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, 2021

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: 001-39512

Metacrine, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**47-2297384**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3985 Sorrento Valley Blvd., Suite C San Diego, California	**92121**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (858) 369-7800

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court. Yes ☒ No ☐

The number of outstanding shares of the registrant's common stock on May 6, 2021 was 26,423,153.

Metacrine, Inc.

Table of Contents

PART I—FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Metacrine, Inc.

Unaudited Condensed Consolidated Balance Sheets
(In thousands, except par value and share amounts)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 19,457	$ 24,393
Short-term investments	65,000	71,783
Prepaid expenses and other current assets	6,257	5,847
Total current assets	90,714	102,023
Property and equipment, net	555	634
Operating lease right-of-use asset	1,415	1,579
Total assets	$ 92,684	$ 104,236
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 325	$ 334
Accrued liabilities	4,149	2,951
Current portion of operating lease liability	762	741
Total current liabilities	5,236	4,026
Operating lease liability, net of current portion	810	1,007
Long-term debt, net of debt discount	9,434	9,372
Other long-term liabilities	544	552
Commitments and contingencies (Note 3)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; authorized shares - 10,000,000 at March 31, 2021 and December 31, 2020, respectively; issued and outstanding shares - none at March 31, 2021 and December 31, 2020, respectively.	-	-
Common stock, $0.0001 par value; authorized shares – 200,000,000 at March 31, 2021 and December 31, 2020, respectively; issued shares – 26,234,612 and 26,005,934 at March 31, 2021 and December 31, 2020, respectively; outstanding shares – 26,209,327 and 25,969,442 at March 31, 2021 and December 31, 2020, respectively.	3	3
Additional paid-in-capital	212,172	210,021
Accumulated other comprehensive income (loss)	(1)	1
Accumulated deficit	(135,514)	(120,746)
Total stockholders' equity	76,660	89,279
Total liabilities and stockholders' equity	$ 92,684	$ 104,236

See accompanying notes to the unaudited condensed consolidated financial statements.

Metacrine, Inc.

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

	Three Months Ended March 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 10,857	$ 6,361
General and administrative	3,696	1,601
Total operating expenses	14,553	7,962
Loss from operations	(14,553)	(7,962)
Other income (expense):		
Interest income	36	229
Interest expense	(244)	(253)
Other expense	(7)	(126)
Total other income (expense)	(215)	(150)
Net loss	$ (14,768)	$ (8,112)
Other comprehensive loss:		
Unrealized loss on available-for-sale securities, net	(2)	(68)
Comprehensive loss	$ (14,770)	$ (8,180)
Net loss per share, basic and diluted	$ (0.57)	$ (3.23)
Weighted average shares of common stock outstanding, basic and diluted	26,007,692	2,509,319

See accompanying notes to the unaudited condensed consolidated financial statements.

Metacrine, Inc.

Unaudited Condensed Consolidated Statements of Cash Flows
(In thousands)

	Three Months Ended March 31,	
	2021	**2020**
Operating activities:		
Net loss	$ (14,768)	$ (8,112)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	79	68
Stock-based compensation	1,520	503
Non-cash interest expense	62	70
Amortization (accretion) of premiums/discounts on investments, net	170	(59)
Amortization of right-of-use asset	164	152
Change in fair value of warrant liability	-	106
Changes in operating assets and liabilities		
Prepaid expenses and other current assets	(410)	(6)
Accounts payable and accrued liabilities	1,189	(1,190)
Lease liability	(176)	(134)
Net cash used in operating activities	(12,170)	(8,602)
Investing activities:		
Purchases of property and equipment	-	(73)
Purchases of short-term investments	(12,784)	(7,944)
Sale and maturities of short-term investments	19,395	13,690
Net cash provided by investing activities	6,611	5,673
Financing activities:		
Proceeds from exercise of common stock options	623	3
Repurchase of unvested common stock	-	(2)
Payment of initial public offering costs	-	(10)
Net cash provided by (used in) financing activities	623	(9)
Net decrease in cash and cash equivalents	(4,936)	(2,938)
Cash and cash equivalents at beginning of period	24,393	15,668
Cash and cash equivalents at end of period	$ 19,457	$ 12,730
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 181	$ 183
Supplemental non-cash investing and financing activities:		
Issuance costs in accounts payable and accrued liabilities	$ -	$ 229
Change in unpaid property and equipment purchases	$ -	$ 69
Vesting of common stock	$ 8	$ 24

See accompanying notes to the unaudited condensed consolidated financial statements.

Metacrine, Inc.

Unaudited Condensed Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
For the Three Months Ended March 31, 2021 and 2020
(In thousands, except share amounts)

	Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
Balance at December 31, 2020	—	$ —	25,969,442	$ 3	$ 210,021	$ 1	$ (120,746)	$ 89,279
Stock-based compensation	—	—	—	—	1,520	—	—	1,520
Exercise of stock options	—	—	228,678	—	623	—	—	623
Vesting of early exercised stock options	—	—	11,207	—	8	—	—	8
Unrealized loss on investment securities	—	—	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	—	—	(14,768)	(14,768)
Balance at March 31, 2021	—	$ —	26,209,327	$ 3	$ 212,172	$ (1)	$ (135,514)	$ 76,660

	Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' deficit
Balance at December 31, 2019	85,093,688	$122,465	2,484,848	$ —	$ 5,164	$ 41	$ (83,442)	$ (78,237)
Stock-based compensation	—	—	—	—	503	—	—	503
Exercise of stock options	—	—	955	—	3	—	—	3
Vesting of early exercised stock options	—	—	48,766	—	24	—	—	24
Unrealized loss on investment securities	—	—	—	—	—	(68)	—	(68)
Net loss	—	—	—	—	—	—	(8,112)	(8,112)
Balance at March 31, 2020	85,093,688	$122,465	2,534,569	$ —	$ 5,694	$ (27)	$ (91,554)	$ (85,887)

See accompanying notes to the unaudited condensed consolidated financial statements.

Note 1. Organization and Summary of Significant Accounting Policies

Organization

Metacrine, Inc. (the "Company") was incorporated in the state of Delaware on September 17, 2014 and is based in San Diego, California. The Company is a clinical-stage biopharmaceutical company focused on building an innovative pipeline of differentiated drugs to treat liver and gastrointestinal diseases.

Principles of Consolidation and Basis of Presentation

In May 2019, the Company established a wholly-owned Australian subsidiary, Metacrine, Pty Ltd, in order to conduct various clinical activities for its product candidates. The unaudited condensed consolidated financial statements include the accounts of the Company and Metacrine, Pty Ltd. The functional currency of both the Company and Metacrine, Pty Ltd is the U.S. dollar. Assets and liabilities that are not denominated in the functional currency are remeasured into U.S. dollars at foreign currency exchange rates in effect at the balance sheet date except for nonmonetary assets, which are remeasured at historical foreign currency exchange rates in effect at the date of transaction. Net realized and unrealized gains and losses from foreign currency transactions and remeasurement are reported in other income (expense) in the unaudited condensed consolidated statements of operations and comprehensive loss. Intercompany accounts and transactions have been eliminated in consolidation.

The Company's unaudited condensed consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP") and applicable regulations of the U.S. Securities and Exchange Commission ("SEC"). The Company's unaudited condensed consolidated financial statements should be read in conjunction with the audited financial statements included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 filed on March 18, 2021. Certain amounts in the unaudited condensed consolidated financial statements have been reclassified to conform to their current year presentation.

Initial Public Offering

On September 18, 2020, the Company closed its initial public offering ("IPO") of 6,540,000 shares of common stock at a public offering price of $13.00 per share. The Company raised $76.9 million in net proceeds from the IPO after deducting underwriters' discounts and commissions of $6.0 million and issuance costs of $2.2 million.

Upon closing of the Company's IPO, all of the Company's outstanding preferred stock were automatically converted into 16,685,014 shares of common stock.

Liquidity and Capital Resources

From its inception through March 31, 2021, the Company has devoted substantially all its efforts to organizing and staffing, business planning, raising capital, researching, discovering and developing its pipeline in FXR and other drug targets, and general and administrative support for these operations and has funded its operations primarily with the net proceeds from the issuance of convertible preferred stock, common stock, and long-term debt. The Company has incurred net losses and negative cash flows from operations since inception and had an accumulated deficit of $135.5 million and $120.7 million as of March 31, 2021 and December 31, 2020, respectively. Management expects the Company will incur substantial operating losses for the foreseeable future in order to complete clinical trials and launch and commercialize any product candidates for which it receives regulatory approval. The Company will need to raise additional capital through a combination of equity offerings, debt financings, collaborations, and other similar arrangements. The Company's ability to raise additional capital may be adversely impacted by potential worsening of economic conditions in the United States and worldwide resulting from the COVID-19 pandemic. If the disruption persists and deepens, the Company could experience an inability to access additional capital. As of March 31, 2021, the Company had available cash, cash equivalents, and short-term investments of $84.5 million and working capital of $85.5 million to fund future operations. Management has prepared cash flow forecasts which indicate that, based on the Company's current cash resources available and working capital, the Company will have sufficient resources to fund its operations for at least one year after the date the financial statements are issued.

Use of Estimates

The preparation of the Company's unaudited condensed consolidated financial statements requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities. Significant estimates in the Company's unaudited condensed consolidated financial statements include accruals for research and development expenses and stock-based compensation. These estimates and assumptions are based on current facts, historical experience, and various other factors believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially and adversely from these estimates. To the extent there are material differences between the estimates and actual results, the Company's future results of operations will be affected.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less when purchased to be cash equivalents. Cash and cash equivalents include cash in readily available checking accounts, money market funds, and commercial paper. The carrying amounts reported in the unaudited condensed consolidated balance sheets for cash and cash equivalents are valued at cost, which approximates fair value.

Short-Term Investments

Short-term investments primarily consist of commercial paper, corporate debt securities, and U.S. government and agency bonds. The Company has classified these investments as available-for-sale securities, as the sale of such investments may be required prior to maturity to implement management strategies, and therefore has classified all short-term investments with maturity dates beyond three months at the date of purchase as current assets in the accompanying unaudited condensed consolidated balance sheets. Any premium or discount arising at purchase is amortized and/or accreted to interest income as an adjustment to yield using the straight-line method over the life of the instrument. Short-term investments are reported at their estimated fair value. The Company reviews its short-term investments in unrealized loss positions at each reporting date to assess whether the decline in their fair value is due to credit-related factors. The credit portion of unrealized losses and any subsequent improvements are recorded in other income (expense) through an allowance account. Unrealized gains and losses that are not credit-related are included in other comprehensive (income) loss as a component of stockholders' equity until realized. Realized gains and losses are determined using the specific identification method and are included in other income (expense).

Fair Value Measurement

The Company accounts for certain assets and liabilities at their fair value. The Company uses the following fair value hierarchy to indicate the extent to which the inputs used to determine fair value are observable in the market:

- *Level 1:* Inputs are based on quoted prices for identical assets in active markets.
- *Level 2:* Inputs, other than Level 1, that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- *Level 3:* Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, and short-term investments. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

Property and Equipment, Net

Property and equipment are stated at cost and depreciated on a straight-line basis over the estimated useful life of the related assets (generally three to five years). Leasehold improvements are stated at cost and amortized on a straight-line basis over the lesser of the remaining lease term or the estimated useful life of the leasehold improvements. Repairs and maintenance costs are charged to expense as incurred.

Leases

At the inception of a contractual arrangement, the Company determines whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. Lease terms are determined at the commencement date by considering whether renewal options and termination options are reasonably assured of exercise. For its long-term operating leases, the Company recognizes a lease liability and a right-of-use ("ROU") asset on its unaudited condensed consolidated balance sheets and recognizes lease expense on a straight-line basis over the lease term. The lease liability is determined as the present value of future lease payments using the discount rate implicit in the lease or, if the implicit rate is not readily determinable, an estimate of the Company's incremental borrowing rate. The ROU asset is based on the lease liability, adjusted for any prepaid or deferred rent. The Company aggregates all lease and non-lease components for each class of underlying assets into a single lease component and variable charges for common area maintenance and other variable costs are recognized as expense as incurred. The Company has elected to not recognize a lease liability or ROU asset in connection with short-term operating leases and recognizes lease expense for short-term operating leases on a straight-line basis over the lease term. The Company does not have any financing leases.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, such as property and equipment, for impairment whenever events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the

carrying amount of the assets exceeds the fair value of the assets. Fair value would be assessed using discounted cash flows or other appropriate measures of fair value. The Company did not recognize any impairment losses during the three months ended March 31, 2021 and 2020.

Research and Development Costs

All costs of research and development are expensed in the period incurred. Research and development costs primarily consist of salaries and related expenses for personnel, stock-based compensation, external research and development costs incurred under agreements with contract research organizations, investigative sites and consultants to conduct our preclinical, toxicology and clinical studies, laboratory supplies, costs related to compliance with regulatory requirements, costs related to manufacturing the Company's product candidates for clinical trials and preclinical studies, facilities, depreciation, and other allocated expenses. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the related goods are delivered or services performed.

The Company has entered into various research and development contracts with clinical research organizations, clinical manufacturing organizations and other companies. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and payments made in advance of performance are reflected in the accompanying unaudited condensed consolidated balance sheets as prepaid expenses. The Company records accruals for estimated costs incurred for ongoing research and development activities. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the services, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the prepaid or accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

Patent Costs

Costs related to filing and pursuing patent applications are recorded as general and administrative expenses and expensed as incurred since recoverability of such expenditures is uncertain.

Stock-Based Compensation

Stock-based compensation expense represents the cost of the grant date fair value of stock option grants recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. The Company estimates the fair value of stock option grants using the Black-Scholes option pricing model and recognizes forfeitures as they occur.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. The only component of other comprehensive loss is unrealized gains (losses) on available-for-sale securities. Comprehensive gains (losses) have been reflected in the unaudited condensed consolidated statements of operations and comprehensive loss and as a separate component in the unaudited condensed consolidated statements of convertible preferred stock and stockholders' equity (deficit) for all periods presented.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company and its chief operating decision-maker view the Company's operations and manages its business in one operating segment.

Recent Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-13, Financial Instruments — Credit Losses, to improve financial reporting by requiring timely recording of credit losses on loans and other financial instruments held by financial institutions and other organizations. The ASU requires the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. This guidance will become effective for the Company beginning January 1, 2023, with early adoption permitted. The Company early adopted ASU No. 2016-13 during the first quarter of 2021. The standard did not have a material impact on the Company's unaudited condensed consolidated financial statements.

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. ASU No. 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in ASC 740 and also improves consistent application by clarifying and amending existing guidance. The Company adopted ASU No. 2019-12 during the first quarter of 2021. The standard did not have a material impact on the Company's unaudited condensed consolidated financial statements.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and dilutive common stock equivalents outstanding for the period determined using the treasury-stock and if-converted methods. Dilutive common stock equivalents are comprised of convertible preferred stock, preferred and common stock warrants, unvested common stock subject to repurchase, and options outstanding under the Company's stock option plan.

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive are as follows (in common stock equivalent shares):

	March 31,	
	2021	**2020**
Common stock options	3,688,965	1,769,104
Unvested common stock	25,285	144,514
Common stock warrant	23,122	—
Preferred stock warrant	—	23,122
Convertible preferred stock	—	16,685,014
Total	3,737,372	18,621,754

Note 2. Balance Sheet Details

Prepaid expenses and other current assets consist of the following (in thousands):

	March 31, 2021	**December 31, 2020**
Prepaid research and development	$ 4,770	$ 4,473
Prepaid expenses	1,011	610
Other current assets	283	570
Interest receivable	193	194
Total prepaid expenses and other current assets	$ 6,257	$ 5,847

Property and equipment consist of the following (in thousands):

	March 31, 2021	December 31, 2020
Laboratory equipment	$ 1,104	$ 1,104
Computer equipment and software	215	215
Furniture and fixtures	178	178
Leasehold improvements	146	146
Property and equipment, gross	1,643	1,643
Less accumulated depreciation and amortization	(1,088)	(1,009)
Property and equipment, net	$ 555	$ 634

Depreciation expense was $0.1 million for each of the three months ended March 31, 2021 and 2020.

Accrued liabilities consist of the following (in thousands):

	March 31, 2021	December 31, 2020
Accrued research and development	$ 2,287	$ 676
Accrued compensation	1,004	1,671
Other accrued liabilities	858	604
Total accrued liabilities	$ 4,149	$ 2,951

Note 3. Commitments and Contingencies

Operating Leases

The Company entered into a five-year noncancelable operating lease in June 2017 for its corporate headquarters in San Diego, California under an agreement that commenced in March 2018. Under the terms of the agreement, there is no option to extend the lease and the Company is subject to additional charges for common area maintenance and other costs. Monthly rental payments due under the lease commenced in March 2018 and escalate throughout the lease term.

Information related to the Company's operating lease is as follows (in thousands):

	Three Months Ended March 31, 2021	2020
Operating lease expense (including variable costs of $88 and $82 during the three months ended March 31, 2021 and 2020)	$ 285	$ 279
Cash paid for amounts included in the measurement of lease liabilities	$ 209	$ 180

As of March 31, 2021 and December 31, 2020, the remaining lease term of the Company's operating lease was 24 months and 27 months, respectively. As of March 31, 2021 and December 31, 2020, the discount rate on the Company's operating lease was 8.0%.

