

**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 September 30, 2023

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: 001-38916

**Bicycle Therapeutics plc**

(Exact Name of Registrant as Specified in its Charter)

**England and Wales**

(State or other jurisdiction of  
incorporation or organization)

**Blocks A & B, Portway Building, Granta Park  
Great Abington, Cambridge, United Kingdom**  
(Address of principal executive offices)

**Not Applicable**

(I.R.S. Employer  
Identification No.)

**CB21 6GS**  
(Zip Code)

Registrant's telephone number, including area code: +44 1223 261503

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value £0.01 per share*	n/a	The Nasdaq Stock Market LLC
American Depositary Shares, each representing one ordinary share, nominal value £0.01 per share	BCYC	The Nasdaq Stock Market LLC

\* Not for trading, but only in connection with the listing of the American Depositary Shares on the Nasdaq Global Select Market.

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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   
Non-accelerated filer

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

As of October 30, 2023, the registrant had 37,715,666 ordinary shares, nominal value £0.01 per share, and 4,705,882 non-voting ordinary shares, nominal value £0.01 per share, outstanding.

**Table of Contents**

	<u>Page</u>
<b><u>PART I - FINANCIAL INFORMATION</u></b>	<b><u>1</u></b>
<u>Item 1. Financial Statements (unaudited)</u>	1
<u>Condensed Consolidated Balance Sheets</u>	1
<u>Condensed Consolidated Statements of Operations and Comprehensive Loss</u>	2
<u>Condensed Consolidated Statements of Shareholders' Equity</u>	3
<u>Condensed Consolidated Statements of Cash Flows</u>	5
<u>Notes to Condensed Consolidated Financial Statements</u>	6
<u>Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	38
<u>Item 3. Quantitative and Qualitative Disclosure About Market Risk</u>	54
<u>Item 4. Controls and Procedures</u>	55
<b><u>PART II - OTHER INFORMATION</u></b>	<b>55</b>
<u>Item 1. Legal Proceedings</u>	55
<u>Item 1A. Risk Factors</u>	56
<u>Item 2. Unregistered Sales of Equity Securities and Use of Proceeds</u>	113
<u>Item 3. Defaults Upon Senior Securities</u>	113
<u>Item 4. Mine Safety Disclosures</u>	113
<u>Item 5. Other Information</u>	113
<u>Item 6. Exhibits</u>	114
<b><u>SIGNATURES</u></b>	

## SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements may be identified by such forward-looking terminology as “will,” “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Any forward-looking statement involves known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by such forward-looking statement. Forward-looking statements include statements, other than statements of historical fact, about, among other things:

- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to advance our product candidates into, and successfully complete, clinical trials;
- our reliance on the success of our product candidates in our *Bicycle*<sup>®</sup> Toxin Conjugate, or BTC<sup>™</sup>, *Bicycle* tumor-targeted immune cell agonist<sup>®</sup>, or *Bicycle* TICA<sup>™</sup> and other pipeline programs;
- our ability to utilize our screening platform to identify and advance additional product candidates into clinical development;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- our ability to develop sales and marketing capabilities;
- the pricing, coverage and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate our business without infringing the intellectual property rights and proprietary technology of third parties;
- costs associated with defending intellectual property infringement, product liability and other claims;
- regulatory development in the United States, the United Kingdom and other jurisdictions and changes to laws and regulations of England and Wales, and other jurisdictions;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the amount of and our ability to satisfy interest and principal payments under our debt facility with Hercules Capital, Inc., or Hercules;
- the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;

- our ability to maintain and establish collaborations or obtain additional grant funding;
- the rate and degree of market acceptance of any approved products;
- developments relating to our competitors and our industry, including competing therapies;
- our ability to effectively manage our anticipated growth;
- our ability to attract and retain qualified employees and key personnel;
- future revenue, hiring plans, expenses, capital expenditures, capital requirements and share performance;
- the impact of public health crises and other adverse global economic conditions on our operations and the potential disruption in the operations and business of our third-party manufacturers, contract research organizations, or CROs, other service providers, and collaborators with whom we conduct business;
- recent adverse developments affecting the financial services industry;
- potential business interruptions resulting from geo-political actions, such as war and terrorism, or the perception that such hostilities may be imminent;
- our failure or perceived failure to comply with existing or future laws, regulations, contracts, self-regulatory schemes, standards, and other obligations related to data privacy and security (including security incidents) that could harm our business, increase the costs of our products or services, limit their use or adoption, and otherwise negatively affect our operating results and business; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

Although we believe that we have a reasonable basis for each forward-looking statement contained in this Quarterly Report on Form 10-Q, these statements are based on our estimates or projections of the future that are subject to known and unknown risks and uncertainties and other important factors that may cause our actual results, level of activity, performance, experience or achievements to differ materially from those expressed or implied by any forward-looking statement. These risks, uncertainties and other factors are described in greater detail under the caption “Risk Factors” in Part II. Item 1A and elsewhere in this Quarterly Report on Form 10-Q. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur. Undue reliance should not be placed on any forward-looking statement.

