engaged in, or planning or preparing to engage in, business activity competitive with any line of business engaged in (or planned to be engaged in) by the Company or its affiliates; provided, however, that Executive may purchase or otherwise acquire up to (but not more than) 1% of any class of securities of any enterprise (without participating in the activities of such enterprise) if such securities are listed on any national or regional securities exchange. In addition, Executive will be subject to certain restrictions (including restrictions continuing after Executive's employment ends) under the terms of the Proprietary Agreement.

8. Termination of Employment; Severance and Change in Control Benefits.

8.1 At-Will Employment. Executive's employment relationship is at-will. Either Executive or the Company may terminate the employment relationship at any time, with or without Cause (as defined in the Severance Plan) or advance notice.

8.2 Covered Termination Unrelated to Change in Control. In the event Executive's employment with the Company is terminated due to a Covered Termination (as defined in the Severance Plan) at any time except during the Change in Control Protection Period (as defined in the Severance Plan), then Executive shall be entitled to the benefits (the "**Severance Benefits**") provided under, and subject to the terms and conditions of, the Severance Plan, subject to Executive's compliance with the terms and conditions of the Severance Plan, including but not limited to Executive's execution (and non-revocation) of a general release of claims in a form reasonably satisfactory to the Company (the "**Release Requirement**").

8.3 Covered Termination During Change in Control Protection Period. In the event Executive's employment with the Company is terminated due to a Covered Termination during the Change in Control Protection Period, then in lieu of (and not additional to) the Severance Benefits described in Section 9.2, Executive shall be entitled to the benefits (the "**Change in Control Benefits**") provided under, and subject to the terms and conditions of, the Severance Plan, including the Release Requirement.

8.4 Termination for Cause; Resignation without Good Reason; Death or Disability. Executive will not be eligible for, or entitled to any severance benefits, including (without limitation) the Severance Benefits and Change in Control Benefits listed in Sections 9.2 and 9.3 above and stated under the Severance Plan, if the Company terminates Executive's employment for Cause, if Executive resigns his employment without Good Reason, or Executive's employment terminates due to Executive's death or disability.

9. Arbitration and Dispute Resolution. To ensure the rapid and economical resolution of disputes that may arise in connection with Executive's employment with the Company, Executive and the Company agree that any and all disputes, claims, or causes of action, in law or equity, including but not limited to statutory claims, arising from or relating to the enforcement, breach, performance, or interpretation of this Agreement, Executive's employment with the Company, or the termination of Executive's employment from the Company, will be resolved pursuant to the Federal Arbitration Act, 9 U.S.C. §1-16, and to the fullest extent permitted by law, by final, binding and confidential arbitration conducted in San Diego, California in accordance with the then-current Employment Arbitration and Mediation Procedures of the American Arbitration Association ("**AAA**") or its successors, (which can be found at <http://www.adr.org/employment>, and which will be provided to Executive on request). In addition, all claims, disputes, or causes of action under this Section, whether by Executive or the Company, must be brought in an individual capacity, and shall not be brought as a plaintiff (or claimant) or class member in any purported class or representative proceeding, nor joined or consolidated with the claims of any other person or entity. The arbitrator may not consolidate the claims of more than one person or entity and may not preside over any form of representative or class proceeding. To the extent that the preceding sentences regarding class claims or proceedings are found to violate applicable law or are otherwise found unenforceable, any claim(s) alleged or brought on behalf of a class shall proceed in a court of law rather than by arbitration. This Section shall not