Future minimum noncancelable operating lease payments and information related to the lease liability are as follows (in thousands):

	March 31, 2021
Remaining during 2021	$ 645
2022	876
2023	183
Total lease payments	1,704
Imputed interest	(132)
Lease liability	1,572
Less current portion of lease liability	762
Lease liability, net of current portion	$ 810

License Agreement with the Salk Institute

In November 2016, the Company and The Salk Institute for Biological Studies ("The Salk") entered into the Amended and Restated Exclusive FXR License Agreement, which was amended in February 2017 and July 2018, pursuant to which The Salk granted the Company an exclusive, worldwide license to certain FXR related intellectual property to make, use, offer for sale, import, export, and distribute products covered by such intellectual property ("FXR Licensed Products") and a non-exclusive, worldwide license to use certain technical information to research, develop, test, make, use, offer for sale, import, export and distribute FXR Licensed Products. The Company is required to use commercially reasonable efforts to achieve certain diligence milestones with respect to the FXR Licensed Products, including with respect to developing, producing and selling FXR Licensed Products. The Company is also required to pay The Salk up to $6.5 million in milestone payments upon the completion of certain clinical and regulatory milestones, certain of which payments the Company may defer under certain circumstances. The Company is also obligated to pay The Salk a low single-digit percentage royalty on net sales, with a minimum annual royalty payment due beginning with the first commercial sale of each FXR Licensed Product. The applicable minimum annual royalty payment amount depends on the number of years that have elapsed since the first commercial sale of an FXR Licensed Product and is in the hundreds-of-thousands-of-dollars range. In addition, if the Company chooses to sublicense the FXR Licensed Product to any third parties, the Company must pay to The Salk a low single-digit percentage of all sublicensing revenue. In addition, in the event of a change of control, the Company is required to pay The Salk a low single-digit percentage of any payments and consideration that it receives in consideration of the change of control. The Company has accrued $0.4 million in milestone payments based upon the achievement of certain regulatory milestones as of March 31, 2021.

Contingencies

In the event the Company becomes subject to claims or suits arising in the ordinary course of business, the Company would accrue a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

Note 4. Long-Term Debt

Long-term debt –consists of the following (in thousands):

	March 31, 2021	December 31, 2020
Long-term debt	$ 10,000	$ 10,000
Unamortized debt discount	(566)	(628)
Long-term debt, net of debt discount	$ 9,434	$ 9,372

On August 27, 2019, the Company entered into a Loan and Security Agreement (the "Loan Agreement", and all amounts borrowed thereunder the "Term Loan") with a lender (the "Lender"). The Company borrowed $10.0 million under the Term Loan at the inception of the Loan Agreement. The remaining borrowings available under the Loan Agreement have expired.

The Term Loan bears interest at a floating annual rate equal to the greater of (i) the prime rate used by the Lender plus 2% (5.25% at March 31, 2021 and December 31, 2020, respectively), and (ii) 7.25%. The monthly payments are interest-only until September 1, 2022. Subsequent to the interest-only period, the Term Loan will be payable in equal monthly installments of principal plus accrued and unpaid interest, through the maturity date of September 1, 2023 ("Maturity Date"). In addition, the Company is obligated to pay a final payment fee of 5.25% of the original principal amount of the Term Loan on the Maturity Date. As of March 31, 2021 and December 31, 2020, the final payment fee of $0.5 million has been recorded as a long-term liability. The Company may elect to prepay all, but not less than all, of the Term Loan prior to the Maturity Date, subject to a prepayment fee of up to 3.0% of the then outstanding principal balance. After repayment, no Term Loan amounts may be borrowed again.

The Company's obligations under the Loan Agreement are secured by a security interest in substantially all of its assets, other than its intellectual property. The Loan Agreement includes customary affirmative and negative covenants and also includes standard events of default, including an event of default based on the occurrence of a material adverse event, and a default under any agreement with a third party resulting in a right of such third party to accelerate the maturity of any debt in excess of $0.3 million. The negative covenants include, among others, restrictions on the Company transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying cash dividends or making other distributions, making investments, creating liens, selling assets and making any payment on subordinated debt, in each case subject to certain exceptions. Upon the occurrence and continuance of an event of default, the Lender may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement. As of March 31, 2021 and December 31, 2020, the Company was in compliance with all applicable covenants under the Loan Agreement.

In connection with the Loan Agreement, the Company issued the Lender a warrant (the "Lender Warrant") to purchase shares of the Company's Series C convertible preferred stock at an exercise price of $10.812 per share and expiring on August 27, 2029. The number of Series C convertible preferred shares issuable upon exercise of the warrant is an amount equal to (i) 2.5% of the aggregate Term Loan funded under the Loan Agreement divided by (ii) $10.812. Upon the funding of the Term Loan, the Lender Warrant was

initially exercisable for 117,924 shares of Series C convertible preferred stock. The Lender Warrant was automatically converted into a warrant to purchase 23,122 shares of common stock upon completion of the Company's IPO.

The initial $0.2 million fair value of the Lender Warrant, $0.5 million final payment fee, and $0.3 million of debt issuance costs were recorded as a debt discount and are being amortized to interest expense using the effective interest method over the term of the Term Loan. For the three months ended March 31, 2021 and 2020, the Company recognized $0.2 million and $0.3 million of interest expense, including $0.1 million and $0.1 million of debt discount amortization, respectively, in connection with the Loan Agreement. As of March 31, 2021 and December 31, 2020, the Company had an outstanding Term Loan of $10.0 million and accrued interest of $0.1 million, respectively.

Future minimum principal and interest payments under the Term Loan, including the final payment fee, as of March 31, 2021 are as follows (in thousands):

	March 31, 2021
Remaining in 2021	$ 554
2022	4,438
2023	6,949
Total principal and interest payments	11,941
Less interest and final payment fee	(1,941)
Long-term debt	$ 10,000

Note 5. Fair Value of Financial Instruments

The following tables summarize the Company's financial instruments measured at fair value on a recurring basis:

		Fair Value Measurements At Reporting Date Using		
	Total	Quoted Prices in Active Markets For Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
As of March 31, 2021				
Assets:				
Commercial paper	$ 27,387	$ —	$ 27,387	$ —
Corporate debt securities	16,467	—	16,467	—
U.S. government and agency securities	21,146	—	21,146	—
Total assets measured at fair value	$ 65,000	$ —	$ 65,000	$ —
As of December 31, 2020				
Assets:				
Commercial paper	$ 27,136	$ —	$ 27,136	$ —
Corporate debt securities	26,506	—	26,506	—
U.S. government and agency securities	18,141	—	18,141	—
Total assets measured at fair value	$ 71,783	$ —	$ 71,783	$ —

Note 6. Short-Term Investments

The following tables summarize short-term investments (in thousands):

	As of March 31, 2021			
		Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Commercial paper	$ 27,387	$ —	$ —	$ 27,387
Corporate debt securities	16,472	—	(5)	16,467
U.S. government and agency securities	21,141	5	—	21,146
Total short-term investments	$ 65,000	$ 5	$ (5)	$ 65,000

	As of December 31, 2020			
		Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Commercial paper	$ 27,136	$ —	$ —	$ 27,136
Corporate debt securities	26,510	—	(4)	26,506
U.S. government and agency securities	18,136	5	—	18,141
Total short-term investments	$ 71,782	$ 5	$ (4)	$ 71,783

The following table summarizes the maturities of the Company's short-term investments at March 31, 2021:

	Amortized Cost	Estimated Fair Value
Due in one year or less	$ 55,696	$ 55,693
Due after one year through two years	9,304	9,307
Total short-term investments	$ 65,000	$ 65,000

Note 7. Stockholders' Equity

Equity Incentive Plan

In January 2015, the Company adopted the Metacrine, Inc. 2015 Equity Incentive Plan (as amended, the "2015 Plan"), which provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock unit awards, and stock appreciation rights to its employees, members of its board of directors, and consultants. In August 2020, the Company's Board of Directors approved the 2020 Equity Incentive Plan (the "2020 Plan"), which is the successor and continuation of the 2015 Plan. No additional awards may be granted under the 2015 Plan and all outstanding awards under the 2015 Plan remain subject to the terms of the 2015 Plan. As of March 31, 2021, there were 3,166,412 shares authorized and available for issuance under the 2020 Plan.

Recipients of incentive stock options are eligible to purchase shares of the Company's common stock at an exercise price equal to no less than the estimated fair market value of such stock on the date of grant. The maximum term of options granted under the 2015 and 2020 Plans (or collectively, the "Equity Plans") is ten years and, in general, the options issued under the Equity Plans vest over a four-year period from the vesting commencement date. The 2015 Plan allows for early exercise of stock options, which may be subject to repurchase by the Company at the lower of (i) the fair market value at the repurchase date or (ii) the original exercise price. The early exercise of stock options is not permitted under the 2020 Plan.

A summary of the Company's unvested shares and unvested stock liability is as follows (in thousands, except share data):

	Number of Unvested Shares	Unvested Stock Liability
Balance at December 31, 2020	36,492	$ 27
Vested shares	(11,207)	(8)
Balance at March 31, 2021	25,285	$ 19

A summary of the Company's stock option activity is as follows (in thousands, except share and per share data):

	Number of Outstanding Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In Years)	Aggregate Intrinsic Value
Balance at December 31, 2020	3,136,076	$ 5.23	7.95	$ 8,963
Granted	783,405	$ 10.00		
Exercised	(228,678)	$ 2.73		
Cancelled	(1,838)	$ 3.01		
Balance at March 31, 2021	3,688,965	$ 6.40	8.46	$ 4,132
Vested and expected to vest at March 31, 2021	3,688,965	$ 6.40	8.46	$ 4,132
Exercisable at March 31, 2021	871,203	$ 2.60	6.26	$ 3,152

The weighted average grant date fair value per share of stock option grants for the three months ended March 31, 2021 and 2020 was $7.34 and $8.01, respectively. The total intrinsic value of stock options exercised during the three months ended March 31, 2021 and 2020 was $1.2 million and $1 thousand, respectively.

The assumptions used in the Black-Scholes option pricing model to determine the fair value of stock option grants were as follows:

	Three Months Ended March 31,	
	2021	2020
Risk-free interest rate	0.6% - 1.0%	0.6% – 0.7%
Expected volatility	88.7% - 89.5%	82.4% – 84.0%
Expected term (in years)	5.8 – 6.07	5.8 – 10.0
Expected dividend yield	0%	0%

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero coupon U.S. Treasury notes with maturities similar to the expected term of the awards.

Expected volatility. Since the Company recently completed its IPO and does not have sufficient trading history for its common stock, the expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biotechnology industry. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determines the expected life assumption using the simplified method, for employees, which is an average of the contractual term of the option and its vesting period. The expected term for nonemployee options is equal to the contractual term.

Expected dividend yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends and, therefore, used an expected dividend yield of zero.

Employee Stock Purchase Plan

In September 2020, the Company's Board of Directors and stockholders adopted and approved the 2020 Employee Stock Purchase Plan (the "ESPP"). The ESPP permits eligible employees, who elect to participate in an offering under the ESPP, to contribute up to 15% of their eligible gross compensation towards the purchase of shares of common stock. Eligible employees can purchase up to 20,000 shares of common stock on a given purchase date. The price at which stock is purchased under the ESPP is equal to 85% of the fair market value of the Company's common stock on the commencement date of each offering period or the relevant purchase date, whichever is lower. Offerings under the ESPP are approximately two years in duration and consist of four purchase periods that are approximately six months in duration. The ESPP is considered a compensatory plan as defined by the authoritative guidance for stock-based compensation. Stock-based compensation expense attributable to the ESPP was $30 thousand for the three months ended March 31, 2021. As of March 31, 2021, there were 665,059 shares of common stock available for future issuance under the ESPP.

Stock-Based Compensation Expense

Stock-based compensation expense recognized for all equity awards has been reported in the unaudited condensed consolidated statements of operations and comprehensive loss as follows (in thousands):

	Three Months Ended March 31,	
	2021	2020
General and administrative	$ 1,026	$ 285
Research and development	494	218
Total stock-based compensation	$ 1,520	$ 503

As of March 31, 2021, unrecognized stock-based compensation cost was $18.7 million, which is expected to be recognized over a remaining weighted average period of approximately 3.1 years.

Common Stock Reserved For Future Issuance

Common stock reserved for future issuance consists of the following:

	March 31, 2021	December 31, 2020
Common stock options outstanding	3,688,965	3,136,076
Shares available for issuance under equity incentive plans	3,166,412	2,907,742
Shares available for issuance under the ESPP	665,059	405,000
Common stock warrant	23,122	23,122
Total	7,543,558	6,471,940

Note 8. 401(k) Plan

The Company maintains a defined contribution 401(k) plan available to eligible employees. Employee contributions are voluntary and are determined on an individual basis, limited to the maximum amount allowable under federal tax regulations. The Company, at its discretion, may make certain matching contributions to the 401(k) plan. As of March 31, 2021, no contributions to the 401(k) plan have been made by the Company.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our unaudited condensed consolidated financial statements and related notes included elsewhere in this Quarterly Report on Form 10-Q and the audited financial statements and related notes and Management's Discussion and Analysis of Financial Condition and Results of Operations included in our Annual Report on Form 10-K for the year ended December 31, 2020. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. You should carefully read the "Risk Factors" section of this Quarterly Report to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing differentiated therapies for patients with liver and gastrointestinal ("GI"), diseases. Our most advanced program targets the farnesoid X receptor ("FXR"), which is central to modulating liver and GI diseases. FXR agonism has been investigated in large-scale clinical trials and has shown clinically relevant improvements in non-alcoholic steatohepatitis ("NASH"), a liver disease characterized by excess liver fat, inflammation, and fibrosis. We believe that potency, sustained exposure and continuous target engagement are key to optimizing therapeutic benefit with an FXR targeted therapy. Leveraging our extensive chemistry and biology expertise, we have built a proprietary library of over 2,500 FXR compounds, and have selected two novel, oral FXR candidates from a unique chemical scaffold, MET409 and MET642, that have the potential to deliver improved tolerability and therapeutic outcomes. MET409 and MET642 were purposefully designed to be differentiated treatments for NASH as potent, sustained FXR agonists, with the ability to be dosed orally once daily. With our program, we believe we can develop differentiated FXR agonist therapies for NASH and other GI diseases.

We are currently evaluating MET409 in a Phase 2a proof-of-concept trial with empagliflozin in patients with type 2 diabetes and NASH. The trial will enroll up to 120 patients in the United States and we expect to report topline data in the fourth quarter of 2021. MET642 is currently being evaluated in a Phase 2a proof-of-concept clinical trial in patients with NASH. We are planning to report preliminary data from an interim analysis in the fourth quarter of 2021 after approximately 60 patients have completed 16 weeks of treatment. We expect to report topline data from up to 180 patients in the study in the first half of 2022.

We anticipate selecting a candidate of MET409 or MET642 for a Phase 2b monotherapy biopsy trial in NASH as early as in the fourth quarter of 2021, and beginning that trial in the first half of 2022.

To date, we have devoted substantially all of our resources to organizing and staffing our company, business, planning, raising capital, researching, discovering and developing our pipeline in FXR and other drug targets and general and administrative support for these operations. We do not have any products approved for sale and have not generated any product sales. We have funded our operations primarily through the private placement of convertible preferred stock, the issuance of long-term debt, and the completion of our IPO. To date, we have raised gross proceeds of approximately $124.8 million from the issuance of convertible preferred stock, $10.0 million under our Loan Agreement with K2 HealthVentures, LLC ("K2") and $85.0 million from our IPO in September 2020. As of March 31, 2021, we had cash, cash equivalents, and short-term investments of $84.5 million.

We have incurred net losses since our inception. Our net losses were $14.8 million and $8.1 million for the three months ended March 31, 2021 and 2020, respectively. As of March 31, 2021, we had an accumulated deficit of $135.5 million. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and preclinical studies and our expenditures on other research and development activities. We expect our expenses and operating losses will increase substantially as product candidates from our FXR program and any future product candidates advance through preclinical studies and clinical trials, and as we expand our clinical, regulatory, quality and manufacturing capabilities, incur significant commercialization expenses for marketing, sales, manufacturing and distribution, if we obtain marketing approval for any of our product candidates, and incur additional costs associated with operating as a public company.

We do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for one or more product candidates, which will not be for many years, if ever. Accordingly, until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our cash needs through a combination of equity offerings, debt financings, additional borrowings under our Loan Agreement, collaborations, and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, reduce or terminate our research and development programs or other operations, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Financial Operations Overview

Research and Development Expenses

To date, our research and development expenses have related primarily to discovery efforts and preclinical and clinical development of our product candidates. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Research and development expenses include:

- salaries, payroll taxes, employee benefits and stock-based compensation charges for those individuals involved in research and development efforts;
- external research and development expenses incurred under agreements with contract research organizations ("CROs") investigative sites and consultants to conduct our preclinical, toxicology and clinical studies;
- costs related to manufacturing our product candidates for clinical trials and preclinical studies, including fees paid to third-party manufacturers;
- laboratory supplies;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, insurance, equipment and other supplies.