In addition, any forward-looking statement in this Quarterly Report on Form 10-Q represents our views only as of the date of this quarterly report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, except as required by applicable law. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

**PART I - FINANCIAL INFORMATION****Item 1. Financial Statements.**

**Bicycle Therapeutics plc**  
**Condensed Consolidated Balance Sheets**  
**(In thousands, except share and per share data)**  
**(Unaudited)**

	<u>September 30,</u> <u>2023</u>	<u>December 31,</u> <u>2022</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 572,086	\$ 339,154
Accounts receivable	—	2,045
Prepaid expenses and other current assets	13,673	9,022
Research and development incentives receivable	17,277	19,162
Total current assets	<u>603,036</u>	<u>369,383</u>
Property and equipment, net	15,599	19,110
Operating lease right-of-use assets	14,597	13,658
Other assets	5,451	8,458
Total assets	<u>\$ 638,683</u>	<u>\$ 410,609</u>
<b>Liabilities and shareholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 8,493	\$ 6,472
Accrued expenses and other current liabilities	34,053	26,452
Deferred revenue, current portion	27,190	20,418
Total current liabilities	<u>69,736</u>	<u>53,342</u>
Long-term debt, net of discount	30,604	30,315
Operating lease liabilities, net of current portion	10,423	10,885
Deferred revenue, net of current portion	107,582	41,455
Other long-term liabilities	4,316	3,829
Total liabilities	<u>222,661</u>	<u>139,826</u>
Commitments and contingencies (Note 11)		
Shareholders' equity:		
Ordinary shares, including non-voting ordinary shares, £0.01 nominal value; 59,612,613 and 57,820,181 shares authorized at September 30, 2023 and December 31, 2022, respectively; 42,384,799 and 29,873,893 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively	550	387
Additional paid-in capital	875,248	601,105
Accumulated other comprehensive income	2,885	387
Accumulated deficit	(462,661)	(331,096)
Total shareholders' equity	<u>416,022</u>	<u>270,783</u>
Total liabilities and shareholders' equity	<u>\$ 638,683</u>	<u>\$ 410,609</u>

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Collaboration revenues	\$ 5,352	\$ 3,040	\$ 21,645	\$ 11,278
Operating expenses:				
Research and development	39,868	22,752	111,799	56,890
General and administrative	16,281	10,047	45,557	38,830
Total operating expenses	56,149	32,799	157,356	95,720
Loss from operations	(50,797)	(29,759)	(135,711)	(84,442)
Other income (expense):				
Interest income	3,985	1,991	7,726	3,117
Interest expense	(814)	(817)	(2,443)	(2,518)
Total other income (expense), net	3,171	1,174	5,283	599
Net loss before income tax provision	(47,626)	(28,585)	(130,428)	(83,843)
Provision for (benefit from) income taxes	2,272	(238)	1,137	(1,104)
Net loss	\$ (49,898)	\$ (28,347)	\$ (131,565)	\$ (82,739)
Net loss per share, basic and diluted	\$ (1.26)	\$ (0.96)	\$ (3.95)	\$ (2.79)
Weighted average ordinary shares outstanding, basic and diluted	39,576,467	29,676,021	33,291,701	29,643,502
Comprehensives loss:				
Net loss	\$ (49,898)	\$ (28,347)	\$ (131,565)	\$ (82,739)
Other comprehensive income:				
Foreign currency translation adjustment	3,762	902	2,498	3,916
Total comprehensive loss	\$ (46,136)	\$ (27,445)	\$ (129,067)	\$ (78,823)

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

**Bicycle Therapeutics plc**  
**Condensed Consolidated Statements of Shareholders' Equity**  
(In thousands, except share data)  
(Unaudited)

	Ordinary Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount				
<b>Balance at December 31, 2022</b>	<u>29,873,893</u>	<u>\$ 387</u>	<u>\$ 601,105</u>	<u>\$ 387</u>	<u>\$ (331,096)</u>	<u>\$ 270,783</u>
Issuance of ADSs upon exercise of share options	877	—	1	—	—	1
Issuance of ADSs, net of commissions and offering expenses of \$0.1 million	100,000	1	2,715	—	—	2,716
Issuance of ADSs upon vesting of restricted share units	56,988	1	—	—	—	1
Share-based compensation expense	—	—	9,042	—	—	9,042
Foreign currency translation adjustment	—	—	—	(316)	—	(316)
Net loss	—	—	—	—	(39,064)	(39,064)
<b>Balance at March 31, 2023</b>	<u>30,031,758</u>	<u>389</u>	<u>612,863</u>	<u>71</u>	<u>(370,160)</u>	<u>243,163</u>
Issuance of ADSs upon exercise of share options	12,389	—	165	—	—	165
Issuance of ADSs, net of commissions and offering expenses of \$0.4 million	520,000	7	12,120	—	—	12,127
Issuance of ADSs upon vesting of restricted share units	21,793	—	—	—	—	—
Share-based compensation expense	—	—	8,193	—	—	8,193
Foreign currency translation adjustment	—	—	—	(948)	—	(948)
Net loss	—	—	—	—	(42,603)	(42,603)
<b>Balance at June 30, 2023</b>	<u>30,585,940</u>	<u>396</u>	<u>633,341</u>	<u>(877)</u>	<u>(412,763)</u>	<u>220,097</u>
Issuance of ADSs upon exercise of share options	13,296	—	139	—	—	139
Issuance of ADSs and non-voting ordinary shares, net of commissions and offering expenses of \$15.5 million	11,764,706	154	234,338	—	—	234,492
Issuance of ADSs upon vesting of restricted share units	20,857	—	—	—	—	—
Share-based compensation expense	—	—	7,430	—	—	7,430
Foreign currency translation adjustment	—	—	—	3,762	—	3,762
Net loss	—	—	—	—	(49,898)	(49,898)
<b>Balance at September 30, 2023</b>	<u>42,384,799</u>	<u>\$ 550</u>	<u>\$ 875,248</u>	<u>\$ 2,885</u>	<u>\$ (462,661)</u>	<u>\$ 416,022</u>

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

**Bicycle Therapeutics plc**  
**Condensed Consolidated Statements of Shareholders' Equity**  
(In thousands, except share data)  
(Unaudited)