apply to any action or claim that cannot be subject to mandatory arbitration as a matter of law, including, without limitation, claims brought pursuant to the California Private Attorneys General Act of 2004, as amended, the California Fair Employment and Housing Act, as amended, and the California Labor Code, as amended, to the extent such claims are not permitted by applicable law(s) to be submitted to mandatory arbitration and the applicable law(s) are not preempted by the Federal Arbitration Act or otherwise invalid (collectively, the “**Excluded Claims**”). In the event Executive intends to bring multiple claims, including one of the Excluded Claims listed above, the Excluded Claims may be filed with a court, while any other claims will remain subject to mandatory arbitration. Executive will have the right to be represented by legal counsel at any arbitration proceeding. Questions of whether a claim is subject to arbitration under this agreement shall be decided by the arbitrator. Likewise, procedural questions which grow out of the dispute and bear on the final disposition are also matters for the arbitrator. The arbitrator shall: (a) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be permitted by law; and (b) issue a written arbitration decision, setting forth the award, if any, and explaining the basis therefor. Executive and the Company shall be entitled to all rights and remedies that either would be entitled to pursue in a court of law. **Both Executive and the Company acknowledge that by agreeing to this arbitration procedure, they waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding.** The Company shall pay all filing fees in excess of those which would be required if the dispute were decided in a court of law and shall pay the arbitrator’s fee. Nothing in this Agreement is intended to prevent either the Company or Executive from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration.

10. General Provisions.

10.1 Notices. Any notices provided must be in writing and will be deemed effective upon the earlier of personal delivery (including personal delivery by fax) or the next day after sending by overnight carrier, to the Company at its primary office location and to Executive at the address as listed on the Company payroll.

10.2 Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal or unenforceable in any respect under any applicable law or rule in any jurisdiction, such invalidity, illegality or unenforceability will not affect any other provision or any other jurisdiction, but this Agreement will be reformed, construed and enforced in such jurisdiction to the extent possible in keeping with the intent of the Parties.

10.3 Waiver. Any waiver of any breach of any provisions of this Agreement must be in writing to be effective, and it shall not thereby be deemed to have waived any preceding or succeeding breach of the same or any other provision of this Agreement.

10.4 Complete Agreement. This Agreement, together with the Severance Plan and the Proprietary Agreement, constitutes the entire agreement between Executive and the Company with regard to the subject matter hereof and is the complete, final, and exclusive embodiment of the Company’s and Executive’s agreement with regard to this subject matter. This Agreement is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other such promises, warranties or

representations. It cannot be modified or amended except in a writing signed by a duly authorized officer of the Company, with the exception of those changes expressly reserved to the Company's discretion in this Agreement.

10.5 Counterparts. This Agreement may be executed in separate counterparts, any one of which need not contain signatures of more than one party, but both of which taken together will constitute one and the same Agreement.

10.6 Headings. The headings of the paragraphs hereof are inserted for convenience only and shall not be deemed to constitute a part hereof nor to affect the meaning thereof.

10.7 Successors and Assigns. This Agreement is intended to bind and inure to the benefit of and be enforceable by Executive and the Company, and their respective successors, assigns, heirs, executors and administrators, except that Executive may not assign any of Executive's duties hereunder and Executive may not assign any of Executive's rights hereunder without the written consent of the Company, which shall not be withheld unreasonably.

10.8 Tax Withholding. All payments and awards contemplated or made pursuant to this Agreement will be subject to withholdings of applicable taxes in compliance with all relevant laws and regulations of all appropriate government authorities. Executive acknowledges and agrees that the Company has neither made any assurances nor any guarantees concerning the tax treatment of any payments or awards contemplated by or made pursuant to this Agreement. Executive has had the opportunity to retain a tax and financial advisor and fully understands the tax and economic consequences of all payments and awards made pursuant to this Agreement.

10.9 Non-Solicitation. Executive agrees that for the one year period after the date Executive's employment ends, Executive will not, as an officer, director, employee, consultant, owner, partner, or in any other capacity, either directly or through others, solicit, induce, encourage, or participate in soliciting, inducing or encouraging any employee, consultant, or independent contractor of the Company to terminate his, his or its relationship with the Company or its affiliates, even if Executive did not initiate the discussion or seek out the contact.