The following table summarizes our research and development expenses allocated by program for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
Third-party research and development expenses:		
FXR program	$ 7,491	$ 3,374
Other research programs	468	538
Total third-party research and development expenses	7,959	3,912
Unallocated expenses	2,898	2,449
Total research and development expenses	$ 10,857	$ 6,361

Unallocated expenses consist primarily of our internal personnel related costs, facility costs, and lab supplies.

We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of our FXR program and discovery of new product candidates. We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future clinical trials and preclinical studies of our product candidates due to the inherently unpredictable nature of preclinical and clinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. We will need to raise substantial additional capital in the future. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Our development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number and scope of preclinical studies;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the phase of development of the product candidate; and
- the efficacy and safety profile of the product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and employee-related costs, including stock-based compensation, for personnel in executive, finance, and other administrative functions. Other significant costs include facility-related costs, legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services, investor relations, and insurance. We anticipate that our general and administrative expenses will increase in the future to support our expanded research and development activities and infrastructure and, if any of our product candidates receive marketing approval,

commercialization activities. We also anticipate increased expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, board of director fees, and investor relations costs associated with operating as a public company.

Total Other Income (Expense)

Total other income (expense) consists primarily of interest income from our cash, cash equivalents, and short-term investments and interest expense under our loan agreement.

Results of Operations

Comparison of the Three Months Ended March 31, 2021 and 2020

The following table summarizes our results of operations for the three months ended March 31, 2021 and 2020:

	Three Months Ended March 31,		
(In Thousands)	**2021**	**2020**	**Change**
Operating expenses:			
Research and development	$ 10,857	$ 6,361	$ 4,496
General and administrative	3,696	1,601	2,095
Total operating expenses	14,553	7,962	6,591
Loss from operations	(14,553)	(7,962)	(6,591)
Other income (expense):			
Interest income	36	229	(193)
Interest expense	(244)	(253)	9
Other expense	(7)	(126)	119
Total other (income) expense	(215)	(150)	(65)
Net loss	$ (14,768)	$ (8,112)	$ (6,656)

Research and Development Expenses. Research and development expenses were $10.9 million and $6.4 million for the three months ended March 31, 2021 and 2020. The increase in research and development expenses of $4.5 million when comparing the three months ended March 31, 2021 and 2020 was primarily due to increases of $4.7 million in clinical trial expenses and $0.3 million in toxicology expenses related to our FXR program and $0.3 million in non-cash stock-based compensation. The increase in research and development expenses was partially offset by a decrease in manufacturing expenses of $0.9 million.

General and Administrative Expenses. General and administrative expenses were $3.7 million and $1.6 million for the three months ended March 31, 2021 and 2020. The increase in general and administrative expenses of $2.1 million when comparing the three months ended March 31, 2021 and 2020 was primarily due to increases of $1.3 million in personnel costs, which included $0.7 million in non-cash stock-based compensation, and $0.8 million in consulting, professional services, and other public company related expenses.

Liquidity and Capital Resources

We have incurred net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. As of March 31, 2021, we had cash, cash equivalents, and short-term investments of $84.5 million.

The following table sets forth a summary of the net cash flow activity for each of the periods indicated:

	Three Months Ended March 31,	
	2021	**2020**
Net cash provided by (used in):		
Operating activities	$ (12,170)	$ (8,602)
Investing activities	6,611	5,673
Financing activities	623	(9)
Net decrease in cash and cash equivalents	$ (4,936)	$ (2,938)

Operating Activities

Net cash used in operating activities was $12.2 million and $8.6 million for the three months ended March 31, 2021 and 2020, respectively. The net cash used in operating activities during the three months ended March 31, 2021 was primarily due to our net loss of $14.8 million, adjusted for $2.0 million of non-cash charges and $0.6 million from changes in operating assets and liabilities. Non-cash charges for the three months ended March 31, 2021 primarily consisted of $1.5 million of stock-based compensation, $0.2 million of amortization on our right-of-use asset, and $0.3 million in other non-cash charges.

Net cash used in operating activities for the three months ended March 31, 2020 was primarily due to our net loss of $8.1 million and $1.3 million from changes in operating assets and liabilities, adjusted for $0.8 million of non-cash charges. Non-cash charges for the three months ended March 31, 2020 primarily consisted of $0.5 million of stock-based compensation, $0.2 million of amortization on our right-of-use asset, and $0.1 million in other non-cash charges.

Investing Activities

Net cash provided by investing activities of $6.6 million for the three months ended March 31, 2021 was due primarily to sales and maturities of short-term investments of $19.4 million, partially offset by purchases of short-term investments of $12.8 million.

Net cash provided by investing activities of $5.7 million for the three months ended March 31, 2020 was due primarily to sales and maturities of short-term investments of $13.7 million, partially offset by purchases of short-term investments of $7.9 million and purchases of property and equipment of $0.1 million.

Financing Activities

Net cash provided by financing activities of $0.6 million for the three months ended March 31, 2021 was due primarily to proceeds from exercises of common stock options.

Net cash used in financing activities of $9 thousand for the three months ended March 31, 2020 was due primarily to the payment of initial public offering costs.

Loan Agreement

We borrowed $10.0 million from our Loan Agreement with K2 in August 2019, as amended in March 2020. The remaining borrowings available under the Loan Agreement have expired.

The Term Loan bears interest at a floating annual rate equal to the greater of (i) the prime rate used by lender plus 2.0% (resulting in an interest rate of 5.25% at March 31, 2021 and December 31, 2020), and (ii) 7.25%. The monthly payments are interest-only until September 1, 2022. Subsequent to the interest-only period, the Term Loan will be payable in equal monthly installments of principal plus accrued and unpaid interest, through September 1, 2023, the Term Loan Maturity Date. In addition, we are obligated to pay a final payment fee of 5.25% of the original principal amount of the Term Loan at the maturity date. We may elect to prepay all, but not less than all, of the term loan prior to the maturity date, subject to a prepayment fee of up to 3.0% of the then outstanding principal balance. After repayment, no term loan amounts may be borrowed again.

Our obligations under the Loan Agreement are secured by a security interest in substantially all of our assets, other than our intellectual property. The loan agreement includes customary affirmative and negative covenants and also includes standard events of default, including an event of default based on the occurrence of a material adverse event, and a default under any agreement with a third party resulting in a right of such third party to accelerate the maturity of any debt in excess of $0.3 million. The negative covenants include, among others, restrictions on us transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying cash dividends or making other distributions, making investments, creating liens, selling assets and making any payment on subordinated debt, in each case subject to certain exceptions. Upon the occurrence and continuance of an event of default, the lender may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the loan agreement. As of March 31, 2021, we were in compliance with all applicable covenants under the Loan Agreement.

Funding Requirements

We believe that our existing cash, cash equivalents, and short-term investments will be sufficient to meet our anticipated cash requirements through at least the next 12 months. In particular, we expect our cash, cash equivalents, and short-term investments, will allow us to fund our ongoing MET409 Phase 2a combination clinical trial in NASH through completion, fund our ongoing MET642 Phase 2a monotherapy clinical trial in NASH through completion, fund a Phase 2a monotherapy clinical trial of either MET409 or MET642 in UC through initial partial enrollment, and fund a Phase 2b monotherapy clinical trial of either MET409 or MET642 in NASH through initial partial enrollment. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could expend our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

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

- the scope, rate of progress and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing our product candidates and commercial manufacturing activities;
- the cost, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;

- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;
- the timing of any milestone and royalty payments to The Salk, or other future licensors;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the cost associated with commercializing our product candidates, if they receive marketing approval.

Until such time, if ever, as we can generate substantial product revenues to support our cost structure, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and 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 capital expenditures or declaring dividends. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. The COVID-19 pandemic continues to rapidly evolve and has 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 the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the pandemic. If the disruption persists and deepens, we could experience an inability to access additional capital. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our unaudited condensed consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these unaudited condensed consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 1 to our unaudited condensed consolidated financial statements appearing elsewhere in this Quarterly Report, we believe the following accounting policies and estimates to be most critical to the preparation of our consolidated financial statements.

Accrued Expenses

We make estimates of our accrued research and development expenses for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost.

We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation Expense

Stock-based compensation expense represents the cost of the grant date fair value of equity awards recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. We estimate the fair value of all stock option grants using the Black-Scholes option pricing model and recognize forfeitures as they occur. Estimating the fair value of equity awards as of the grant date using valuation models, such as the Black-Scholes option pricing model, is affected by assumptions regarding a number of variables, including the fair value of the underlying common stock on the date of grant, the risk-free interest rate, the expected stock price volatility, the expected term of stock options, and the expected dividend yield. Before the closing of our IPO, we were required to estimate the fair value of the common stock underlying our stock-based awards when performing fair value calculations. Our determinations of the fair value of our common stock were made using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Accounting and Valuation Guide: *Valuation of Privately Held Company Equity Securities Issued as Compensation,* or the Practice Aid. Since the completion of our IPO, the fair value of equity awards have been determined based upon our closing stock price on The Nasdaq Global Market on the date of grant.

Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop. See Note 7 to our unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted the three months ended March 31, 2021 and 2020. As of March 31, 2021, the unrecognized stock-based compensation expense relating to stock options was $18.7 million and is expected to be recognized over a weighted average period of approximately 3.1 years.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. As of March 31, 2021, our cash, cash equivalents, and short-term investments consisted of cash, money market funds, commercial paper, corporate debt securities and U.S. government and agency securities. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature and low risk profile of the instruments in our portfolio, a 10% change in market interest rates would not have a material impact on our financial condition and/or results of operations.

Our outstanding long-term debt bears interest at a floating annual rate equal to the greater of (i) the prime rate used by Lender plus 2.0% (5.25% at March 31, 2021), and (ii) 7.25%. The impact of a 10% change in market interest rates would be less than $0.1 million annually and would not have a material impact on our financial condition and/or results of operations.

Foreign Currency

In May 2019, we formed a wholly-owned Australian subsidiary, Metacrine, Pty Ltd. The functional currency of Metacrine, Pty Ltd is the United States dollar. Assets and liabilities of Metacrine, Pty Ltd that are not denominated in the functional currency are remeasured into U.S. dollars at foreign currency exchange rates in effect at the reporting date except for nonmonetary assets and capital accounts, which are remeasured at historical foreign currency exchange rates in effect at the date of transaction. Expenses are generally remeasured at foreign currency exchange rates which approximate average rates in effect during each period. Net realized and unrealized gains and losses from foreign currency transactions and remeasurement are reported in other income (expense) in the unaudited condensed consolidated statements of operations.

In addition to the activities of Metacrine, Pty Ltd, we incur expenses, including for manufacturing of clinical trial materials, outside the United States based on contractual obligations denominated in currencies other than the U.S. dollar, including Euros. At the end of each reporting period, these liabilities are converted to U.S. dollars at the then-applicable foreign exchange rate. As a result, our business is affected by fluctuations in exchange rates between the U.S. dollar and foreign currencies. We do not enter into foreign currency hedging transactions to mitigate our exposure to foreign currency exchange risks. Exchange rate fluctuations may adversely affect our expenses, results of operations, financial position, and cash flows. However, to date, these fluctuations have not been significant and a movement of 10% in the U.S. dollar exchange rate would not have a material effect on our results of operations.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe inflation has had a material effect on our results of operations during the periods presented.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on that

evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that, as of the end of the period covered by this Quarterly Report on Form 10-Q, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Changes in Internal Control over Financial Reporting

Due to a transition period established by SEC rules applicable to newly public companies, our management is not required to evaluate the effectiveness of our internal control over financial reporting until after the filing of our Annual Report on Form 10-K for the year ended December 31, 2021. As a result, this Quarterly Report on Form 10-Q does not address whether there have been any changes in our internal control over financial reporting.

PART II—OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

From time to time, we are subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this Quarterly Report, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

ITEM 1A. RISK FACTORS

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Quarterly Report and our other filings with the Securities and Exchange Commission before making investment decisions regarding our common stock.

Summary Risk Factors

We may be unable, for many reasons, including those that are beyond our control, to implement our business strategy. In particular, risks associated with our business include:

- We are an early stage biopharmaceutical company with a very limited operating history. We have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have never generated any revenue from product sales and may never be profitable.
- We are highly dependent on the success of our FXR program, which consists of our product candidates MET409 and MET642, each of which is in early stage clinical development, and we may not be able to successfully obtain regulatory or marketing approval for, or successfully commercialize, either or both of these product candidates in any of the indications for which we plan to develop them.
- MET409 and MET642 are FXR agonists, a class of drugs from which there are no approved therapies in the diseases for which we are currently pursuing clinical trials, and our initial target indication is NASH, for which there are no approved therapies. This makes it difficult to predict the timing and costs of clinical development for these product candidates.
- We will need to obtain substantial additional funding to complete the development and any commercialization of MET409 and MET642 and any future product candidates. If we are unable to raise this capital when needed, we may be forced to delay, reduce or eliminate our research and development programs or other operations.
- We are very early in our development efforts and we have limited experience conducting clinical trials in humans.
- The development and commercialization of drug products is subject to extensive regulation, and we may not obtain regulatory approvals for MET409 or MET642 in any of the indications for which we plan to develop them, or any future product candidates.
- Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.
- Some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. This is acutely relevant for our development of MET409 and MET642 for the treatment of patients with NASH and IBD (including UC), diseases for which there are significant competition for clinical trial subjects.
- Adverse side effects or other safety risks associated with our product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon product candidates, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.
- Our business could be adversely affected by the effects of health pandemics or epidemics, including the recent COVID-19 pandemic.
- The lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to the market penetration of MET409 and MET642 for the treatment of NASH, if ever commercialized.
- We face substantial competition, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us. If their product candidates are shown to be safer or more effective than ours, then our commercial opportunity will be reduced or eliminated.
- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.
- The trading price of our common stock may be volatile and fluctuate substantially or may decline regardless of our operating performance, which could result in substantial losses.

Investing in our common stock is speculative and involves a high degree of risk. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. This report also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated

in the forward-looking statements as a result of a number of factors, including the risks described below. You should consider all of the risk factors described when evaluating our business. We have marked with an asterisk (*) those risk factors that reflect changes from the similarly titled risk factors included in the Annual Report

Risk Factors

Risks Related to Our Business and to the Discovery, Development and Regulatory Approval of MET409, MET642 and Future Product Candidates

We are an early stage biopharmaceutical company with a very limited operating history. We have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have never generated any revenue from product sales and may never be profitable.*

We are an early stage biopharmaceutical company with a very limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. We were incorporated in 2014 and commenced operations in 2015. To date, our operations have been limited to organizing and staffing our company, business planning, raising capital, researching, discovering and developing our pipeline in FXR and other drug targets, and general and administrative support for these operations. Our product candidates, MET409 and MET642, are in early clinical development, while our other research and development programs are in the discovery stage. We have not yet demonstrated an ability to successfully complete any late stage clinical trials and have never completed the development of any product candidate. We have never generated any revenue from product sales and have incurred net losses each year since we commenced operations. For the three months ended March 31, 2021 and 2020, our net losses were $14.8 million and $8.1 million, respectively. As of March 31, 2021, we had an accumulated deficit of $135.5 million. We expect to incur increasing levels of operating losses for the foreseeable future as we execute our plan to continue our discovery, research and development activities, including the ongoing and planned clinical development of MET409 and MET642, and incur the additional costs of operating as a public company. We expect that it will be several years, if ever, before we have a product candidate ready for potential regulatory approval and commercialization. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital.

To become and remain profitable, we must develop and eventually commercialize a product with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we succeed in obtaining approval for and commercializing one or more of our product candidates, we may never generate revenues that are significant enough to achieve profitability. In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. Furthermore, 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 or when, or if, we will be able to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We are highly dependent on the success of our FXR program, which consists of our product candidates MET409 and MET642, each of which is in early stage clinical development, and we may not be able to successfully obtain regulatory or marketing approval for, or successfully commercialize, either or both of these product candidates in any of the indications for which we plan to develop them.

Our future success will depend almost entirely on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or both of MET409 and MET642, in any of the indications for which we plan to develop them, including NASH or IBD, which may never occur. We have no significant product candidates in our pipeline other than MET409 and MET642. We currently generate no revenues from sales of any drugs and we may never be able to develop or commercialize a marketable drug.

Before we can market and sell a drug in the United States or foreign jurisdictions, we will need to commence and complete additional clinical trials, manage clinical, preclinical and manufacturing activities, obtain necessary regulatory approvals from the FDA in the United States and from similar foreign regulatory agencies in other jurisdictions, obtain manufacturing supply, build a commercial organization or enter into a marketing collaboration with a third party, and in some jurisdictions, obtain reimbursement authorization, among other things. We cannot assure you that we will be able to successfully complete the necessary clinical trials and/or obtain regulatory approvals and develop sufficient commercial capabilities for MET409, MET642 or any other product candidates. We have not submitted a NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate. Further, a product candidate may not receive regulatory approval even if it is successful in clinical trials. If we do not receive regulatory approvals, our business, prospects, financial condition and results of operations will be adversely affected. Even if we obtain regulatory approvals, we may never generate significant revenues from any commercial sales of a marketable drug. If one of our product candidates is approved and we fail to successfully commercialize it, we may be unable to generate sufficient revenues to sustain and grow our business and our business, prospects, financial condition and results of operations will be adversely affected.