	Ordinary Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount				
<b>Balance at December 31, 2021</b>	<u>29,579,364</u>	<u>\$ 384</u>	<u>\$ 567,637</u>	<u>\$ (3,388)</u>	<u>\$ (218,379)</u>	<u>\$ 346,254</u>
Issuance of ADSs upon exercise of share options	30,074	1	449	—	—	450
Issuance of ADSs upon vesting of restricted share units	35,000	—	—	—	—	—
Share-based compensation expense	—	—	10,198	—	—	10,198
Foreign currency translation adjustment	—	—	—	920	—	920
Net loss	—	—	—	—	(27,564)	(27,564)
<b>Balance at March 31, 2022</b>	<u>29,644,438</u>	<u>385</u>	<u>578,284</u>	<u>(2,468)</u>	<u>(245,943)</u>	<u>330,258</u>
Issuance of ADSs upon exercise of share options	21,879	—	195	—	—	195
Share-based compensation expense	—	—	5,673	—	—	5,673
Foreign currency translation adjustment	—	—	—	2,094	—	2,094
Net loss	—	—	—	—	(26,828)	(26,828)
<b>Balance at June 30, 2022</b>	<u>29,666,317</u>	<u>385</u>	<u>584,152</u>	<u>(374)</u>	<u>(272,771)</u>	<u>311,392</u>
Issuance of ADSs upon exercise of share options	12,114	—	159	—	—	159
Share-based compensation expense	—	—	5,368	—	—	5,368
Foreign currency translation adjustment	—	—	—	902	—	902
Net loss	—	—	—	—	(28,347)	(28,347)
<b>Balance at September 30, 2022</b>	<u>29,678,431</u>	<u>\$ 385</u>	<u>\$ 589,679</u>	<u>\$ 528</u>	<u>\$ (301,118)</u>	<u>\$ 289,474</u>

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

**Bicycle Therapeutics plc**  
**Condensed Consolidated Statements of Cash Flows**  
(In thousands)  
(Unaudited)

	Nine Months Ended Ended September 30,	
	2023	2022
<b>Cash flows from operating activities:</b>		
Net loss	\$ (131,565)	\$ (82,739)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation expense	24,665	21,239
Depreciation and amortization	4,892	2,303
Non-cash interest	289	359
Deferred income tax provision (benefit)	3,588	(2,640)
Changes in operating assets and liabilities:		
Accounts receivable	2,482	348
Research and development incentives receivable	2,192	(3,064)
Prepaid expenses and other assets	(4,615)	(2,137)
Operating lease right-of-use assets	3,116	2,015
Accounts payable	3,835	4,931
Accrued expenses and other current liabilities	6,084	5,495
Operating lease liabilities	(2,983)	(1,446)
Deferred revenue	74,238	(969)
Other long-term liabilities	442	503
Net cash used in operating activities	<u>(13,340)</u>	<u>(55,802)</u>
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(2,878)	(17,539)
Net cash used in investing activities	<u>(2,878)</u>	<u>(17,539)</u>
<b>Cash flows from financing activities:</b>		
Proceeds from the issuance of ADSs and non-voting ordinary shares, net of issuance costs	249,335	—
Proceeds from the exercise of share options and sale of ordinary shares	306	804
Net cash provided by financing activities	<u>249,641</u>	<u>804</u>
<b>Effect of exchange rate changes on cash, cash equivalents and restricted cash</b>	57	(4,674)
Net increase (decrease) in cash, cash equivalents and restricted cash	233,480	(77,211)
Cash, cash equivalents and restricted cash at beginning of period	339,154	438,680
Cash, cash equivalents and restricted cash at end of period	<u>\$ 572,634</u>	<u>\$ 361,469</u>
<b>Reconciliation of cash, cash equivalents and restricted cash</b>		
Cash and cash equivalents	\$ 572,086	\$ 361,469
Restricted cash included in other assets	548	—
Total cash, cash equivalents and restricted cash	<u>\$ 572,634</u>	<u>\$ 361,469</u>
<b>Supplemental disclosure of cash flow information</b>		
Cash paid for interest	\$ 2,059	\$ 2,099
Cash paid for income taxes	\$ 664	\$ 1,203
Cash paid for amounts included in the measurement of operating lease liabilities	\$ 4,188	\$ 2,245
Changes in purchases of property and equipment in accounts payable and accrued expenses	\$ (1,689)	\$ 318
Non-cash impact right-of-use asset and operating lease liabilities	\$ 3,898	\$ 3,120

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

**Bicycle Therapeutics plc**  
**Notes to Condensed Consolidated Financial Statements**  
**(Unaudited)**

**1. Nature of the business and basis of presentation**

Bicycle Therapeutics plc (collectively with its subsidiaries, the “Company”) is a clinical-stage biopharmaceutical company developing a novel class of medicines, which the Company refers to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic properties of a small molecule. The Company’s initial internal programs are focused on oncology indications with high unmet medical need. The Company is evaluating BT8009, a *Bicycle*<sup>®</sup> Toxin Conjugate (“BTC<sup>™</sup>”) targeting Nectin-4, in a Company-sponsored Phase I/II clinical trial, BT5528, a BTC targeting Ephrin type-A receptor 2 (“EphA2”), in a Company-sponsored Phase I/II clinical trial, and BT7480, a *Bicycle* tumor-targeted immune cell agonist<sup>®</sup> (“*Bicycle* TICA<sup>™</sup>”) targeting Nectin-4 and agonizing CD137, in a Company-sponsored Phase I/II clinical trial. In addition, BT1718, a BTC that is being developed to target tumors that express Membrane Type 1 matrix metalloproteinase, is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial sponsored and fully funded by the Centre for Drug Development of Cancer Research UK. The Company’s discovery pipeline in oncology includes *Bicycle*-based systemic immune cell agonists and *Bicycle* TICAs. Beyond the Company’s wholly owned oncology portfolio, the Company is collaborating with biopharmaceutical companies.