10.10 Non-disparagement. Executive agrees not to disparage the Company and its affiliates, and the Company's and its affiliates' officers, directors, employees, shareholders, investors and agents, in any manner likely to be harmful to them or their business, business reputation or personal reputation; provided that Executive may respond accurately and fully to any question, inquiry or request for information when required by legal process or as part of a government investigation. Notwithstanding the foregoing, nothing herein shall limit Executive's right to voluntarily communicate with the Equal Employment Opportunity Commission, United States Department of Labor, the National Labor Relations Board, the Securities and Exchange Commission, other federal government agency or similar state or local agency or to discuss the terms and conditions of Executive's employment with others to the extent expressly permitted by Section 7 of the National Labor Relations Act.

10.11 Choice of Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the laws of the State of California.

IN WITNESS WHEREOF, the parties have executed this Agreement on the day and year first written above.

TURNING POINT THERAPEUTICS, INC.

By: /s/Athena Countouriotis
Athena Countouriotis, M.D.
Chief Executive Officer

EXECUTIVE

/s/ Brian Sun
Brian Sun

TURNING POINT THERAPEUTICS, INC.
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY
ADOPTED: APRIL 5, 2019
AS AMENDED: MARCH 24, 2022

Each member of the Board of Directors (the “**Board**”) of Turning Point Therapeutics, Inc. (the “**Company**”) who is a non-employee director of the Company (each such member, a “**Non-Employee Director**”) will receive the compensation described in this Non-Employee Director Compensation Policy (the “**Director Compensation Policy**”) for his or her Board service.

The Director Compensation Policy may be amended at any time in the sole discretion of the Board or the Compensation Committee of the Board.

A Non-Employee Director may decline all or any portion of his or her compensation by giving notice to the Company prior to the date cash is to be paid or equity awards are to be granted, as the case may be.

Annual Cash Compensation

Each Non-Employee Director will receive the cash compensation set forth below for service on the Board. The annual cash compensation amounts will be payable in equal quarterly installments, in arrears following the end of each quarter in which the service occurred, pro-rated for any partial months of service. All annual cash fees are vested upon payment.

1. Annual Board Service Retainer:
 - a. All Eligible Directors: \$40,000
 2. Annual Board Chair Service Retainer (in lieu of Board Service Retainer):
 - a. Chair of the Board: \$70,000
 3. Annual Committee Member Service Retainer:
 - a. Member of the Audit Committee: \$10,000
 - b. Member of the Compensation Committee: \$7,500
 - c. Member of the Nominating and Corporate Governance Committee: \$5,000
 - d. Member of the Corporate Strategy Committee: \$7,500
 4. Annual Committee Chair Service Retainer (in lieu of Committee Member Service Retainer):
 - a. Chair of the Audit Committee: \$20,000
 - b. Chair of the Compensation Committee: \$15,000
 - c. Chair of the Nominating and Corporate Governance Committee: \$10,000
 - d. Chair of the Corporate Strategy Committee: \$15,000
- 1.

Equity Compensation

Equity awards will be granted under the Company's 2019 Equity Incentive Plan (the "**Plan**"). All stock options granted under this policy will be Nonstatutory Stock Options (as defined in the Plan), with a term of ten years from the date of grant and an exercise price per share equal to 100% of the Fair Market Value (as defined in the Plan) of the underlying common stock of the Company on the date of grant.

Automatic Equity Grants.

(i)Initial Grant for New Directors. Without any further action of the Board, each person who is elected or appointed for the first time to be a Non-Employee Director will automatically, upon the date of his or her initial election or appointment to be a Non-Employee Director (or, if such date is not a market trading day, the first market trading day thereafter), be granted a Nonstatutory Stock Option to purchase shares of common stock of the Company with an aggregate grant date fair value equal to \$800,000 (the "**Initial Option Grant**"). Each Initial Option Grant will vest in a series of 36 successive equal monthly installments over the three-year period measured from the date of grant.

(ii)Annual Grant. Without any further action of the Board, at the close of business on the date of each annual meeting of the Company's stockholders (each such annual meeting, an "**Annual Meeting**"), each person who is then a Non-Employee Director (other than any Non-Employee Director elected to the Board at such Annual Meeting) will automatically be granted a Nonstatutory Stock Option to purchase shares of common stock of the Company with an aggregate grant date fair value equal to \$400,000 (the "**Annual Option Grant**"); provided, however, that the Annual Option Grant granted to any Non-Employee Director that was appointed to the Board following the prior year's Annual Meeting and prior to the current year's Annual Meeting shall be pro-rated based on the number of days served on the Board by such Non-Employee Director prior to the current year's Annual Meeting divided by 365. Each Annual Option Grant will vest on the one-year anniversary of the date of grant.