MET409 and MET642 are FXR agonists, a class of drugs from which there are no approved therapies in the diseases for which we are currently pursuing clinical trials, and our initial target indication is NASH, for which there are no approved therapies. This makes it difficult to predict the timing and costs of clinical development for these product candidates.

We have concentrated our product research and development efforts on our FXR agonists, including MET409 and MET642, and our future success depends on the successful development of this therapeutic approach to disease. To date, there are no FXR agonists approved for the treatment of the diseases for which we are currently pursuing clinical trials. Additionally, the first indication for which we intend to develop MET409 and MET642 is NASH, a disease for which there are no approved therapies. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. While other companies are in later stages of clinical trials for their FXR agonists than we are, there is not a tested and successful approval path for drugs in this class that we can use as an example and we expect that such a path for regulatory approval for NASH treatments may continue to evolve in the near term as these other companies refine their regulatory approval strategies and interact with regulatory authorities. As an example, the FDA recently denied accelerated approval for Intercept Pharmaceuticals, Inc.'s drug candidate, OCA, based on the surrogate histologic endpoint of improvement of fibrosis as shown by liver biopsy with no worsening of NASH in lieu of clinical outcomes such as overall survival and time to transplant. Such evolution may impact our future clinical trial designs, including trial size and approval endpoints, in ways that we cannot predict today. As we advance our product candidates, we will be required to consult with the FDA and equivalent foreign authorities and comply with applicable guidelines. The FDA and equivalent foreign authorities may require that we perform additional studies beyond those that we currently expect. As a result, our expenses could increase materially beyond what we currently anticipate, and the timing of any potential product approval may be delayed. As an example, the FDA has suggested, and we have agreed, to include scans and other blood tests with respect to our anticipated Phase 2a clinical trial of MET642 which resulted in increases to our anticipated study costs. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient revenue to maintain our business.

We will need to obtain substantial additional funding to complete the development and any commercialization of MET409, MET642 and any future product candidates. If we are unable to raise this capital when needed, we may be forced to delay, reduce or eliminate our research and development programs or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations and expect our expenses to increase substantially during the next few years. The development of biopharmaceutical product candidates is capital intensive. As our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our clinical, regulatory, quality and manufacturing capabilities. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses for marketing, sales, manufacturing and distribution. We expect to incur additional costs associated with operating as a public company. 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, 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 the net proceeds from our initial public offering, together with our cash and cash equivalents at March 31, 2021, will enable us to fund our operating expenses and capital expenditure requirements through at least the next 12 months. 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 the progress of our drug development activities and changes in regulation of what is necessary to develop a therapy for NASH and obtain approval. Our future capital requirements will depend on many factors, including:

- the scope, rate of progress and costs of our drug discovery, preclinical development activities, laboratory testing and clinical trials for our product candidates;
- the number and scope of clinical programs we decide to pursue;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the cost, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of our product candidates;
- the costs associated with being a public company;
- the timing of any milestone and royalty payments to current or future licensors;
- the extent to which we acquire or in-license other product candidates and technologies;
- the cost associated with commercializing our product candidates, if they receive marketing approval; and
- the severity, duration, and impact of the ongoing COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product 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 many years, if at all. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations, including through a combination of equity offerings, debt financing, additional borrowings under our loan agreement, collaborations and other similar arrangements. Adequate additional financing may not be available to us on acceptable terms, or at all. 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. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or other operations.

The terms of our loan agreement place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our operating and financial flexibility.

In August 2019, we entered into a loan and security agreement, or the loan agreement, with K2, as amended in March 2020. We borrowed $10.0 million in the first tranche under the loan agreement. Our obligations under the loan agreement are secured by a security interest in substantially all of our assets, other than our intellectual property. The loan agreement includes customary affirmative and negative covenants, as well as standard events of default, including an event of default based on the occurrence of a material adverse event. The negative covenants include, among others, restrictions on us transferring collateral, incurring additional indebtedness, engaging in mergers or acquisitions, paying cash dividends or making other distributions, making investments, creating liens, selling assets and making any payment on subordinated debt, in each case subject to certain exceptions. These restrictive covenants could limit our flexibility in operating our business and our ability to pursue business opportunities that we or our stockholders may consider beneficial. In addition, K2 could declare a default upon the occurrence of any event that it interprets could have material adverse effect, as defined in the loan agreement. Upon the occurrence and continuance of an event of default, K2 may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the loan agreement. Any declaration by K2 of an event of default could significantly harm our business and prospects and could cause the price of our common stock to decline. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay these outstanding obligations at the time any event of default occurs. Further, if we raise any additional capital through debt financing, the terms of such additional debt could further restrict our operating and financial flexibility.

We are very early in our development efforts and we have limited experience conducting clinical trials in humans.

We are early in our development efforts and we have limited experience conducting clinical trials in humans. Because of the early stage of our development efforts, and because the regulatory landscape in NASH is still evolving, we are still in the process of determining the clinical development path forward for MET409 and MET642 in this indication. To date, MET409 and MET642 have only been evaluated for safety and toxicology in animals for up to 13 weeks and 16 weeks, respectively, in completed preclinical studies, MET409 has been evaluated for safety in a 14-day Phase 1 clinical trial and 12-week Phase 1b clinical trial, and MET642 has been evaluated for safety in a 14-day Phase 1 clinical trial. Their longer-term toxicity is unknown. We are currently conducting six-month rat and nine-month non-human primate GLP toxicology studies for MET409 and MET642 to support longer-term clinical trials. Adverse safety and toxicology findings may emerge as we conduct longer studies. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because later-stage clinical trials may be conducted in broader patient populations and involve different study designs. For instance, the results of our completed Phase 1b proof-of-concept clinical trial of MET409 in NASH patients may not be predictive of the results of any future clinical trial. Furthermore, our future clinical trials will need to demonstrate sufficient safety and efficacy in larger patient populations for approval by regulatory authorities. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

To date, we have had only limited interactions with the FDA regarding our plans for future MET409 and MET642 clinical trials. We may not learn of certain information or the amount or type of data that the FDA may require for approval of our product candidates until after we have additional interactions with the FDA. In part because of our limited infrastructure, experience conducting clinical trials as a company and regulatory interactions, we cannot be certain that our clinical trials will be initiated on time, that our planned clinical trials will be completed on time, if at all, that our planned development programs would be acceptable to the FDA or other comparable foreign regulatory authorities, or that, if approval is obtained, such product candidates can be successfully commercialized.

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on our ability to successfully complete the above activities and any other activities required for the successful development and eventual commercialization of one or more of our product candidates. The success of our product candidates will further depend on factors such as:

- completion of preclinical studies, including ongoing and future long-term toxicology studies, our ongoing Phase 2a Combination Trial of MET409 with empagliflozin in patients with Type 2 diabetes and NASH and our ongoing Phase 2a clinical trial of MET642 with favorable results;
- authorization by the FDA to proceed with clinical trials under INDs or similar regulatory authorizations by comparable foreign regulatory authorities for our future clinical trials;
- successful enrollment in, and completion of, clinical trials with favorable results;
- demonstrating safety and efficacy to the satisfaction of applicable regulatory authorities;
- receipt of marketing approvals from applicable regulatory authorities;

- establishing manufacturing capabilities or arrangements with third-party manufacturers for clinical supply and, if and when approved, for commercial supply;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in combination with others;
- 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 patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates;
- maintaining a continued acceptable safety profile of any product following approval; and
- disruptions or difficulties, or other restrictions, in initiating, enrolling, conducting or completing trials due to the recent COVID-19 pandemic.

If we do not achieve one or more of these factors in a timely manner, we could experience significant delays or an inability to successfully obtain marketing approval and commercialize our product candidates, which would materially harm our business.

The development and commercialization of drug products is subject to extensive regulation, and we may not obtain regulatory approvals for MET409 or MET642 in any of the indications for which we plan to develop them, or any future product candidates.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing and distribution and other possible activities relating to MET409 and MET642 as well as any other product candidate that we may develop in the future, are subject to extensive regulation in the United States and foreign jurisdictions. Marketing approval of drug candidates in the United States requires the submission of an NDA to the FDA and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of an 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.

Regulatory approval of an NDA is not guaranteed, and the approval process is an expensive and uncertain process that may take several years. The FDA and foreign regulatory entities also have 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 product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. 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 our product candidates and other products with the same mechanism of action may not be predictive of the results of our clinical trials. In particular, while we have conducted certain preclinical studies of MET409 and MET642, a Phase 1b proof-of-concept clinical trial of MET409, and a Phase 1 clinical trial of MET642, we do not know whether these product candidates will perform in current and future clinical trials as they have performed in these prior studies. For example, in preclinical animal studies with our FXR agonist product candidates, we have observed improvement in colon inflammation on a level similar to a mouse antibody which targets IL-12/23, but there is no guarantee that a similar improvement will be observed in our 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 biopharmaceutical 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. Furthermore, as more product candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change.

The FDA and similar foreign authorities could delay, limit or deny approval of a product candidate for many reasons, including because they:

- may not deem our product candidate to be adequately safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- may determine that adverse events experienced by participants in our clinical trials represents 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 of our product candidates;
- may not approve the manufacturing processes or facilities associated with our product 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.

In order to evaluate the potential of our FXR program as part of a combination therapy for NASH, we are currently evaluating MET409 in combination with empagliflozin, an antidiabetic agent that has previously shown clinical benefits in NASH in a Phase 2a clinical trial. Additionally, we are currently conducting a Phase 2a clinical trial to evaluate MET642 in patients with NASH. We may also use other agents in future clinical trials. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidate. There is also a risk that safety, efficacy, manufacturing or supply issues could arise with the antidiabetic agent that is used in the combination therapy. This could result in our own products being removed from the market or being less successful commercially.

Generally, public concern regarding the safety of drug 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.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may 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.

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

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming and uncertain as to outcome. In addition, we may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product 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.

The FDA or comparable foreign regulatory authorities may require that we perform additional studies beyond those that we currently expect. As an example, the FDA has suggested, and we have agreed, to include scans and other blood tests with respect to our anticipated Phase 2a clinical trial of MET 642 which resulted in increases to our anticipated study costs. As a result, our expenses could increase materially beyond what we currently anticipate, and the timing of any potential product approval may be delayed. Any such delays in the commencement or completion of our ongoing and planned clinical trials for our product candidates could significantly affect our product development costs. We do not know whether our planned trials will begin on time 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 studies;
- obtaining regulatory authorizations to commence a trial or reaching a consensus with regulatory authorities on trial design;
- 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;
- IRBs 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;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-up;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects 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;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMP regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;

- 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 GCPs or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- 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; or
- disruptions caused by man-made or natural disasters, or public health pandemics or epidemics or other business interruptions, including the ongoing COVID-19 pandemic.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. 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 or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, 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 for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, conducting clinical trials in foreign countries (for example, our Phase 1 clinical trial of MET409 was conducted in the Netherlands and our Phase 1 clinical trial of MET642 was conducted in Australia) presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Moreover, certain of our scientific advisors or consultants who receive compensation in connection with such services are likely to be investigators for our future clinical trials. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that our financial relationships with principal investigators, some of whom we engage as consultants, have created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority 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 or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. We may make formulation or manufacturing changes to our product candidates, in which case we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

We may not be able to initiate or continue clinical trials for our product 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 or analogous regulatory authorities outside the United States. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. This is acutely relevant for our development of MET409 and MET642 for the treatment of patients with NASH and IBD (including UC), diseases for which there are significant competition for clinical trial subjects. Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- invasive procedures required to obtain evidence of drug performance during the clinical trial;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- reluctance of physicians to encourage patient participation in clinical trials;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and

- disruptions caused by man-made or natural disasters, or public health pandemics or epidemics, or other business interruptions, including the ongoing COVID-19 pandemic.

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

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

As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with the use of our product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates, used as a monotherapy or in combination with another medication, could result in the delay, suspension or termination of clinical trials by us, the FDA or other regulatory authorities for a number of reasons. If we elect or are required to delay, suspend or terminate any clinical trial of any product candidates that we develop, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of the product candidate at issue. Any of these occurrences may harm our business, prospects, financial condition and results of operations significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development 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 the product candidate if approved. We may also be required to modify our study plans based on findings in our ongoing clinical trials. Many compounds that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the compound. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

It is possible that, as we test our product candidates in larger, longer and more extensive clinical trials including with different dosing regimens, or as the use of these product candidates becomes more widespread if they receive 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 subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly.

In addition, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or a contraindication;
- we may be required to implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, 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 interim, topline or preliminary data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We 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 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 or interim data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects and disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. See the description of risks under the heading “Risks Related to our Common Stock” for more disclosure related to the risk of volatility in our stock price.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is 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 topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

We have completed a Phase 1 clinical trial for MET409 in the Netherlands and a Phase 1 clinical trial for MET642 in Australia, and may conduct additional clinical trials of MET409, MET642 and other future product candidates outside of the United States. However, the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.

In 2019, we completed a Phase 1 clinical trial for MET409 in the Netherlands and in December 2020 we completed a Phase 1 clinical trial of MET642 in Australia. We are currently conducting a Phase 2a Combination trial of MET409 with empagliflozin in patients with Type 2 diabetes and NASH and a Phase 2a clinical trial of MET642 in patients with NASH in the United States.

Although the FDA and foreign equivalents may accept data from clinical trials conducted entirely outside the United States and not under an IND, acceptance of such study data is generally subject to certain conditions. For example, the FDA requires the clinical trial to have been conducted in accordance with GCPs, and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. In addition, when studies are conducted only at sites outside of the United States, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional potential risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, which would likely require us to conduct additional clinical trials. Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

Even if any of our product candidates receives marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, hospitals, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. There are no currently-approved therapies for the treatment of NASH, which may mean that we are required to use more resources to educate the medical community than we are anticipating, if either or both of MET409 and MET642 is approved for the treatment of this disease. If our product 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 product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- our ability to offer our therapies for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- potential product liability claims;
- the timing of market introduction of our products as well as competitive drugs;
- the effectiveness of our or any of our potential future sales and marketing strategies;
- publicity relating to the product;
- sufficient third-party coverage and adequate reimbursement;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

We currently have no marketing and sales organization and 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 marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We may have to seek collaborators, especially for marketing and sales outside of the United States, or invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that our product candidates will be approved, if at all. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. Even if we determine to perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by our product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and cGCPs, for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, undesirable side effects caused by the product, problems encountered by our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, either before or after product approval, may result in, among other things:

- restrictions on the marketing or manufacturing of the product;
- requirements to include additional warnings on the label;
- requirements to create a medication guide outlining the risks to patients;
- withdrawal of the product from the market;
- voluntary or mandatory product recalls;
- requirements to change the way the product is administered or for us to conduct additional clinical trials;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- harm to our reputation.

Additionally if any of our product candidates receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of the therapy outweigh its risks, which may include, among other things, a medication guide outlining the risks for distribution to patients and a communication plan to health care practitioners. Any of these events could prevent us from achieving or maintaining market acceptance of the product or the particular product candidate at issue and could significantly harm our business, prospects, financial condition and results of operations.

In addition, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. 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 sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may

arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

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

Because we have limited financial and managerial resources, we must prioritize our research programs and will need to focus our product candidates on the potential treatment of certain indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. 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 product 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 product candidate, we may also relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our inability to design such product candidates with the pharmacological properties that we desire; and
- potential product candidates may, on further study, be shown to have harmful side effects, limited to no efficacy or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenues in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products, if any, will be harmed.

Our business could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations.*

Our business could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic, in regions where we have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third-party manufacturers and CROs upon whom we rely. The COVID-19 pandemic has resulted in governments implementing numerous containment measures, such as travel bans and restrictions, particularly quarantines, stay at home orders and business limitations and shutdowns.

We are following, and plan to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. In March 2020, we implemented a remote work-from-home policies for most of our employees. The effects of the stay at home order and our work-from-home policies may negatively impact productivity, increase risks associated with cyber security, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results, and financial condition.

Quarantines, stay at home and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases, may impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. In particular, some of our suppliers of certain materials used in the production of our drug products are located in China and Europe, where there have been government-imposed quarantines. While many of these materials may be obtained by more than

one supplier, restrictions resulting from the COVID-19 pandemic may disrupt our supply chain or limit our ability to obtain sufficient materials for our product candidates.