The accompanying condensed consolidated financial statements include the accounts of Bicycle Therapeutics plc and its wholly owned subsidiaries, BicycleTx Limited, BicycleRD Limited and Bicycle Therapeutics Inc. All intercompany balances and transactions have been eliminated on consolidation.

The accompanying condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“GAAP”). The Company has reclassified the deferred income tax benefit within its condensed consolidated statements of cash flows in prior periods to conform to current period presentation.

*Liquidity*

As of September 30, 2023, the Company had cash and cash equivalents of \$572.1 million.

The accompanying condensed consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. Since inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital. The Company has funded its operations primarily with proceeds from the sale of its ordinary shares, non-voting ordinary shares, convertible preferred shares and American Depositary Shares (“ADSs”), including offerings pursuant to its at-the-market offering program (“ATM”), proceeds received from its collaboration arrangements (Note 9) and borrowings from the Loan Agreement with Hercules Capital, Inc. (“Hercules”) (Note 6).

On July 17, 2023, the Company completed an underwritten public offering of its securities, pursuant to which it issued and sold 6,117,648 ADSs, representing the same number of ordinary shares, nominal value £0.01 per share, which included 1,411,764 ADSs sold upon the underwriters’ full exercise of their option to purchase additional ADSs, and 4,705,882 non-voting ordinary shares, nominal value £0.01 per share, at a public offering price of \$21.25 per ADS or non-voting ordinary share, respectively. The transaction resulted in gross proceeds to the Company of \$230.0 million, and after deducting underwriting discounts, commissions, and offering expenses of \$14.9 million, net proceeds to the Company of \$215.1 million.

On June 5, 2020, the Company entered into a Sales Agreement (the “Sales Agreement”) with Cantor Fitzgerald & Co. and Oppenheimer & Co. Inc. (the “Sales Agents”) with respect to an ATM program pursuant to which the Company may offer and sell through the Sales Agents, from time to time at the Company’s sole discretion, ADSs, each

ADS representing one ordinary share. During the three and nine months ended September 30, 2023, the Company issued and sold 941,176 and 1,561,176 ADSs, respectively, representing the same number of ordinary shares, for gross proceeds of \$20.0 million and \$35.3 million, respectively, resulting in net proceeds of \$19.4 million and \$34.2 million, respectively, after deducting sales commissions and offering expenses of \$0.6 million and \$1.1 million, respectively. No ADSs were issued or sold pursuant to the Sales Agreement during the three or nine months ended September 30, 2022.

The Company has incurred recurring losses since inception, including net losses of \$49.9 million and \$131.6 million for the three and nine months ended September 30, 2023, respectively, and \$28.3 million and \$82.7 million for the three and nine months ended September 30, 2022, respectively. As of September 30, 2023, the Company had an accumulated deficit of \$462.7 million. The Company expects to continue to generate operating losses in the foreseeable future. The Company expects that its cash will be sufficient to fund its operating expenses and capital expenditure requirements through at least twelve months from the issuance date of these interim condensed consolidated financial statements.

The Company expects its expenses to increase substantially in connection with ongoing activities, particularly as the Company advances its preclinical activities and clinical trials for its product candidates in development. Accordingly, the Company will need to obtain additional funding in connection with continuing operations. If the Company is unable to raise funding when needed, or on attractive terms, it could be forced to delay, reduce or eliminate its research or drug development programs or any future commercialization efforts. There is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of delays in initiating or continuing research programs and clinical trials, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, if approved, dependence on key personnel and collaboration partners, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations, and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. Even if the Company's research and development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

## **2. Summary of significant accounting policies**

The Company's significant accounting policies are disclosed in the audited consolidated financial statements for the year ended December 31, 2022 included in the Company's Annual Report on Form 10-K for the year ended December 31, 2022, which was filed with the Securities and Exchange Commission (the "SEC"), on February 28, 2023 (the "2022 Annual Report"). Since the date of such consolidated financial statements, there have been no changes to the Company's significant accounting policies, other than those disclosed below.

### ***Use of estimates***

The preparation of condensed consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these condensed consolidated financial statements include, but are not limited to, the accrual for research and development expenses, revenue recognition, share-based compensation expense, valuation of right-of-use assets and liabilities, and income taxes, including the valuation allowance for deferred tax assets. The Company bases its estimates on historical experience, known trends and other market-specific or other relevant factors that it believes to be reasonable under the circumstances. Estimates are periodically reviewed in light of reasonable changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates or assumptions.

### ***Significant risks and uncertainties***

The Company currently operates in a period of economic uncertainty which has been significantly impacted by the global health crises, domestic and global monetary and fiscal policy, bank failures, geopolitical conflicts such as the ongoing wars in Ukraine and Israel, rising inflation and interest rates, and fluctuations in monetary exchange rates. While the Company has experienced limited financial impacts at this time, the Company continues to monitor these factors and events and the potential effects each may have on the Company's business, financial condition, results of operations and growth prospects.

### ***Unaudited interim financial information***

Certain information in the footnote disclosures of these financial statements has been condensed or omitted pursuant to the rules and regulations of the SEC. These unaudited condensed consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements and notes thereto for the year ended December 31, 2022 included in the Company's 2022 Annual Report.

The accompanying condensed consolidated balance sheet as of September 30, 2023, condensed consolidated statements of operations and comprehensive loss and condensed consolidated statements of shareholders' equity for the three and nine months ended September 30, 2023 and 2022, and condensed consolidated statements of cash flows for the nine months ended September 30, 2023 and 2022, and the related financial information disclosed in these notes are unaudited. The unaudited interim financial statements have been prepared on the same basis as the audited annual financial statements for the year ended December 31, 2022, and, in the opinion of management, reflect all adjustments, consisting of normal recurring adjustments, necessary for the fair statement of the Company's financial position as of September 30, 2023, the results of its operations for the three and nine months ended September 30, 2023 and 2022, and its cash flows for the nine months ended September 30, 2023 and 2022. The results for the three and nine months ended September 30, 2023 are not necessarily indicative of the results to be expected for the year ending December 31, 2023, any other interim periods, or any future year or period.