Vesting; Change in Control. All vesting is subject to the Non-Employee Director's "**Continuous Service**" (as defined in the Plan) on each applicable vesting date. Notwithstanding the foregoing vesting schedules, for each Non-Employee Director who remains in Continuous Service with the Company until immediately prior to the closing of a "**Change in Control**" (as defined in the Plan), the shares subject to his or her then-outstanding equity awards that were granted pursuant to this policy will become fully vested immediately prior to the closing of such Change in Control.

Remaining Terms. The remaining terms and conditions of each award, including transferability, will be as set forth in the Company's Director Option Grant Package in the form adopted from time to time by the Board.

Compensation Limit

Notwithstanding anything to the contrary herein, the aggregate value of all compensation granted or paid, as applicable, to any individual for service as a Non-Employee Director with respect to any calendar year, including Initial Option Grants and Annual Option Grants granted and cash fees paid by the Company to such Non-Employee Director, will not exceed (i) \$500,000 in total value or (ii) in the event such Non-Employee Director is first appointed or elected to the Board during such calendar year, \$1,000,000 in total value, in each case calculating the value of any equity awards based on the grant date fair value of such equity awards for financial reporting purposes (the “**Compensation Limit**”). The Company shall have the sole discretion to reduce any compensation contemplated hereunder in order to comply with the Compensation Limit.

Expenses

The Company will reimburse Non-Employee Director for ordinary, necessary and reasonable out-of-pocket travel expenses to cover in-person attendance at and participation in Board and committee meetings; *provided*, that the Non-Employee Director timely submit to the Company appropriate documentation substantiating such expenses in accordance with the Company’s travel and expense policy, as in effect from time to time.

3.

FIRST AMENDMENT TO LEASE

This FIRST AMENDMENT TO LEASE ("**First Amendment**") is made and entered into as of August 31, 2021 (the "**Effective Date**"), by and between HCP CALLAN ROAD, LLC, a Delaware limited liability company ("**Landlord**"), and TURNING POINT THERAPEUTICS, INC., a Delaware corporation ("**Tenant**").

RECITALS:

A. Landlord and Tenant are parties to the Lease dated May 20, 2021 (the "**Lease**"), pursuant to which Landlord leases to Tenant and Tenant leases from Landlord the Premises consisting of the entirety of the building commonly known as Building A ("**Building A**") to be located at 3020/3030 Callan Road, San Diego, California 92121, and the building commonly known as Building B ("**Building B**") to be located at 3020/3030 Callan Road, San Diego, California 92121.

B. The parties desire to amend the Lease on the terms and conditions set forth in this First Amendment.

AGREEMENT:

NOW, THEREFORE, in consideration of the foregoing recitals and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. **Terms.** All capitalized terms when used herein shall have the same respective meanings as are given such terms in the Lease unless expressly provided otherwise in this First Amendment. As of the Effective Date, all references to the "**Lease**" in the Lease and in this First Amendment shall mean the Lease as modified by this First Amendment.

2. **Exhibit B – Work Letter.** Notwithstanding anything to the contrary in the Lease, (a) the following sentence is hereby added to the end of Section 2.2.2 of the Tenant Work Letter attached as **Exhibit B** to the Lease: "Landlord shall, upon Tenant's prior written request, pay disbursements of the Tenant Improvement Allowance, or any portion thereof, which is then due and approved by Landlord pursuant to the terms of the Tenant Work Letter, directly to the Contractor or any of the other Tenant's Agents, as directed by Tenant," and (b) Section 2.2.2.1(A) of the Tenant Work Letter attached as **Exhibit B** to the Lease shall be amended and restated in its entirety as follows: "(A) the amounts so requested by Tenant, as set forth in this Section 2.2.2.1, above, less a ten percent (10%) retention for amount being paid to the Contractor (the aggregate amount of such retentions to be known as the "**Final Retention**"), but such retention shall not be withheld from amounts being paid to any of the other Tenant's Agents, and"