In addition, our clinical trials may be affected by the COVID-19 pandemic. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic. Some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients, principal investigators and site staff (who as healthcare providers may have heightened exposure to COVID-19) may be hindered, which would adversely affect our clinical trial operations. Disruptions or restrictions on our ability to travel to monitor data from our clinical trials, or to conduct clinical trials, or the ability of patients enrolled in our studies to travel, or the ability of staff at study sites to travel, as well as temporary closures of our facilities or the facilities of our clinical trial partners and their contract manufacturers, would negatively impact our clinical trial activities. In addition, we rely on independent clinical investigators, CROs and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, including the collection of data from our clinical trials, and the outbreak may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us. Similarly, our preclinical trials could be delayed and/or disrupted by the COVID-19 pandemic. As a result, the expected timeline for data readouts of our preclinical studies and clinical trials and certain regulatory filings may be negatively impacted, which would adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, the COVID-19 pandemic may cause interruption or delays in the operation of the FDA or other regulatory authorities which could negatively affect our planned clinical trials.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, it is currently resulting in significant disruption of global financial markets. This disruption, if sustained or recurrent, could make it more difficult for us to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global pandemic of COVID-19 continues to rapidly evolve. The ultimate impact of the COVID-19 pandemic or a similar health pandemic or epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. These effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely. To the extent the COVID-19 pandemic adversely affects our operations, it may also have the effect of heightening many of the other risks described in this “Risk Factors” section.

The lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to the market penetration of MET409 and MET642 for the treatment of NASH, if ever commercialized.

Liver biopsy is the standard approach for the diagnosis of inflammation and fibrosis associated with NASH. However, the procedure-related morbidity and, in rare cases, mortality, sample errors, costs, patient discomfort and thus lack of patient interest in undergoing the procedure limit its use. As such, only patients with a high risk of NASH, which includes patients with metabolic syndrome and an indication of NAFLD are generally sent for liver biopsy. Because NASH tends to be asymptomatic until the disease progresses, many individuals with NASH remain undiagnosed until the disease has reached its late stages, if at all. The lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to the market penetration of MET409 and MET642 for the treatment of NASH, if ever commercialized, as many practitioners and patients may not be aware that a patient suffers from NASH and requires treatment. As such, use of MET409 and MET642 for the treatment of NASH might not be as wide-spread as our actual target market and this may limit the commercial potential of such product candidates.

A further challenge to the market penetration for our NASH product candidates is that currently a liver biopsy is the standard approach for measuring improvement in NASH patients. Because it would be impractical to subject all patients that take MET409 and/or MET642, if approved, to regular and repeated liver biopsies, it will be difficult to demonstrate effectiveness to practitioners and patients unless and until a reliable non-invasive method for the diagnosis and monitoring of NASH becomes available, as to which there can be no assurance.

While non-invasive diagnostic approaches are being advanced, none of these has been clinically validated, and the timetable for commercial validation, if at all, is uncertain. Moreover, such diagnostics may also be subject to regulation by FDA or other regulatory authorities as medical devices and may require premarket clearance or approval.

We face substantial competition, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us. If their product candidates are shown to be safer or more effective than ours, then our commercial opportunity will be reduced or eliminated.

The development and commercialization of new products is highly competitive. We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop small molecules and biologics for the treatment of liver and GI diseases. 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 more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

We are aware of both private and public companies with development programs in NASH. These companies include, but are not limited to, 89Bio, Inc., Akero Therapeutics, Inc., Allergan, Inc., Bristol-Myers Squibb Company, CymaBay Therapeutics, Inc., Eli Lilly and Company, Enanta Pharmaceuticals, Inc., ENYO Pharma SA, Intercept Pharmaceuticals, Inc., Inventiva S.A., Gilead Sciences, Inc., Madrigal Pharmaceuticals, Inc., NGM Biopharmaceuticals, Inc., Novartis AG, Novo Nordisk A/S, Pfizer, Inc., Sanofi S.A., Shire plc, Terns Pharmaceuticals, Inc. and Viking Therapeutics, Inc. Several companies, including some of those mentioned above, have active research and development programs on FXR and are further along in development than we are with MET409 and MET642. Our commercial opportunity could be substantially limited in the event that our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or cheaper than our comparable products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of our product's entry. We believe the competitive factors that will determine the success of our programs will be the efficacy, safety, pricing and reimbursement and convenience of our product candidates.

Major, currently-marketed IBD therapies include, but are not limited to, infliximab (marketed as Remicade by Janssen Biotech, Inc.), adalimumab (marketed as Humira by Pfizer, Inc.), vedolizumab (marketed as Entyvio by Takeda Pharmaceuticals, Inc.), ustekinumab (marketed as Stelara by Janssen Biotech, Inc.) and tofacitinib (marketed as Xeljanz by Pfizer, Inc.), and we are aware of several companies with development programs in this indication, including, but not limited to, Abbvie Inc., Janssen Pharmaceuticals, Inc., Pfizer, Inc. and Takeda Pharmaceuticals, Inc.

As more product candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Consequently, the results of our clinical trials for product candidates in those class will likely need to show a risk benefit profile that is competitive with or more favorable than those products and product candidates in order to obtain marketing approval or, if approved, a product label that is favorable for commercialization. If the risk benefit profile is not competitive with those products or product candidates, we may have developed a product that is not commercially viable, that we are not able to sell profitably or that is unable to achieve favorable pricing or reimbursement. In such circumstances, our future product revenues and financial condition would be materially and adversely affected.

Many of our competitors, such as large pharmaceutical and biotechnology companies like Allergan, Bristol-Myers Squibb, Eli Lilly and Company, Gilead, Novartis, Novo Nordisk and Pfizer have longer operating histories and significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and 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 and management personnel, establishing clinical trial sites and subject enrollment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience and availability of coverage and reimbursement. If we are not successful in developing, commercializing and achieving higher levels of reimbursement than our competitors, we will not be able to compete against them and our business would be materially harmed.

If the market opportunities for any product that we or our strategic partners develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer.

We are focused on the development of treatments for liver and GI diseases. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidates are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. If any of our estimates are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse material impact on our business.

Risks Related to Manufacturing and Our Reliance on Third Parties

We contract with third parties for the manufacturing and supply of product candidates for use in preclinical testing and clinical trials, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.

We do not have any manufacturing facilities. We produce, in our laboratory, relatively small quantities of compounds for evaluation in our research programs. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial supply if any of our product candidates are approved. We currently do not have long-term agreements with any of our third-party manufacturers and do not have any contractual relationships for the manufacture of commercial supplies of any of our product candidates, if they are approved. This reliance increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. This could be particularly problematic where we rely on a single-source supplier, as is currently the case for the manufacture of the drug substance and the drug product for MET409 and MET642. In addition, if we were to experience an unexpected loss of supply of our product candidates for any reason, including as a result of manufacturing, supply or storage issues, our business would be harmed, and we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials.

Furthermore, all entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for MET409, MET642 and future product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to the FDA's GLP regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Comparable foreign regulatory authorities may require compliance with similar requirements. The facilities and quality systems of our third-party contractor manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of our product candidates. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP regulations, but we are nevertheless responsible for their failures to comply with applicable laws and regulations, including cGMP.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do so on commercially reasonable terms, if at all. Further, we may be unable to use the product produced by that manufacturer, or if the manufacturer has manufactured product for our commercial sale, if and when we obtain approval, we could be subject to a recall of such product.

Any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third-party manufacture our product candidates. The process of changing manufacturers is extensive and time consuming and could cause delays or interruptions in our drug development. Further, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

Our or a third party's failure to execute on our manufacturing requirements, to do so on commercially reasonable terms and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our product candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our product candidates;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of our product candidates; and
- in the event of approval to market and commercialize our product candidates, an inability to meet commercial demands for our product or any other future product candidates.

In order to conduct later-stage clinical trials of our product candidates, we will need to manufacture them in large quantities. We, or our manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we or our manufacturing partners are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and marketing approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Additionally, our third-party manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes, or unstable political environments, or health pandemics or epidemics such as the ongoing COVID-19 pandemic. For example, many of our raw materials for manufacture of MET409 are produced in China, and MET642 in Europe, which could impact our ability to manufacture and supply material for clinical and commercial supply. If our contract manufacturers were to encounter any manufacturing difficulties or delays due to these factors, our ability to provide our product candidates to patients in clinical trials, or to provide product for treatment of patients if and when approved, would be jeopardized.

We rely, and intend 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 or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are, and expect to remain, dependent on third parties to conduct our ongoing and planned clinical trials of our product candidates, and any future preclinical and clinical trials of any other product candidates. The timing of the initiation and completion of these trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Specifically, we expect CROs, clinical investigators, and consultants to 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, the Competent Authorities of the Member States of the EEA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these 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 or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure 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 performs in a substandard manner, or terminates its engagement 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, clinical trial investigators for our clinical trial may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities 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 or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our product 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 drug 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 our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our products.

Even if we receive marketing approval, we may not be able to successfully commercialize our product candidates due to unfavorable pricing regulations or third-party coverage and reimbursement policies, which could make it difficult for us to sell our product candidates profitably.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product 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 products, 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 product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, by any future laws limiting drug prices and by any future relaxation of laws that presently restrict imports of product from countries where they may be sold at lower prices than in the United States.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting reimbursement policies, but also have their own methods and approval process apart from Medicare coverage and reimbursement determinations.

Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;

- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded therapeutics and therapeutics administered under the supervision of a physician. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private 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.

Reimbursement may impact the demand for, and the price of, any product for which we obtain marketing approval. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the successful commercialization of new products. Further, the adoption and implementation of any future governmental cost containment or other health reform initiative may result in additional downward pressure on the price that we may receive for any approved product.

Outside of the United States, many countries require approval of the sale price of a product before it can be marketed and the pricing review period only begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some of these countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product 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 product 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 product candidates, even if such product candidates obtain marketing approval.

We may wish to acquire rights to future assets through in-licensing or may attempt to form collaborations in the future with respect to our product candidates, but may not be able to do so, which may cause us to alter or delay our development and commercialization plans.

The development and potential commercialization of our product candidates will require substantial additional capital to fund expenses. We may, in the future, decide to collaborate with biopharmaceutical companies for the development and potential commercialization of product candidates. We will face significant competition in seeking appropriate collaborators. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. If and when we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the following:

- the design or results of clinical trials;
- the likelihood of approval by the FDA or comparable foreign regulatory authorities;
- the potential market for the product candidate;
- the costs and complexities of manufacturing and delivering such product candidate to patients;
- the potential of competing products;
- the existence of uncertainty with respect to our ownership of technology or other rights, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and
- industry and market conditions generally.

The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under any license agreements from entering into agreements on certain terms or at all with potential collaborators. Collaborations are complex and time consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators

and changes to the strategies of the combined company. As a result, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay one or more of our other development programs, delay the potential commercialization or reduce the scope of any planned sales or marketing activities for such product candidate, or increase our expenditures and undertake development, manufacturing or commercialization activities at our own expense. If we elect to increase our expenditures to fund development, manufacturing or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue. Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development approval of a product candidate is delayed, the safety of a product candidate is questioned or sales of an approved product candidate are unsatisfactory.

Risks Related to Our Intellectual Property

Our commercial success depends on our ability to obtain and maintain sufficient intellectual property protection for our product candidates and other proprietary technologies.

Our commercial success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and various foreign jurisdictions such as Europe, China, and Japan with respect to our product candidates, proprietary technologies, and their uses, and the manufacture and formulation thereof, that we develop. If we are unable to obtain or maintain patent protection with respect to our product candidates, proprietary technologies, and their uses, our business, financial condition, results of operations and prospects could be materially harmed. Given that the development of our product candidates, proprietary technologies, and their uses is at an early stage, our intellectual property portfolio with respect to certain aspects of our product candidates and proprietary technologies is also at an early stage.

We generally seek to protect our proprietary position by filing patent applications in the United States, Europe, China, Japan and other foreign jurisdictions related to our product candidates, proprietary technologies and their uses which are important to our business. Our pending and future patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to obtain the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. Obtaining and enforcing patents is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain and/or enforce patents that may issue based on our patent applications, at a reasonable cost or in a timely manner, including as a result of the ongoing COVID-19 pandemic. It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection.

Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, independent contractors, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek adequate patent protection.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including Supreme Court decisions, that have increased uncertainties as to the ability to enforce patent rights in the future. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa.

Further, we may not be aware of all third-party intellectual property rights potentially relating to our research programs and product candidates, or their intended uses, and as a result the potential impact of such third-party intellectual property rights upon the patentability of our own patents and patent applications, as well as the potential impact of such third-party intellectual property upon our freedom to operate, is highly uncertain. Because patent applications are maintained as confidential for a certain period of time (for example, 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), until the relevant application is published, we may be unaware of third-party patents that may be infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no

assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Our patents or pending patent applications may be challenged in the courts or patent offices in the United States, Europe, China, Japan and other foreign jurisdictions. 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, derivations, reexaminations, or inter parties review proceedings, in the United States or oppositions or similar proceedings in foreign jurisdictions, challenging our patent rights. The legal threshold for initiating such proceedings may be low, so that even proceedings with a low probability of success might be initiated. An adverse determination in any such challenges may result in loss of exclusivity or in 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.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop and market our products.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. There can be no assurance that our operations do not, or will not in the future, infringe existing or future third-party patents. Identification of third-party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to our research and other operations or necessary for the commercialization of our product candidates in any jurisdiction.

Numerous U.S. and foreign patents and pending patent applications exist in our market that are owned by third parties. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our products. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. Patent applications in the United States and elsewhere are typically published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Certain U.S. applications that will not be filed outside the U.S. can remain confidential until patents issue. In addition, patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived. Furthermore, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our products or the use of our products. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These patent applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our research programs, product candidates, their respective methods of use, manufacture and formulations thereof, and could result in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

We cannot ensure that patent rights relating to inventions described and claimed in our pending patent applications will be issued or that patents based on our patent applications will not be challenged and rendered invalid and/or unenforceable.

We have patent applications in our portfolio relating to our research programs and product candidates that are pending at the patent offices in the U.S., Europe, China, Japan and other foreign jurisdictions. However, we cannot predict:

- if and when patents may be issued based on our patent applications, including as a result of the delays at the applicable patent office as a result of the ongoing COVID-19 pandemic;
- the scope of protection of any patent issuing based on our patent applications;

- whether the claims of any patent issuing based on our patent applications will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- whether the patent applications that we own or in-license will result in issued patents with claims that cover our product candidates or uses thereof; and/or
- whether, as the COVID-19 pandemic continues to spread around the globe, we may experience patent office interruption or delays to our ability to timely secure patent coverage to our product candidates.

We cannot be certain that the claims in our pending patent applications directed to our product candidates, as well as technologies relating to our research programs will be considered patentable by the USPTO or by patent offices in foreign countries. One aspect of the determination of patentability of our inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim relevant to our business. There is no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. Even if the patents do issue based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our product candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

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

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may allege that we have infringed or misappropriated their intellectual property. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities, and there may be additional delays in such proceeding due to the ongoing COVID-19 pandemic. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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 rights with respect to our products candidates. Third parties may assert infringement claims against us based on existing or future intellectual property rights. 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 use. 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 product candidates, or methods of use 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 able to do this. Proving invalidity of third-party patents may be difficult and uncertain. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in defending our rights in these proceedings, which could have a material adverse effect on our business and operations, including as a result of additional delays in such proceedings due to the ongoing COVID-19 pandemic. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product 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 product 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 a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product 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.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property that relate to our research programs and product candidates, their respective methods of use, manufacture and formulations thereof. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent that we own or have licensed 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 our patents is upheld, the court will construe the claims of our patents 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 at issue. 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. 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 by competitors, a court may decide not to grant an injunction against further infringing activity by competitors 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. Moreover, we cannot assure you 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, and there may be additional delays as a result of the ongoing COVID-19 pandemic. Even if we ultimately prevail in such infringement 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.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing any one of our issued patents or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such an infringement claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Patents are of national or regional effect, and although we have two issued United States patents for our product candidate MET409 and pending patent applications in the United States, Europe, China, Japan and other foreign jurisdictions for both MET409 and MET642, filing, prosecuting and defending patents on all of our research programs and product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These competitor products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Various companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many countries do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights.

Various countries outside the United States have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. As a result, a patent owner may have limited remedies in certain circumstances, 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. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. As such, we do not know the degree of future protection that we will have on our technologies, products and product candidates. While we will endeavor to try to protect our technologies, products and product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time consuming, expensive and unpredictable.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act, or Leahy-Smith Act, was signed into law in the United States. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first inventor to file" system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, including with respect to any delays due to the ongoing COVID-19 pandemic. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either file any patent application related to our product candidates or invent any of the inventions claimed in our patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing 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. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents relating to our research programs and product candidates. Obtaining and enforcing patents in the biopharmaceutical 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, rules and regulations in the United States and other countries could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future. For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained.

Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, 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 governmental fees on patents and/or patent applications will be due to be paid to the USPTO and various foreign patent agencies at various stages over the lifetime of our patents and/or patent applications. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. In addition, the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply with these provisions. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance (including as a result of the ongoing COVID-19 pandemic) can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction, including as a result of failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If such an event were to occur, including with respect to the patents and patent applications covering our research programs and product candidates, as well as their respective methods of use, manufacture and formulations thereof, it could have a material adverse effect on our business, as for example, competitors might be able to enter the market earlier than would otherwise have been the case.