### ***Accounts receivable***

Accounts receivable generally represents amounts due under the Company's collaboration agreements. The Company makes judgments as to its ability to collect outstanding receivables and estimates credit losses at the reporting date resulting from the inability of its customers to make required payments. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices. As of September 30, 2023, the Company has no accounts receivable. To date, the Company has not had any write-offs of bad debt, and the Company did not have an allowance for credit losses as of September 30, 2023.

### ***Recently adopted accounting pronouncements***

There have been no recent accounting pronouncements, changes in accounting pronouncements or recently adopted accounting guidance during the three and nine months ended September 30, 2023, that are of significance or potential significance to the Company.

### **3. Fair value of financial assets and liabilities**

Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable: Level 1, Quoted prices in active markets for identical assets or liabilities; Level 2, Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data; Level 3, unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The carrying values of cash and cash equivalents, accounts receivable, research and development incentives receivable, prepaid expenses other current assets, accounts payable and accrued expenses and other current liabilities approximate their fair values due to the short-term nature of these assets and liabilities. As of September 30, 2023, and December 31, 2022, the carrying value of the long-term debt approximates its fair value, which was determined using unobservable Level 3 inputs, including quoted interest rates from a lender for borrowings with similar terms. As of September 30, 2023, and December 31, 2022, there were no assets or liabilities measured at fair value on a recurring basis.

*Cash, cash equivalents and restricted cash*

The Company considers all highly liquid investments that are readily convertible to known amounts of cash with original maturities of three months or less at the date of purchase to be cash equivalents. As of September 30, 2023 and December 31, 2022, the Company's cash equivalents included interest-bearing money market funds and 30-day term deposits, which are considered Level 1 assets. The Company had \$63.4 million and \$276.1 million of cash equivalents as of September 30, 2023 and December 31, 2022, respectively.

As of September 30, 2023, the Company had \$0.5 million of restricted cash related to a collateralized letter of credit in connection with the Company's lease for office and laboratory space in Cambridge, Massachusetts, which is included within other assets in the Company's condensed consolidated balance sheet.

**4. Property and equipment, net**

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

	<u>September 30,</u> <u>2023</u>	<u>December 31,</u> <u>2022</u>
Laboratory equipment	\$ 15,087	\$ 14,872
Leasehold improvements	10,547	10,736
Computer equipment and software	537	441
Furniture and office equipment	823	924
	<u>26,994</u>	<u>26,973</u>
Less: Accumulated depreciation and amortization	(11,395)	(7,863)
	<u>\$ 15,599</u>	<u>\$ 19,110</u>

As of September 30, 2023, property and equipment not yet placed in service was immaterial. As of December 31, 2022, approximately \$2.3 million of laboratory equipment was not yet placed in service. Depreciation expense was \$1.7 million and \$4.9 million for the three and nine months ended September 30, 2023, respectively, and \$1.3 million and \$2.2 million for the three and nine months ended September 30, 2022, respectively.

**5. Accrued expenses and other current liabilities**

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

	<u>September 30,</u> <u>2023</u>	<u>December 31,</u> <u>2022</u>
Accrued employee compensation and benefits	\$ 9,760	\$ 9,928
Accrued external research and development expenses	18,010	10,859
Accrued professional fees	1,319	1,068
Current portion of operating lease liabilities	4,661	3,125
Other	303	1,472
	<u>\$ 34,053</u>	<u>\$ 26,452</u>

## 6. Long-term debt

On September 30, 2020 (the “Closing Date”), Bicycle Therapeutics plc and its subsidiaries (the “Borrowers”) entered into a loan and security agreement (the “Loan Agreement”) with Hercules, which provided for aggregate maximum borrowings of up to \$40.0 million, consisting of (i) a term loan of \$15.0 million, which was funded on the Closing Date, (ii) subject to customary conditions, an additional term loan of up to \$15.0 million available from the Closing Date through March 15, 2021, and (iii) subject to the Borrowers achieving certain performance milestones and satisfying customary conditions and available until March 15, 2022, an additional term loan of \$10.0 million.

On March 10, 2021 (“the Amendment Closing Date”), the Borrowers entered into the First Amendment to the Loan and Security Agreement (the “First Amendment to LSA”) with Hercules, in its capacity as administrative agent and collateral agent, and the lenders named in the First Amendment to LSA. Pursuant to the First Amendment to LSA, payments on borrowings under the Company’s debt facility with Hercules were interest-only until the first payment was due on August 1, 2023, which date was extended from November 1, 2022, followed by equal monthly payments of principal and interest through the scheduled maturity date on October 1, 2024 (the “Maturity Date”). If the Company achieved certain performance milestones, the interest-only period could be extended, with the first principal payment due on February 1, 2024, which date was extended from May 1, 2023. On the Amendment Closing Date and pursuant to the terms of the First Amendment to LSA, the Company borrowed the additional term loan of \$15.0 million that had been available from September 30, 2020 to March 15, 2021. In November 2021, the performance milestones were achieved, and the interest only period was extended until February 1, 2024. On March 15, 2022, the additional term loan of \$10.0 million expired unexercised.