3. **California Required Disclosures.** As required by Section 1938(e) of the California Civil Code, Landlord hereby states as follows: "A Certified Access Specialist (CASp) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises." In furtherance of the foregoing, Landlord and Tenant hereby agree as follows: (a) any CASp inspection requested by Tenant shall be conducted, at Tenant's sole cost and expense, by a CASp designated by Landlord, subject to Landlord's reasonable rules and requirements; (b) Tenant, at its sole cost and expense, shall be responsible for making any improvements or repairs within the Premises to correct violations of construction-related accessibility standards identified by such CASp inspection; and (c) if such CASp inspection requested by Tenant shall require any improvements or repairs to the Building or Project (outside the Premises) to correct violations of construction-related accessibility standards, then Tenant shall reimburse Landlord upon demand, as Additional Rent, for the cost to Landlord of performing such improvements or repairs.

4. **Broker.** Landlord and Tenant hereby warrant to each other that they have had no dealings with any real estate broker or agent in connection with the negotiation of this First Amendment, and that they know of no real estate broker or agent who is entitled to a commission in connection with this First Amendment. Each party agrees to indemnify and defend the other party against and hold the other party harmless from and against any and all claims, demands, losses, liabilities, lawsuits, judgments, and costs and expenses (including, without limitation, reasonable attorneys' fees) with respect to any leasing commission or equivalent compensation alleged to be owing on account of the indemnifying party's dealings with any real estate broker or agent, occurring by, through, or under the indemnifying party. The terms of this Section 4 shall survive the expiration or earlier termination of the term of the Lease, as hereby amended.

5. **Counterparts.** This First Amendment may be executed in counterparts with the same effect as if both parties hereto had executed the same document. Both counterparts shall be construed together and shall constitute a single document. Signatures of the parties transmitted by electronic mail PDF format shall be deemed to constitute originals and may be relied upon, for all purposes, as binding the transmitting party hereto. The parties intend to be bound by the signatures transmitted by electronic mail PDF format, are aware that the other party will rely on such signature, and hereby waive any defenses to the enforcement of the terms of this First Amendment based on the form of signature. At the request of either party, an original of any such PDF scanned document transmitted via email is to be sent to such requesting party.

6. **No Further Modification.** Except as specifically set forth in this First Amendment, all of the terms and provisions of the Lease shall remain unmodified and in full force and effect.

[SIGNATURES FOLLOW ON NEXT PAGE]

STYLEREF zExhibitLabel

* MERGEFORMAT

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IN WITNESS WHEREOF, this First Amendment has been executed as of the day and year first above written.

"LANDLORD"

HCP CALLAN ROAD, LLC,
a Delaware limited liability company

By: _____
Name: _____
Its:

By: _____
Name: _____
Its:

"TENANT"

TURNING POINT THERAPEUTICS, INC.,
a Delaware corporation

By: __
Name: __
Its:

By __
Name: __
Its:

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Athena Countouriotis, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Turning Point Therapeutics, 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: May 10, 2022

By: _____
/s/ Athena Countouriotis
Athena Countouriotis, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Paolo Tombesi, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Turning Point Therapeutics, 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.
-

**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 the Quarterly Report of Turning Point Therapeutics, Inc. (the "Company") on Form 10-Q for the period ended March 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; 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: May 10, 2022

By: _____
/s/ Athena Countouriotis
Athena Countouriotis, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

This certification accompanies the Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.

**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 the Quarterly Report of Turning Point Therapeutics, Inc. (the "Company") on Form 10-Q for the period ended March 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; 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: May 10, 2022

By: _____ /s/ Paolo Tombesi
Paolo Tombesi
Executive Vice President & Chief Financial Officer
(Principal Financial Officer)

This certification accompanies the Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.