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

We may be subject to claims that former employees, consultants, independent contractors, collaborators or other third parties have an interest in our patents or other intellectual property as an owner, co-owner, inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for our product candidates, our commercial success may be materially harmed.

A patent term extension based on regulatory delay may be available in the United States. Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (the “Hatch-Waxman Act”). The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, only a single patent can be extended for each FDA approved product as compensation for the patent term lost during the FDA regulatory review process, and any patent can be extended only once, for a single product. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the product as approved. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have registered trademarks with the appropriate agencies in the United States, Europe, and China. Our future trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive determined to be infringing on other

marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

Moreover, any name we have proposed to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. 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.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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 product candidates that are similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our future licensors or collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our future licensors or collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors 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;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in-license will result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries;
- the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties;
- if enforced, a court may not hold that our patents are valid, enforceable and infringed;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- 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;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Elements of our

product candidates, including processes for their preparation and manufacture, may involve proprietary know-how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know-how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Trade secrets and unpatented know-how can be difficult to trace, protect and enforce. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We and any third parties with whom we share facilities enter into written agreements that include confidentiality and intellectual property obligations to protect each party's property, potential trade secrets, proprietary know-how and information. We further seek to protect our potential trade secrets, proprietary know-how and information in part, by entering into non-disclosure and confidentiality agreements with parties who are given access to them, such as our corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. With our consultants, contractors and outside scientific collaborators, these agreements typically include invention assignment obligations. Although we have taken steps to protect our trade secrets and unpatented know-how, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets and unpatented know-how, and we may not be able to obtain adequate remedies for such breaches. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. 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 inside and outside the United States are less willing or unwilling to protect trade secrets.

Trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles and the movement of skilled personnel from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. Because from time to time we expect to rely on third parties in the development, manufacture and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. 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 them 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 competitive position would be harmed.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who previously worked with other companies, including our competitors or potential competitors. We could in the future be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of current or former employers or competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an individual to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged intellectual property, proprietary information, know-how or trade secrets of a current or former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management and other employees. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies that are essential to our product candidates, if such technologies are found to incorporate or be derived from the trade secrets or other proprietary information of the current or former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent

discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Although these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will likely expect to be granted rights to publish data arising out of such collaboration, and any joint research and development programs may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

In the future, we may need to obtain additional licenses of third-party technology that may not be available to us or are available only on commercially unreasonable terms, and which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.

From time to time, we may be required to license technologies relating to our therapeutic research programs from additional third parties to further develop or commercialize our product candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our product candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our product candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities, or the ongoing COVID-19 pandemic;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future products or that results 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 current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

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

We are highly dependent on the services of our key personnel.

We are highly dependent on the services of our key personnel, Preston Klassen, M.D., who serves as our President and Chief Executive Officer, Patricia Millican, who serves as our Chief Financial Officer, and Hubert Chen, M.D., who serves as our Chief Medical Officer. Although we have entered into agreements with them regarding their employment, they are not for a specific term and each of them may terminate their employment with us at any time, though we are not aware of any present intention of these individuals to leave us.

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

As of March 31, 2021, we had 39 full-time employees. As we advance our research and development programs, 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, quality, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must:

- identify, recruit, integrate, maintain and motivate additional qualified personnel;
- manage our development efforts effectively, including the initiation and conduct of clinical trials for our product candidates; and
- improve our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to develop, manufacture and commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert financial and other resources, and a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time, to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain third-party contract organizations, advisors and consultants to provide certain services, including assuming substantial responsibilities for the conduct of our clinical trials and the manufacture of our product candidates. We cannot assure you that the services of such third-party contract organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by our vendors or consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of our product candidates or otherwise advance our business. We cannot assure you that we will be able to properly manage our existing vendors or consultants or find other competent outside vendors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

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

Our industry has experienced a high rate of turnover in recent years. Our ability to compete in the highly competitive biopharmaceuticals industry depends upon our ability to attract, retain and motivate highly skilled and experienced personnel with scientific, medical, 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 biopharmaceutical 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 biopharmaceutical companies. Many of the other biopharmaceutical 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 product candidates and to grow our business and operations as currently contemplated.

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) U.S. laws and regulations or those of foreign jurisdictions, 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 or (iv) 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 have adopted a code of conduct applicable to all of our employees, 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, individual 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.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our product candidates before we

receive marketing approval from the applicable regulatory authority in that foreign market, and we may never receive such marketing approval for any of our product candidates. To obtain marketing approval in many foreign countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

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

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

Our internal information technology systems, or those of our third-party CROs, contractors, consultants or others who process sensitive information on our behalf, may fail or suffer security breaches, loss or leakage of data and other compromises, any of which could result in a material disruption of our product candidates' development programs, compromise sensitive information related to our business or prevent us from accessing such information, expose us to liability or otherwise adversely affect our business.*

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we may collect, store, transmit, or otherwise process information (including but not limited to intellectual property, proprietary business information and personal data of employees, clinical trial participants and others). It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such information. We also have outsourced certain of our operations to third parties, and as a result we manage a number of third-parties who have access to our information.

Given our (and that of our third-party CROs, contractors, consultants or others who process sensitive information on our behalf) information technology systems' size and complexity and the increasing amounts of information that they maintain, these systems are potentially vulnerable to breakdown, damage or disruptions caused by several potential sources, such as corruption, system malfunction, natural disasters, public health epidemics (such as the COVID-19 pandemic), terrorism, war, telecommunication and electrical failures, fraudulent activity, cyber-attacks by sophisticated nation-state and nation-state supported actors, as well as security breaches from inadvertent or intentional actions (such as theft or error) by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware (such as malicious code, viruses and worms), phishing attacks, ransomware, denial-of-service attacks, social engineering schemes and other means that affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure as well as lead to unauthorized access, disclosure or acquisition of information. The techniques used to sabotage or to obtain unauthorized access to our information technology systems or those upon whom we rely to process our information change frequently, and we have not always been able in the past and may be unable in the future to anticipate such techniques or implement adequate preventative measures or to stop security breaches in all instances. The recovery systems, security protocols, network protection mechanisms and other security measures that we have integrated into our information technology systems, which are designed to protect against, detect and minimize security breaches, may not be adequate to prevent or detect service interruption, system failure or data loss. Third parties may also attempt to and successfully exploit vulnerabilities in, or obtain unauthorized access to, platforms, systems, networks and/or physical facilities utilized by us or our third-party CROs, contractors, consultants or others upon whom we rely. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, and/or inappropriate disclosure of, or inappropriate access to information, we could incur liability and reputational damage and the further development and commercialization of our drug candidates could be delayed.

We cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems 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, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our or our vendors' information technology systems or security breaches could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the

prevention of access to, information (including trade secrets or other intellectual property, proprietary business information and personal data), which could result in financial, legal, business and reputational harm to us.

We may be required to comply with laws, regulations, rules, industry standards, and other legal obligations that require us to maintain the security of personal data. We may also have contractual and other legal obligations to notify collaborators, our clinical trial participants, or other relevant stakeholders of security breaches. Failure to prevent or mitigate cyberattacks could result in unauthorized access to data, including personal data. Most jurisdictions have enacted laws requiring companies to notify individuals, regulatory authorities, and others of security breaches involving certain types of data. Such disclosures are costly, could lead to negative publicity, may cause our collaborators or other relevant stakeholders to lose confidence in the effectiveness of our security measures and require us to expend significant capital and other resources to respond to and/or alleviate problems caused by the actual or perceived security breach. In addition, the costs to respond to a cybersecurity event or to mitigate any identified security vulnerabilities could be significant, including costs for remediating the effects of such an event, paying a ransom, restoring data from backups, and conducting data analysis to determine what data may have been affected by the breach. In addition, our efforts to contain or remediate a security breach or any vulnerability exploited to cause a breach may be unsuccessful, and efforts and any related failures to contain or remediate them could result in interruptions, delays, harm to our reputation, and increases to our insurance coverage.

In addition, litigation resulting from security breaches may adversely affect our business. Unauthorized access to our information technology systems could result in litigation with our collaborators, our clinical trial participants, or other relevant stakeholders. These proceedings could force us to spend money in defense or settlement, divert management's time and attention, increase our costs of doing business, or adversely affect our reputation. We could be required to fundamentally change our business activities and practices in response to such litigation, which could have an adverse effect on our business. If a security breach were to occur and the confidentiality, integrity or availability of our data or the data of our collaborators were disrupted, we could incur significant liability, which could negatively affect our business and damage our reputation.

Further, failures or significant downtime of our information technology or telecommunication systems or those used by our third-party service providers could cause significant interruptions in our operations and adversely impact the confidentiality, integrity and availability of sensitive or confidential information, including preventing us from conducting clinical trials, tests or research and development activities and preventing us from managing the administrative aspects of our business.

We may not have adequate insurance coverage.*

We may not have adequate insurance coverage or otherwise protect us from, or adequately mitigate, liabilities or damages. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

We are subject to stringent and changing privacy and information security laws, regulations, standards, policies and contractual obligations related to data privacy and security. Our actual or perceived failure to comply with such data privacy and security obligations could lead to government enforcement actions (which could include civil or criminal fines or penalties), a disruption of our clinical trials or commercialization of our products, private litigation, changes to our business practices, increased costs of operations, and adverse publicity that could otherwise negatively affect our operating results and business. Compliance or the failure to comply with such obligations could increase the costs of our products, could limit their use or adoption, and could otherwise negatively affect our operating results and business.*

Regulation of data (including personal data) is evolving, as federal, state, and foreign governments continue to adopt new, or modify existing, laws and regulations addressing data privacy and security, and the collection, processing, storage, transfer, and use of data. These new or proposed laws and regulations are subject to differing interpretations and may be inconsistent among jurisdictions, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data. Moreover, we are subject to the terms of our privacy and security policies, representations, certifications, standards, publications, contracts and other obligations to third parties related to data privacy, security and processing. These and other requirements could require us or our collaborators to incur additional costs to achieve compliance, limit our competitiveness, necessitate the acceptance of more onerous obligations in our contracts, restrict our ability to use, store, transfer, and process data, impact our or our collaborators' ability to process or use data in order to support the provision of our products, affect our or our collaborators' ability to offer our products in certain locations, cause regulators to reject, limit or disrupt our clinical trial activities, result in increased expenses, reduce overall demand for our products, and make it more difficult to meet expectations of relevant stakeholders.

We and any potential collaborators may be subject to federal, state and foreign data protection laws and regulations including, without limitation, laws that regulate personal data such as health data. For example, in the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state personal information laws (e.g., the California Consumer Privacy Act of 2018 ("CCPA")), state data breach notification laws, state health information privacy laws and federal and state consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act), govern the collection, use, disclosure and protection of health-related and other personal data. These laws and regulations could apply to our operations, the operations of our collaborators, or other relevant stakeholders upon whom we depend. In addition, we may obtain personal data (including 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 Health Insurance Portability and Accountability Act ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"). Depending on the facts and circumstances, we could be subject to

significant penalties if we violate HIPPA. Additionally, we could be subject to criminal penalties if we knowingly 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 CCPA became effective on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal data, opt out of certain personal data sharing and receive detailed information about how their personal data is used. The CCPA requires covered businesses to provide new disclosures to California residents. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although there are limited exemptions for clinical trial data and the CCPA's implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, the CCPA may increase our compliance costs and potential liability. It is anticipated that the CCPA will be expanded on January 1, 2023, when the CPRA becomes operative. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive information, establish restrictions on the retention of personal data, expand the types of data breaches subject to the CCPA's private right of action and establish a new California Privacy Protection Agency to implement and enforce the new law. These laws demonstrate our vulnerability to the evolving regulatory environment related to personal data. As we expand our operations, these and similar laws may increase our compliance costs and potential liability.

Foreign data protection laws, such as, without limitation, the EU's GDPR and EU member state implementing legislation, may also apply to health-related and other personal data that we process, including, without limitation, personal data relating to clinical trial participants. European data protection laws impose strict obligations on the ability to process health-related and other personal data of European data subjects, including in relation to security (which requires the adoption of administrative, physical and technical safeguards designed to protect such information), collection, use and transfer or personal data. European data protection laws may affect our use, collection, analysis, and transfer (including cross-border transfer) of such personal data. These include, without limitation, several requirements relating to transparency related to communications with data subjects regarding the processing of their personal data, obtaining the consent of the individuals to whom the personal data relates, limitations on the retention of personal data, increased requirements pertaining to health data, establishing a legal basis for processing, notification of data processing obligations or security incidents to the competent national data protection authorities and/or data subjects, the security and confidentiality of the personal data, various rights that data subjects may exercise with respect to their personal data, and strict rules and restrictions on the transfer of personal data outside of Europe (including from the European Economic Area (EEA), Switzerland and United Kingdom)..

European data protection laws prohibit, without an appropriate legal basis, the transfer of personal data to countries outside of Europe, such as to the United States, which are not considered relevant authorities to provide an adequate level of data protection. A decision by the Court of Justice of the European Union, or the "Schrems II" ruling, invalidated the EU-U.S. Privacy Shield Framework, and raised questions about whether the European Commission's Standard Contractual Clauses, or SCCs, one of the primary alternatives to the Privacy Shield, can lawfully be used for personal data transfers from Europe to the United States or most other countries. Similarly, the Swiss Federal Data Protection and Information Commissioner recently opined that the Swiss-U.S. Privacy Shield is inadequate for transfers of personal data from Switzerland to the U.S. The United Kingdom, whose data protection laws are similar to those of the European Union, has similarly determined that the EU-U.S. Privacy Shield is not a valid mechanism for lawfully transferring personal data from the United Kingdom to the United States. The European Commission recently proposed updates to the SCCs, and additional regulatory guidance has been released that seeks to impose additional obligations on entities that rely on the SCCs. Given that, at present, there are few, if any, alternatives to the SCCs, any transfers by us or our vendors of personal data from Europe may not comply with European data protection laws, which may increase our exposure to such laws' sanctions for violations of its cross-border transfer restrictions and may prohibit our transfer of European personal data outside of Europe, require that we process personal data only with Europe and may adversely impact our operations, product development and ability to provide our products. Additionally, other countries have passed or are considering passing laws requiring local data residency and/or restricting the international transfer of data.

Further, the UK's decision to leave the EU, often referred to as Brexit, and ongoing developments in the UK have created uncertainty regarding data protection regulation in the UK. Following December 31, 2020, and the expiry of transitional arrangements between the UK and EU, the data protection obligations of the GDPR continue to apply to UK-related Processing of personal data in substantially unvaried form under the so-called 'UK GDPR' (i.e., the GDPR as it continues to form part of UK law by virtue of section 3 of the EU (Withdrawal) Act 2018, as amended). However, going forward, there is increasing risk for divergence in application, interpretation and enforcement of the data protection laws as between the UK and EEA. Furthermore, the relationship between the UK and the EEA in relation to certain aspects of data protection law remains uncertain. For example, it is unclear whether transfers of personal data from the EEA to the UK will be permitted to take place on the basis of a future adequacy decision of the European Commission, or whether a 'transfer mechanism' such as the SCCs will be required. Under the post-Brexit Trade and Cooperation Agreement between the EU and the UK, the UK and EU have agreed that transfers of personal data to the UK from EEA member states will not be treated as 'restricted transfers' to a non-EEA country for a period of up to four months from January 1, 2021, plus a potential further two months extension, or the "Extended Adequacy Assessment Period". Although the current maximum duration of the Extended Adequacy Assessment Period is six months, it may end sooner, for example, in the event that the European Commission adopts an adequacy decision in respect of the UK, or the UK amends the UK GDPR and/or makes certain changes regarding data transfers under the UK GDPR/Data Protection Act 2018 without the consent of the EU (unless those amendments or decisions are made simply to keep relevant UK laws aligned with the EU's data protection regime). If the European Commission does not adopt an 'adequacy decision' in respect of the UK prior to the expiry of the Extended Adequacy Assessment Period, from that point onwards the UK will be an 'inadequate third country' under the GDPR and transfers of personal data from the EEA to the UK will require a 'transfer mechanism' such as the Standard Contractual Clauses.

The increase of foreign privacy and security legal frameworks with which we must comply, increases our compliance burdens and exposure to substantial fines and penalties for non-compliance. For example, under the GDPR, entities that violate the GDPR can face fines of up to the greater of 20 million Euros or 4% of their worldwide annual turnover (revenue). Additionally, regulators could prohibit our use of personal data subject to the GDPR. The GDPR has increased our responsibility and potential liability in relation to personal data that we process, requiring us to put in place additional mechanisms to comply with the GDPR and other foreign data protection requirements.

We publish privacy policies and other documentation regarding our collection, processing, use and disclosure of personal data, and/or other confidential information. Although we endeavor to comply with our published policies and documentation, we may at times fail to do so or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our employees or contractors fail to comply with our published policies and documentation. Such failures can subject us to potential foreign, local, state and federal action if they are found to be deceptive, unfair, or misrepresentative of our actual practices.