On July 15, 2022, the Borrowers entered into the Second Amendment to the Loan and Security Agreement (the “Second Amendment to LSA”) with Hercules. Pursuant to the Second Amendment to LSA, the rate at which the borrowings under the Loan Agreement bear interest was decreased and capped. Under the Second Amendment to LSA, interest is paid at an annual rate of the *Wall Street Journal* prime rate plus 4.55%, with a minimum annual rate of at least 8.05%, capped at a rate no greater than 9.05%. In addition, among other amendments, the Second Amendment to LSA extended the interest-only period to April 1, 2025, extended the Maturity Date to July 1, 2025, and provided the Borrowers, at their request, the potential for additional term loans, subject to satisfaction of customary conditions, in an aggregate principal amount of up to \$45.0 million, and as such the aggregate maximum borrowings under the Loan Agreement increased to \$75.0 million.

At the Borrowers’ option, the Borrowers may prepay all or any portion greater than \$5.0 million of the outstanding borrowings, subject to a prepayment premium equal to (i) 1.5% of the principal amount outstanding if the prepayment occurs after the first anniversary of the Closing Date but on or prior to December 31, 2023, and (ii) 1.0% of the principal amount outstanding if the prepayment occurs thereafter but prior to the Maturity Date. The Loan Agreement also provides for an end of term charge (the “End of Term Charge”), payable upon maturity or the repayment of obligations under the Loan Agreement, equal to 5.0% of the principal amount repaid. Borrowings under the Loan Agreement are collateralized by substantially all of the Borrower’s personal property and other assets, other than their intellectual property. Hercules has a perfected first-priority security interest in certain cash accounts. The Loan Agreement contains customary affirmative and restrictive covenants and representations and warranties, including a covenant against the occurrence of a change in control, as defined in the agreement. There are no financial covenants. The Loan Agreement also includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, cross acceleration to third-party indebtedness, certain events relating to bankruptcy or insolvency, and the occurrence of certain events that could reasonably be expected to have a material adverse effect. Upon the occurrence of an event of default, a default interest rate of an additional 5.0% may be applied to the outstanding principal and interest payments due, and Hercules may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement. The Company has determined that the risk of subjective acceleration under the material adverse events clause is not probable and therefore has classified the outstanding principal in long-term liabilities based on scheduled principal payments.

The Company incurred fees and transaction costs totaling \$0.6 million associated with the initial term loan, which are recorded as a reduction to the carrying value of the long-term debt in the condensed consolidated balance sheets. The fees, transaction costs, and the End of Term Charge are amortized to interest expense through the Maturity

Date using the effective interest method. The Company evaluated the First Amendment to LSA and the Second Amendment to LSA and concluded that these amendments represent modifications to the Loan Agreement, and as such, the fees and transaction costs associated with term loan will continue to be amortized to interest expense through the Maturity Date. The effective interest rate of the Hercules borrowings was 10.8% at September 30, 2023.

The Company assessed all terms and features of the Loan Agreement in order to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the debt. The Company determined that all features of the Loan Agreement are clearly and closely associated with a debt host and, as such, do not require separate accounting as a derivative liability. Interest expense associated with the Loan Agreement for the three and nine months ended September 30, 2023 was \$0.8 million and \$2.3 million, respectively, and for the three and nine months ended September 30, 2022, was \$0.8 million and \$2.5 million, respectively.

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

	September 30, 2023	December 31, 2022
Term loan payable	\$ 30,000	\$ 30,000
End of term charge	881	682
Unamortized debt issuance costs	(277)	(367)
Carrying value of term loan	<u>\$ 30,604</u>	<u>\$ 30,315</u>

Future principal payments, including the End of Term Charge, are as follows (in thousands):

Year Ending December 31,	
2023	\$ —
2024	—
2025	31,500
Total	<u>\$ 31,500</u>

## 7. Ordinary shares

The Company's ordinary shares are divided into two classes: (i) ordinary shares and (ii) non-voting ordinary shares. Each holder of ordinary shares is entitled to one vote per ordinary share and to receive dividends when and if such dividends are recommended by the board of directors and declared by the shareholders. Holders of ADSs are not treated as holders of the Company's ordinary shares, unless they withdraw the ordinary shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the ordinary shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of the Company's ordinary shares, other than the rights that they have pursuant to the deposit agreement with the depositary.

The non-voting ordinary shares have the same rights and restrictions as the ordinary shares and otherwise rank *pari passu* in all respects with the ordinary shares except for the following:

- a holder of non-voting ordinary shares shall, in relation to the non-voting ordinary shares held, have no right to receive notice of, or to attend or vote at, any general meeting of shareholders save in relation to a variation of class rights of the non-voting ordinary shares;
- the non-voting ordinary shares shall be re-designated as ordinary shares by the Company's board of directors, or a duly authorized committee or representative thereof, upon receipt of a re-designation notice and otherwise subject to the terms and conditions set out in the terms of issue. A holder of non-voting ordinary shares shall not be entitled to have any non-voting ordinary shares re-designated as ordinary shares where such re-designation would result in such holder thereof beneficially owning (for purposes of section 13(d) of the Exchange Act), when aggregated with "affiliates" and "group" members with whom

such holder is required to aggregate beneficial ownership for the purposes of section 13(d) of the Exchange Act, in excess of 9.99% of any class of the Company's securities registered under the Exchange Act (which percentage may be increased or decreased on a holder-by-holder basis subject to the provisions set out in the terms of issue); and

- the non-voting ordinary shares shall be re-designated as ordinary shares automatically upon transfer of a non-voting ordinary share by its holder to any person that is not an "affiliate" or "group" member with whom such holder is required to aggregate beneficial ownership for purposes of section 13(d) of the Exchange Act. This automatic re-designation shall only be in respect of the non-voting ordinary shares that are subject to such transfer.

As of September 30, 2023, and December 31, 2022, the Company had not declared any dividends.