Compliance with U.S. federal and state as well as foreign data protection 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, or perceived failure, to comply with federal, state, and foreign data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties, fines or penalties), private litigation, a diversion of management attention, adverse publicity and negative effects on our operating results and business. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages if we fail to comply with applicable data protection laws, privacy policies or data protection obligations related to information security or security breaches. Moreover, clinical trial participants or subjects about whom we or our collaborators obtain information, as well as the providers who share this information with us, may limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, contracts, privacy notices, or breached other 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. Compliance with data protection laws may be time consuming, require additional resources and could result in increased expenses, reduce overall demand for our products and make it more difficult to meet expectations of or commitments to our relevant stakeholders.

Any of these matters could adversely affect materially our business, financial condition, or operational results.

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

Our headquarters and main research facility are located in the greater San Diego area, which in the past has experienced severe earthquakes and fires. If these earthquakes, fires, other natural disasters, health pandemics or epidemics, terrorism and similar unforeseen events beyond our control, including for example the ongoing COVID-19 pandemic, prevented us from using all or a significant portion of our headquarters or research facility, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We do not have a disaster recovery or business continuity plan in place and may incur substantial expenses as a result of the absence or limited nature of our internal or third party service provider disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our ability to conduct our clinical trials, our development plans and business.

Our ability to use our net operating loss carryforwards and certain other tax attributes to offset future taxable income or taxes 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 losses for tax years beginning on or prior to December 31, 2017 will carry forward to offset future taxable income, if any, until such unused losses expire. Under legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, as modified by the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, unused federal losses generated in tax years beginning after December 31, 2017 may be carried forward indefinitely but the deductibility of such federal net operating loss carryforwards, or NOLs, in tax years beginning after December 31, 2020 is limited to 80% of current year taxable income. Also, under the CARES Act, NOLs arising in 2018, 2019 and 2020 can be carried back five years. Many states have similar laws. 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, or 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 not completed a Section 382 study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since our formation due to the complexity and cost associated with such a study and the fact that there may be additional such ownership changes in the future. As a result, if we earn net taxable income our NOLs generated in tax years beginning before December 31, 2017 may expire prior to being used, our NOLs generated tax years beginning after December 31, 2017 will be subject to a percentage limitation in tax years beginning after December 31, 2020 and, if we undergo an ownership change (or if we previously underwent an ownership change), our ability to use all of our pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes may be limited. 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 NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. As a result,

even if we attain profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

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

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

- delay or termination of clinical trials;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial subjects;
- initiation of investigations by regulators;
- significant costs to defend the related litigation and diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We currently hold $10 million in aggregate product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as our product candidates advance through clinical trials and if we successfully commercialize any products. 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.

Changes in healthcare law and implementing regulations, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and may have a significant adverse effect on our business and results of operations.*

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Among policy makers and payors in the United States and elsewhere, including in the EU, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "Affordable Care Act") substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things: (i) introduced a new average manufacturer price definition for drugs and biologics that are inhaled, infused, instilled, implanted or injected and not generally dispensed through retail community pharmacies; (ii) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and expanded rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well; (iii) established a branded prescription drug fee that pharmaceutical manufacturers of branded prescription drugs must pay to the federal government; (iv) expanded the list of covered entities eligible to participate in the 340B drug pricing program by adding new entities to the program; (v) established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts (which through subsequent legislative amendments, was increased to 70% from 50%) 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; (vi) extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; (vii) expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (viii) created a licensure framework for follow on biologic products; and (ix) established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services (CMS) to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, the Tax Cuts and Jobs Act included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Further, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. Moreover, on December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act. On December 18, 2019, the U.S. Court of Appeals for the

5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The United States Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. On February 10, 2021, the Biden administration withdrew the federal government's support for overturning the Affordable Care Act. Although the Supreme Court has not yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and will remain open through August 15, 2021. The executive order also instructs 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 Affordable Care Act. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and our business..

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011 and subsequent laws, which began in 2013 and will remain in effect through 2030, unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2021. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

New laws may result in additional reductions in Medicare and other healthcare funding, which may materially adversely affect customer demand and affordability for our products and, accordingly, the results of our financial operations. Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, 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. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the Department of Health and Human Services ("HHS") finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, individual states in the United States are increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs, once marketing approval is obtained.

In the EU, coverage and reimbursement status of any product candidates for which we obtain regulatory approval are provided for by the national laws of EU Member States. The requirements may differ across the EU Member States. Also at a national level, actions have been taken to enact transparency laws regarding payments between pharmaceutical companies and health care professionals.

We will be subject to applicable fraud and abuse, transparency, government price reporting and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.*

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any future product candidates for which we obtain marketing approval. Our current and future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may affect the business or

financial arrangements and relationships through which we would research, market, sell and distribute our products. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has also been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other the other hand. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal civil and criminal false claims laws, such as the False Claims Act ("FCA"), and civil monetary penalty laws, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, false, fictitious or fraudulent claims for payment or approval by the federal government, and knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. For example, pharmaceutical companies have been prosecuted under the FCA in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Criminal prosecution is also possible for making or presenting a false, fictitious or fraudulent claim to the federal government. Government enforcement agencies and private whistleblowers have investigated pharmaceutical companies for or asserted liability under the FCA for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product, providing consulting fees and other benefits to physicians to induce them to prescribe products, engaging in promotion for "off-label" uses, and submitting inflated best price information to the Medicaid Rebate Program. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;
- HIPAA, among other things, imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by HITECH and its implementing regulations, which imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon entities subject to the law, such as health plans, healthcare clearinghouses and certain healthcare providers and their respective business associates that perform services for them that involve individually identifiable health information, as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys; general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the federal transparency requirements under the Physician Payments Sunshine Act, which requires, among other things, certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid, or the Children's Health Insurance Program to annually report to HHS information related to payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and physician ownership and investment interests, including such ownership and investment interests held by a physician's immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding its payments and other transfers of value during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives; and
- analogous state and foreign laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state and foreign laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, track and report gifts,

compensation and other remuneration provided to physicians, other health care providers and other health care entities, or drug pricing, and/or ensure the registration and compliance of sales personnel and other federal, state and foreign laws that govern the privacy and security of health information or personally identifiable information in certain circumstances, including state health information privacy and data breach notification laws which govern the collection, use, disclosure and protection of health-related and other personal information, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus requiring additional compliance efforts.

We have entered into consulting and scientific advisory board arrangements with physicians and other healthcare providers, some of whom are compensated with stock options including some who could influence the use of our product candidates, if approved. Because of the complex and far-reaching nature of these laws, regulatory agencies may view these transactions as prohibited arrangements that must be restructured, or discontinued, or for which we could be subject to other significant penalties. We could be adversely affected if regulatory agencies interpret our financial relationships with providers who may influence the ordering of and use our product candidates, if approved, to be in violation of applicable laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies, healthcare providers and other third parties, including charitable foundations, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time- and resource-consuming and can divert management's attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. If our operations are found to be in violation of any of these laws or any other current or future governmental laws and 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, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could substantially disrupt our 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.

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, collectively, Trade Laws, 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 Trade 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.

Requirements associated with being a public company will increase our costs significantly, as well as divert significant company resources and management attention.

We are subject to the reporting requirements of the Exchange Act, or the other rules and regulations of the SEC, or any securities exchange relating to public companies. Sarbanes-Oxley, as well as rules subsequently adopted by the SEC, and The Nasdaq Global Market to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Compliance with the various reporting and other requirements applicable to public companies requires considerable time and attention of management. We cannot assure you that we will satisfy our obligations as a public company on a timely basis.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. In addition, as a public company, it may

be more difficult or more costly for us to obtain certain types of insurance, including directors' and officers' liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified personnel to serve on our board of directors, our board committees or as executive officers.

We may also be subject to more stringent state law requirements. For example, on September 30, 2018, California Governor Jerry Brown signed into law Senator Bill 826, which generally requires public companies with their principal executive office in California to have a minimum number of females on the company's board of directors. Each public company with principal executive offices in California is required to have at least one female on its board of directors, and by December 31, 2021, will be required to have at least two females on its board of directors if the company has at least five directors, and at least three females on its board of directors if the company has at least six directors. Additionally, on September 30, 2020, California enacted AB 979, requiring public companies with their principal executive office in California to each have at least one director from an underrepresented community based on ethnicity and sexual orientation by December 31, 2021. By December 31, 2022, each of these companies will be required to have at least two directors from such underrepresented communities if such company has more than four but fewer than nine directors, or at least three directors from underrepresented communities if the company has nine or more directors. The new law does not provide a transition period for newly listed companies. The current composition of our board of directors includes two female directors and one director from underrepresented communities. In order to meet the requirements of applicable California law, we expect to onboard the requisite number of female and diverse directors. If we fail to comply with these new laws, we could be fined by the California Secretary of State, with a $100,000 fine for the first violation and a $300,000 fine for each subsequent violation, and our reputation may be adversely affected. We cannot assure that we can recruit, attract and/or retain qualified members of the board and meet gender and diversity quotas as required by California law (provided that such laws are not repealed before the compliance deadlines), which may cause certain investors to divert their holdings in our securities and expose us to financial penalties and/or reputational harm.

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

We, and the third parties with whom we share our facilities, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Each of our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Each of 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. We could be held liable for any resulting damages in the event of contamination or injury resulting from the use of hazardous materials by us or the third parties with whom we share our facilities, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

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

Risks Related to our Common Stock

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

Prior to the completion of our IPO, there was no public market for our common stock. We cannot assure you that an active or liquid market in our common stock will develop, or if it does develop, it may not be sustainable. Our stock price has been, and in the future, may be volatile. 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 of our common stock may fluctuate significantly in response to numerous factors, many of which are beyond our control, including:

- limited daily trading volume resulting in the lack of a liquid market
- our operating performance and the performance of other similar companies;
- our ability to enroll subjects in our ongoing and planned clinical trials;
- results from our ongoing clinical trials and future clinical trials with our current and future product candidates or of our competitors;
- changes in our projected operating results that we provide to the public, our failure to meet these projections or changes in recommendations by securities analysts that elect to follow our common stock;
- regulatory or legal developments in the United States and other countries, including changes in the structure of healthcare payment systems;
- the level of expenses related to future product candidates or clinical development programs;
- our ability to achieve product development goals in the timeframe we announce;

- announcements of clinical trial results, regulatory developments, equity offerings, debt financings, acquisitions, strategic alliances or significant agreements by us or by our competitors;
- the success or failure of our efforts to acquire, license or develop additional product candidates;
- recruitment or departure of key personnel;
- the economy as a whole and market conditions in our industry;
- 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;
- trading activity by a limited number of stockholders who together beneficially own a significant amount of our outstanding common stock;
- the expiration of market standoff or contractual lock-up agreements;
- the size of our market float; and
- any other factors or events, including those described in this “Risk Factors” section.

In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many life sciences companies. Stock prices of many biopharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. For example, the ongoing COVID-19 pandemic has negatively affected the stock market and investor sentiment and has resulted in significant volatility. The price of our common stock may be disproportionately affected as investors may favor traditional profit-making industries and companies during times of market uncertainty and instability. In the past, stockholders have filed securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs, divert resources and the attention of management from our business and adversely affect our business.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, additional borrowings under our loan agreement, collaborations and other similar arrangements. 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. Additional debt financing, if available, may involve agreements that include covenants further limiting or restricting our ability to take specific actions beyond those contained in our existing loan agreement, such as further limitations on our ability to incur additional debt, make capital expenditures or declare dividends.

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

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We currently have research coverage from a limited number of securities or industry analysts. If no or only very few securities analysts commence coverage of us, or if industry analysts cease coverage of us, the trading price for our common stock would be negatively affected. 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 disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a non-binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved.

In addition, as an "emerging growth company" the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. We have not elected to use this extended transition period under the JOBS Act.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (a) December 31, 2025, (b) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion or (c) the date on which we first qualify as a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We do not intend to pay dividends for the foreseeable future.

We have never declared nor paid cash dividends on our capital stock. We currently intend to retain any future earnings to finance the operation and expansion of our business, and we do not expect to declare or pay any dividends in the foreseeable future. In addition, the terms of our loan agreement with K2 preclude us from paying cash dividends. Consequently, stockholders must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment.

The concentration of our stock ownership will likely limit your ability to influence corporate matters, including the ability to influence the outcome of director elections and other matters requiring stockholder approval.

Our executive officers and directors, combined with our stockholders who owned more than 5% of our outstanding capital stock beneficially own shares representing a significant percentage of our common stock. As a result, these stockholders, acting together, will have significant influence over all matters that require approval by our stockholders, including the election of directors and approval of significant corporate transactions. Corporate actions might be taken even if other stockholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other stockholders may view as beneficial.

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 the 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 chairman of the board, 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 (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) and any appellate court therefrom will be the sole and exclusive forum for the following claims or causes of action under the Delaware statutory or common law: (i) any derivative claim or cause of action brought on our behalf; (ii) any claim or cause of action for 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 claim or cause of action 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 (each as may be amended from time to time); (iv) any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws (as each may be amended from time to time, including any right, obligation, or remedy thereunder); (v) any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware; and (vi) any claim or cause of action 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; provided, that, this Delaware forum provision set forth in our of our amended and restated certificate of incorporation and amended and restated bylaws will not apply to claims or causes of action brought to enforce a duty or liability created by the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

Further, our amended and restated certificate of incorporation provides that unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States will be the exclusive forum for resolution of any complaint asserting a cause of action arising under the Securities Act.

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, or Section 203. 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 acquirors 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 may 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 the Court of Chancery of the State of Delaware (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) and any appellate court therefrom shall be the sole and exclusive forum for the following claims or causes of action under the Delaware statutory or common law: (i) any derivative claim or cause of action brought on our behalf, (ii) any action claim or cause of action for breach of fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders, (iii) any claim or cause of action 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 (as each may be amended from time to time); (iv) any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws (as each may be amended from time to time, including any right, obligation, or remedy thereunder); (v) any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware and (vi) any claim or cause of action against us or any of our directors, officers or other employees that is governed by the internal-affairs doctrine; provided, that this Delaware forum provision set forth in our amended and restated certificate of incorporation will not apply to claims or causes of action brought to enforce a duty or liability created by the Securities Act or the Exchange Act, or

any other claim for which the federal courts have exclusive jurisdiction. Further, our amended and restated certificate of incorporation provides that unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States will be the exclusive forum for resolution of any complaint asserting a cause of action arising under the Securities Act. 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 additional costs associated with resolving such action in other jurisdictions.

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 biopharmaceutical 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.

Not applicable.

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	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39512) filed with the SEC on September 18, 2020).
3.2	Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-39512) filed with SEC on September 18, 2020).
4.1	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. 333-248292), filed with the SEC on September 9, 2020).
4.2	Amended and Restated Investor Rights Agreement, dated August 26, 2019, by and among the Registrant and certain of its stockholders (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-248292), filed with the SEC on August 24, 2020).
4.3	Warrant to Purchase Preferred Stock, dated August 27, 2019, issued to K2 Health Ventures Equity Trust LLC (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-248292), filed with the SEC on August 24, 2020).
10.1+	Amended and Restated Consulting Agreement by and between the Registrant and Jeff Jonker dated March 10, 2021.
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1	Certification of Principal Executive Officer and Principal Financial Officer Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. Section 1350.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ Indicates management contract or compensatory plan.

SIGNATURES

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

Metacrine, Inc.

Date: May 13, 2021

By: /s/ Preston Klassen
Preston Klassen, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 13, 2021

By: /s/ Patricia Millican
Patricia Millican
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 10.1

METACRINE, INC.

AMENDED AND RESTATED CONSULTING AGREEMENT

THIS AMENDED AND RESTATED CONSULTING AGREEMENT (this "**Agreement**") is made as of March 10, 2021 (the "**Effective Date**") by and between **METACRINE, INC.**, a Delaware corporation (the "**Company**") located at 3985 Sorrento Valley Blvd, Suite C, San Diego, California 92121, and Jeff Jonker ("**Consultant**") an individual.

Whereas, the Company and Consultant entered into that certain Consulting Services Agreement dated December 9, 2020 (the "**Original Agreement**"); and

Whereas, the parties desire to amend certain terms of the Original Agreement. Accordingly, Company and Consultant agree as follows:

1. ENGAGEMENT OF SERVICES. Consultant agrees to provide consulting services to Company as described in **Exhibit A** hereto (collectively, the "**Services**") during the term of this Agreement. It is anticipated that Consultant will provide up to eight (8) hours of Services per week. Consultant may not subcontract or otherwise delegate Consultant's obligations under this Agreement without Company's prior written consent as it in its sole discretion determines. Consultant shall at all times use commercially reasonable best efforts and all due diligence in performing the Services. All Services shall be performed in accordance with (i) generally accepted professional standards and applicable laws, rules and regulations; (ii) Company policies and procedures; and (iii) to Company's reasonable satisfaction. To the extent any of the Services require Consultant to possess any professional or other licenses, Consultant shall maintain such licensure(s) in good standing throughout the Term (as defined herein).

2. COMPENSATION. In consideration of satisfactorily performing the Services, Company will pay to Consultant the fees on the schedule specified in **Exhibit A** hereto ("**Fees**"). Company will reimburse reasonable out-of-pocket expenses, if any, incurred by Consultant in the performance of the Services provided such are pre-approved in writing by Company ("**Authorized Expenses**") (Fees and Authorized Expenses, collectively, the "**Compensation**"). The Compensation shall be Consultant's sole remuneration unless the parties agree otherwise in writing. Consultant shall submit invoices to Company on a monthly basis for all Services provided and Authorized Expenses incurred during the preceding month. Each invoice shall include a detailed description of the Services performed delineated by project or task, as applicable, and a detailed description of the Authorized Expenses with all required receipts. All invoices must be sent to: ap@metacrine.com. Payment terms are net thirty (30) days. Consultant understands that Company will report Consultant's compensation and reimbursed expenses under this Agreement to the extent Company, in its sole opinion, believes that it is required to do so by applicable laws or regulations.

3. INDEPENDENT CONTRACTOR RELATIONSHIP. Consultant's relationship with Company will be that of an independent contractor and not an employee of Company for any purpose. Consultant is not the agent of Company and is not authorized to make any representation, contract, or commitment on behalf of Company. Consultant will not be entitled to any of the benefits that

Company may make available to its employees. Because Consultant is an independent contractor, Company will not withhold or make payments for social security, make unemployment insurance or disability insurance contributions, or obtain worker's compensation insurance on Consultant's behalf. Consultant accepts exclusive liability for complying with all applicable state and federal laws governing self-employed individuals and agrees to indemnify and defend Company against any and all such taxes or contributions, including penalties and interest.

4. CONFIDENTIALITY.

4.1 Definition. "**Proprietary Information**" means: (a) trade secrets, inventions, mask works, ideas, processes, formulas, source and object codes, data, programs, other works of authorship, know-how, improvements, discoveries, developments, designs and techniques; (b) information regarding plans for research, development, new products, marketing and selling, business plans, budgets and nonpublic financial statements, licenses, prices and costs, suppliers, partners and customers; and (c) information regarding the skills and compensation of other employees of Company. In addition, and notwithstanding any other provision of this Agreement to the contrary, Inventions and Materials (defined below) shall constitute Proprietary Information.

4.2 Non-Use and Non-Disclosure. Consultant agrees that during the Term of this Agreement and for a period of five (5) years after the termination hereof, that it will take all steps reasonably necessary to hold Company's Proprietary Information in trust and confidence, will not use Proprietary Information in any manner or for any purpose not expressly set forth in this Agreement, and will not disclose any such Proprietary Information to any third party without first obtaining Company's express written consent. Consultant agrees that Proprietary Information shall remain the sole property of Company. Consultant further agrees to take all reasonable precautions to prevent any unauthorized disclosure of Proprietary Information.

4.3 Third Party Information. Consultant understands that Company has received and will in the future receive from third parties confidential or proprietary information ("**Third Party Information**") subject to a duty on Company's part to maintain the confidentiality of such information and use it only for certain limited purposes. Consultant agrees to hold Third Party Information in confidence and not to disclose to anyone (other than Company personnel who need to know such information in connection with their work for Company) or to use, except in connection with Consultant's work for Company, Third Party Information unless expressly authorized in writing by an officer of Company.

4.4 Return of Information. Consultant shall upon termination of this Agreement or as earlier requested by Company, return to Company any and all parts of the Proprietary Information provided by Company and will return or destroy (and provide a certificate of destruction) any copies or other tangible or electronic embodiments thereof; provided that Consultant may retain one (1) copy of Company's Proprietary Information for archival purposes, subject to the ongoing obligations of nondisclosure and nonuse. In the event Consultant has any additional copies on Consultant's standard computer backup systems, if not possible to destroy those copies, Consultant

must ensure that access to those backup copies is denied.

5. INTELLECTUAL PROPERTY.

5.1 Ownership of Inventions and Materials. As used herein "**Inventions and Materials**" means all works conceived, created, produced, discovered or tendered by Consultant pursuant to this Agreement in performing the Services hereunder, including without limitation, any copyrightable material, deliverables, software, notes, records, writings, reports, programs, drawings, designs, inventions, improvements, developments, discoveries, trade secrets, etc. in all media formats (paper, computer file, disk, tape, etc.) Consultant agrees that all such Inventions and Materials are the sole and exclusive property of Company. Consultant shall promptly disclose all Inventions and Materials to Company and hereby irrevocably assigns, sells and transfers exclusively to Company all right, title, and interest including, without limitation all copyrights and worldwide intellectual property rights for perpetuity (or for the longest period of time otherwise permitted by law) in the Inventions and Materials. For avoidance of doubt, Inventions and Materials shall not include any pre-existing works (or inventions thereto) independently developed by Consultant outside of the course and scope of this Agreement and made without the use of any Company Proprietary Information, materials, supplies, facilities or equipment, the title and interest of which shall vest in Consultant. Consultant warrants and represents that none of the Services or any Inventions or Materials provided to Company hereunder shall infringe or misappropriate any third-party intellectual property rights.

5.2 Assignment. Consultant agrees to assign (or shall cause to be assigned) and does hereby assign fully to Company all Inventions and Materials and any copyrights, patents, trade secrets, mask work rights and other intellectual property rights relating thereto. Consultant shall deliver the originals and all copies of the same to Company upon the termination of this Agreement. Consultant hereby assigns and agrees to assign to Company or its designee all rights including copyright in any such information and materials.

5.3 Assistance. Consultant agrees to assist Company, or its designee, at the Company's expense, in every proper way to secure Company's rights in the Inventions and Materials and any copyrights, patents, mask work rights or other intellectual property rights relating thereto in any and all countries, including the disclosure to Company of all pertinent information and data with respect thereto, the execution of all applications, specifications, oaths, assignments and all other instruments which Company shall deem necessary in order to apply for and obtain such rights and in order to assign and convey to Company, its successors, assigns and nominees the sole and exclusive right, title and interest in and to such Inventions and Materials, and any copyrights, patents, mask work rights or other intellectual property rights relating thereto. Consultant further agrees that Consultant's obligation to execute or cause to be executed, when it is in Consultant's power to do so, any such instrument or papers shall continue after the termination of this Agreement. Consultant agrees that if Company is unable because of Consultant's unavailability, dissolution, incapacity, or for any other reason, to secure Consultant's signature to apply for or to pursue any application for any United States or foreign patents or mask work or copyright registrations covering the Inventions and Materials assigned to Company and its duly authorized officers and agents as Consultant's agent and attorney in fact, to act for and in Consultant's behalf and stead to execute and file any such applications and to do all other lawfully permitted acts to further the prosecution and issuance of patents, copyright and mask work registrations thereon with the same legal force and effect as if

executed by Consultant.

5.4 License. Consultant agrees that if in the course of performing the Services, Consultant incorporates into any Inventions and Materials developed hereunder any invention, improvement, development concept, discovery or other proprietary information owned by Consultant or in which Consultant has an interest, Company is hereby granted and shall have a nonexclusive, royalty-free, fully paid-up, perpetual, irrevocable, worldwide license, with right to sublicense, to reproduce, prepare derivative works of, publicly perform, publicly display in any form or medium, whether now known or later developed, distribute (by any means known or hereafter developed, including without limitation electronic and Internet distribution), make have made, use, sell, offer for sale, and import such item as part of or in connection with such Inventions and Materials.

5.5 Publications. Consultant shall not present or publish, or submit for publication, any work describing or resulting from the Services without the prior written consent of Company.

6. Conflict of Interest. Consultant represents and warrants that the terms of this Agreement do not violate the terms of any other contractual or legal obligation Consultant may owe to any employer, affiliated institute or other third party or any applicable policy of such employer, affiliated institution or third party. Consultant agrees, during the term of this Agreement, not to accept work or enter into a contract or accept an obligation, inconsistent or incompatible with Consultant's obligations under this Agreement or the scope of Services rendered for Company. In no event shall Consultant use in the performance of the Services, disclose to Company, or induce Company to use any confidential information that belongs to anyone other than Company or Consultant. Consultant will indemnify Company and hold it harmless from and against all claims, liabilities, damages and expenses, including reasonable attorneys' fees and costs of suit, arising out of or in connection with any violation or claimed violation by Company of such third party's rights resulting in whole or in part from Company's use of the work product or deliverables provided by Consultant under this Agreement.

7. Sanctions or Debarment. Consultant represents and warrants that Consultant is not and has never been: (i) sanctioned by the Office of Inspector General ("**OIG**") of the Department of Health and Human Services, barred from participating in government health care programs, or convicted of a criminal offense with respect to health care reimbursement; or (ii) debarred under Section 306(a) or (b) of the Federal Food, Drug and Cosmetic Act, or a stockholder in, or otherwise affiliated with any person or entity who has been so debarred. Consultant shall immediately notify Company, in writing, if the foregoing representation becomes untrue, or if Consultant is notified by the OIG, the FDA or other enforcement agency that an investigation of Consultant has begun which could lead to such sanction, debarment or conviction.

8. Compliance with Law. Each party shall perform its obligations under this Agreement in compliance with all applicable federal and state laws, regulations, guidance, and ethical standards. The parties acknowledge and agree that the Services do not involve the counseling or

promotion of any activity that violates any state or federal law.

9. TERMINATION.

9.1 Term. The term of this Agreement shall commence on December 9, 2020 and shall remain in full force and effect until May 9, 2021 unless terminated earlier as set forth below ("**Term**").

9.2 Termination of Agreement. Either party may terminate this Agreement for convenience, for any or no reason, at any time upon thirty (30) days prior written notice to the other party. Either party may terminate this Agreement for cause upon written notice to the other party, if the other party breaches this Agreement and does not cure the breach within thirty (30) days following receipt of written notice thereof from the non-breaching party. Such right to terminate this Agreement for cause shall be in addition to any other remedies available to the terminating party at law or in equity.

9.3 Noninterference with Business. During the term of this Agreement and for a period of one (1) year immediately following termination of this Agreement by either party, Company and Consultant agree not to solicit or induce any employee or independent contractor to terminate or breach an employment, contractual, or other relationship with the non-soliciting party.

9.4 Pre-Existing Rights; Survival. The termination of this Agreement shall not affect in any way the rights and obligations of either party which have accrued prior to such event or in connection therewith. The following provisions shall survive termination of this Agreement and all definitions necessary to interpret the foregoing: Sections 3, 4, 5, 6, 9.3, 9.4 and 10.

10. GENERAL PROVISIONS.

10.1 Governing Law. This Agreement will be governed by and construed in accordance with the laws of the State of California as applied to transactions taking place wholly within California between California residents.

10.2 Insurance. Upon Company's written request to Consultant, Consultant shall secure and maintain at Consultant's expense commercial general liability and professional liability (errors and omissions) insurance in an amount adequate to cover all loss, damage, liability or costs with respect to the Services performed hereunder within thirty (30) days of such written request. Such insurance shall be with insurers with an A.M. Best rating of A-VIII or better, or equivalent from another rating body. If any insurance required hereunder is on a "claims made basis," Consultant shall arrange for an extended reporting period for four (4) years after the termination of this Agreement. At Company's request, Consultant shall furnish to Company true and correct copies of the certificates of insurance indicating such coverage.

10.3 Product Information/Adverse Event Reporting. To the extent any Services performed by Consultant pursuant to this Agreement result in Consultant's collection, receipt or other form of knowledge of any information about Company's medicinal or biological product(s) ("**Product(s)**"), from any source, in any form, relating to a Medication Error, Product Adverse Events, Product Quality Complaints, and/or Pregnancy Information ("**Reportable Information**"), Consultant represents and warrants that it shall cooperate with Company as set forth in this

provision. Consultant shall preserve the original record of such Reportable Information and within one (1) business day of the day on which such Reportable Information was received or otherwise became known to Consultant, submit a copy of such records and information to Company: (i) identifying and providing full contact information for both the person receiving the Reportable Information and the Consultant personnel submitting it to Company; (ii) stating the date on which the Reportable Information was received by Consultant, and (iii) describing the Product(s) in question and the event underlying the Reportable Information, including identifying the subject thereof. For purposes of this Section, the capitalized terms used herein shall have the following definitions: (1) an "**Adverse Event**" is any undesirable event or experience associated with the use of Product(s) in humans, whether or not expected, and whether or not considered related to or caused by the Product(s), including, but not limited to, an event or experience that occurs in the course of the use of the Product(s) in professional medical practice, including without limitation, from overdose whether accidental or intentional, from abuse, from withdrawal, from a failure of expected pharmacological or biological therapeutic action of the Product(s); (2) a "**Medication Error**" is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer (whether related to professional medical practice, health care products, procedures, and systems including: prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring; and use of Product(s) or otherwise); (3) "**Pregnancy Information**" is any information pertaining to a patient's experience with Product(s) during or affecting pregnancy and (4) a "**Product Quality Complaint**" is any expression of dissatisfaction with the quality of a Product(s) or a reported failure of Product(s) attributes or specifications.

10.4 Severability. In case any one or more of the provisions contained in this Agreement shall, for any reason, be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect the other provisions of this Agreement, and this Agreement shall be construed as if such invalid, illegal, or unenforceable provision had never been contained herein. If moreover, any one or more of the provisions contained in this Agreement shall for any reason be held to be excessively broad as to duration, geographical scope, activity, or subject, it shall be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it shall then appear.

10.5 No Assignment. This Agreement may not be assigned by Consultant without Company's consent, and any such attempted assignment shall be void and of no effect. The Company may assign its rights and obligations hereunder to an affiliate or to any person or entity that succeeds to all or substantially all of the Company's business to which this Agreement relates, whether by merger, acquisition or other means.

10.6 Notices. All notices, requests, and other communications under this Agreement must be in writing and must be mailed by registered or certified mail, postage prepaid and return receipt requested, or delivered by hand to the party to whom such notice is required or permitted to be given. If mailed, any such notice will be considered to have been given five (5) business days after it was mailed, as evidenced by the postmark. If delivered by hand, any such notice will be considered to have been given when received by the party to whom notice is given, as evidenced by written and dated receipt of the receiving party. The mailing address for notice to either party will be the address shown on the signature page of this Agreement. Either party may change its

mailing address by notice as provided by this section.

10.7 Legal Fees. If any dispute arises between the parties with respect to the matters covered by this Agreement which leads to a proceeding to resolve such dispute, the prevailing party in such proceeding shall be entitled to receive its reasonable attorneys' fees, expert witness fees, and out-of-pocket costs incurred in connection with such proceeding, in addition to any other relief it may be awarded.

10.8 Injunctive Relief. A breach of any of the promises or agreements contained in this Agreement may result in irreparable and continuing damage to Company for which there may be no adequate remedy at law, and Company is therefore entitled to seek injunctive relief as well as such other and further relief as may be appropriate.

10.9 Waiver. No waiver by Company of any breach of this Agreement shall be a waiver of any preceding or succeeding breach. No waiver by Company of any right under this Agreement shall be construed as a waiver of any other right. Company shall not be required to give notice to enforce strict adherence to all terms of this Agreement.

10.10 Entire Agreement. This Agreement is the final, complete, and exclusive agreement of the parties with respect to the subject matter hereof. This Agreement supersedes all prior discussions between the parties. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing and signed by the party to be charged. The terms of this Agreement will govern all Services undertaken by Consultant for Company.

[REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

In Witness Whereof, the parties have caused this Consulting Agreement to be executed by their duly authorized representative.

Metacrine, Inc.

By: /s/ Preston Klassen
Preston Klassen, President and CEO

Address: 3985 Sorrento Valley Blvd, Suite C, San Diego, CA 92121

Consultant

By: /s/ Jeff Jonker
Jeff Jonker

EXHIBIT A

SERVICES

Consultant will provide one or more of the following services, as reasonably requested by Company:

- Serve as a senior advisor to the Company in the area of corporate and business development.
- Other projects to be determined by mutual agreement between Consultant and the Chief Executive Officer or their designee.

Compensation:

A. Company will pay Consultant a consulting fee of ten thousand dollars ($10,000) per month during the Term. It is anticipated that Consultant will provide up to eight (8) hours of Services per week. The Consulting fee shall be payable monthly within 30 days of Company receiving an invoice from Consultant detailing the Services provided and the time spent providing such Services, and all of which fees shall be net of any withholding taxes (if applicable).

B. Company will reimburse Consultant for all reasonable expenses, including non-local travel, incurred by Consultant in performing the Services pursuant to this Agreement, provided that Consultant receives written consent from Company's Chief Executive Officer or authorized representative prior to incurring such expenses and submits receipts for such expenses to Company in accordance with Company policy.

Exhibit 31.1

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, Preston Klassen, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 of Metacrine, 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)) 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) 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

   (c) 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 13, 2021

By: /s/ Preston Klassen
Preston Klassen, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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, Patricia Millican, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 of Metacrine, 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)) 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) 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

   (c) 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 13, 2021

By: /s/ Patricia Millican
Patricia Millican
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

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

In connection with the Quarterly Report of Metacrine, Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2021 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 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: May 13, 2021

By: /s/ Preston Klassen
Preston Klassen, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 13, 2021

By: /s/ Patricia Millican
Patricia Millican
Chief Financial Officer
(Principal Financial and Accounting Officer)