As of September 30, 2023, and December 31, 2022, the Company's authorized share capital consisted of 59,612,613 and 57,820,181 ordinary shares, respectively, including ordinary shares and non-voting ordinary shares, with a nominal value of £0.01 per share. Authorized share capital, or shares authorized, comprises (i) the currently issued and outstanding ordinary shares and non-voting ordinary shares, (ii) the remaining ordinary shares available for allotment under the existing authority granted to the Board at the annual general meeting held on June 28, 2021, (iii) ordinary shares issuable on the exercise of outstanding options and (iv) ordinary shares reserved for issuance under the Bicycle Therapeutics plc 2020 Equity Incentive Plan and/or the Bicycle Therapeutics plc 2019 Employee Share Purchase Plan.

As of September 30, 2023, there were 37,678,917 ordinary shares issued and outstanding and 4,705,882 non-voting ordinary shares issued and outstanding.

## **8. Share-based compensation**

### ***Employee incentive pool***

#### ***2020 Equity Incentive Plan***

In June 2020, the Company's shareholders first approved the Bicycle Therapeutics plc 2020 Equity Incentive Plan with Non-Employee Sub-Plan (the "2020 Plan"), under which the Company may grant market value options, market value stock appreciation rights or restricted shares, restricted share units ("RSUs"), performance RSUs and other share-based awards to the Company's employees. The Company's non-employee directors and consultants are eligible to receive awards under the 2020 Non-Employee Sub-Plan to the 2020 Plan. All awards under the 2020 Plan, including the 2020 Non-Employee Sub-Plan, will be set forth in award agreements, which will detail the terms and conditions of awards, including any applicable vesting and payment terms, change of control provisions and post-termination exercise limitations. In the event of a change of control of the Company, as defined in the 2020 Plan, any outstanding awards under the 2020 Plan will vest in full immediately prior to such change of control.

The Company initially reserved up to 4,773,557 ordinary shares for future issuance under the 2020 Plan, representing 574,679 new shares, 544,866 shares that remained available for future issuance under the Company's 2019 Share Option Plan (the "2019 Plan") immediately prior to the effectiveness of the 2020 Plan and up to 3,654,012 shares subject to options that were granted under the 2019 Plan and that were granted pursuant to option contracts granted prior to the Company's IPO, in each case that expire, terminate, are forfeited or otherwise not issued from time to time, if any. On June 27, 2022, the Company's shareholders approved an amendment to the 2020 Plan (the "Amendment") which increased the number of ordinary shares reserved for future issuance by 750,000 shares. Additionally, the number of ordinary shares reserved for issuance pursuant to the 2020 Plan will automatically increase on the first day of January of each year, initially commencing on January 1, 2021, in an amount equal to 5% of the total number of the Company's ordinary shares outstanding on the last day of the preceding year, or a lesser number of shares determined by the Company's board of directors. Pursuant to this "evergreen" provision, on January 1, 2023, the number of shares reserved for issuance under the 2020 Plan was increased by 1,493,694 shares. The Amendment extended the final date upon which an "evergreen" increase may occur under this provision from January 1, 2030, to January 1, 2032. As of September 30, 2023, there were 889,257 shares available for issuance.

Share options issued under the 2020 Plan have a 10-year contractual life and generally vest over either a three-year service period for non-employee directors, or a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date and the balance thereafter in 36 equal monthly installments for employees and consultants. Certain options granted to the Company's non-employee directors vest immediately upon grant or over a one-year service period in four equal quarterly installments.

The Company grants RSUs to non-employee directors and certain employees under the 2020 Plan. Each RSU represents the right to receive one of the Company's ordinary shares upon vesting. RSUs granted to employees vest over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date and the remaining RSUs vest in 12 equal quarterly installments. Certain RSUs granted to the Company's non-employee directors either vest immediately upon grant or over a one-year service period in four equal quarterly installments.

As of September 30, 2023, there were options to purchase 4,620,330 shares and RSUs for 335,104 shares outstanding under the 2020 Plan.

#### *2019 Share Option Plan*

In May 2019, the Company adopted the 2019 Plan, which became effective in conjunction with the IPO. As of September 30, 2023, there were 2,103,250 options to purchase ordinary shares outstanding under the 2019 Plan. In conjunction with the adoption of the 2020 Plan, all shares available for future issuance under the 2019 Plan as of June 29, 2020 became available for issuance under the 2020 Plan and the Company ceased making awards under the 2019 Plan. The 2020 Plan is the successor of the 2019 Plan.

Share options previously issued under the 2019 Plan have a 10-year contractual life, and generally either vest monthly over a three year-service period, or over a four-year service period with 25% of the award vesting on the first anniversary of the vesting commencement date and the balance thereafter in 36 equal monthly installments. Certain awards granted to the Company's non-employee directors were fully vested on the date of grant. The exercise price of share options issued under the 2019 Share Option Plan is not less than the fair value of ordinary shares as of the date of grant.

#### *Employee Share Purchase Plan*

In May 2019, the Company adopted the 2019 Employee Stock Purchase Plan (the "ESPP"), which became effective in conjunction with the IPO. The Company initially reserved 215,000 ordinary shares for future issuance under this plan. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020 and each January 1 thereafter through January 1, 2029, by the lower of: (i) 1% of the outstanding number of ordinary shares on the immediately preceding December 31; (ii) 430,000 ordinary shares or (iii) such lesser number of shares as determined by the Compensation Committee. The number of shares reserved under the ESPP is subject to adjustment in the event of a split-up, share dividend or other change in the Company's capitalization. The number of shares reserved for issuance under the ESPP was increased by 298,738 shares effective January 1, 2023. As of September 30, 2023, the total number of shares available for issuance under the ESPP was 1,200,413 ordinary shares. As of September 30, 2023, there have been no offering periods to employees under ESPP.

**Share-based compensation**

The Company recorded share-based compensation expense in the following expense categories of its condensed consolidated statements of operations and comprehensive loss (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Research and development expenses	\$ 3,357	\$ 2,637	\$ 11,941	\$ 7,643
General and administrative expenses	4,073	2,731	12,724	13,596
	<u>\$ 7,430</u>	<u>\$ 5,368</u>	<u>\$ 24,665</u>	<u>\$ 21,239</u>

**Share options**

The following table summarizes the Company's option activity since December 31, 2022:

	Number of Shares Underlying Share Options	Weighted Average Exercise Price	Weighted Average Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2022	5,898,888	\$ 22.45	7.64	\$ 71,002
Granted	1,859,315	27.57	—	—
Exercised	(26,562)	11.42	—	—
Forfeited	(419,621)	30.69	—	—
Outstanding as of September 30, 2023	<u>7,312,020</u>	\$ 23.32	6.99	\$ 29,629
Vested and expected to vest as of September 30, 2023	7,312,020	\$ 23.32	6.99	\$ 29,629
Options exercisable as of September 30, 2023	4,334,755	\$ 18.39	5.75	\$ 28,069

The weighted average grant-date fair value of share options granted during the nine months ended September 30, 2023 and 2022 was \$20.16 per share and \$32.91 per share, respectively.

The aggregate intrinsic value of share options is calculated as the difference between the exercise price of the share options and the fair value of the Company's ordinary shares. The aggregate intrinsic value of share options exercised was \$0.1 million and \$0.3 million for the three and nine months ended September 30, 2023, respectively and was \$0.1 million and \$1.3 million for the three and nine months ended September 30, 2022, respectively.

Total share-based compensation expense for share options granted was \$6.3 million and \$20.5 million for the three and nine months ended September 30, 2023, respectively, and was \$4.7 million and \$17.1 million for the three and nine months ended September 30, 2022, respectively. Expense for non-employee consultants for the three and nine months ended September 30, 2023 and 2022 was immaterial.

The following table presents, on a weighted average basis, the assumptions used in the Black-Scholes option-pricing model to determine the fair value of share options granted to employees and directors:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Risk-free interest rate	4.1 %	3.0 %	3.9 %	2.0 %
Expected volatility	83.3 %	84.1 %	83.5 %	82.2 %
Expected dividend yield	—	—	—	—
Expected term (in years)	6.1	6.1	6.1	6.0

As of September 30, 2023, total unrecognized compensation expense related to the unvested employee and director share options was \$58.6 million, which is expected to be recognized over a weighted average period of 2.7 years.

*Restricted share units*

The following table summarizes the Company’s RSU activity under the 2020 Plan since December 31, 2022:

	Number of Shares Underlying RSUs	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2022	187,725	\$ 60.86
Granted	321,839	29.59
Vested	(99,638)	51.39
Forfeited	(74,822)	39.55
Unvested at September 30, 2023	335,104	\$ 38.40

The fair value of RSUs that vested during the three and nine months ended September 30, 2023, was \$0.5 million and \$2.6 million, respectively, and for the three and nine months ended September 30, 2022, was zero and \$2.1 million, respectively.

Total share-based compensation expense for RSUs granted was \$1.2 million and \$4.2 million for the three and nine months ended September 30, 2023, respectively, and was \$0.7 million and \$4.1 million for the three and nine months ended September 30, 2022, respectively. As of September 30, 2023, the total unrecognized compensation expense related to unvested RSUs was \$11.0 million, which is expected to be recognized over a weighted-average period of 2.7 years.

**9. Significant agreements**

For the three and nine months ended September 30, 2023 and 2022, the Company recognized revenue for its collaborations with Bayer Consumer Care AG (“Bayer”), Novartis Pharma AG (“Novartis”), Ionis Pharmaceuticals, Inc. (“Ionis”), Genentech, Inc. (“Genentech”), the Dementia Discovery Fund (“DDF”), and AstraZeneca AB (“AstraZeneca”). The following table summarizes the revenue recognized in the Company’s condensed consolidated statements of operations and comprehensive loss from these arrangements (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
<b>Collaboration revenues</b>				
Bayer	\$ 434	\$ —	\$ 434	\$ —
Novartis	772	—	772	—
Ionis	2,782	2,195	8,123	6,764
Genentech	1,364	798	11,112	3,144
Dementia Discovery Fund	—	47	—	205
AstraZeneca	—	—	1,204	1,165
Total collaboration revenues	\$ 5,352	\$ 3,040	\$ 21,645	\$ 11,278

***Bayer Collaboration Agreement***

On May 4, 2023, the Company and Bayer entered into a collaboration and license agreement (the “Bayer Collaboration Agreement”), pursuant to which the parties will perform research and discovery activities under a mutually agreed upon research plan during a research term up to a specified number of years per target program to generate radiopharmaceutical compounds incorporating optimized *Bicycle* constructs directed to two specified targets,

under the oversight of a joint research committee. In addition, Bayer has a one-time right to expand the collaboration to include a third target program, and with respect to each of the up to three target programs, Bayer has an option, exercisable within a specified period of time following the effective date of the Bayer Collaboration Agreement, to generate, develop and commercialize non-radiopharmaceutical compounds directed to the applicable target, either itself or in collaboration with the Company. Bayer also has certain limited target substitution rights, in certain cases subject to specified additional payments.

For each collaboration program, Bayer may elect, at its sole discretion, to progress compounds arising from activities under the research programs into further preclinical development of potential products directed to the target of such collaboration program. On a target-by-target basis, if Bayer elects to progress development candidates directed to such target into further clinical development, Bayer will be required to use commercially reasonable efforts to develop and seek regulatory approval in certain major markets for products directed to the applicable target.

Bayer agreed to pay an upfront payment to the Company of \$45.0 million, which was received in July 2023. All other payments under the Bayer Collaboration Agreement will be made in British Pound Sterling. If Bayer elects to expand the collaboration to include an additional target program, it will be required to make a one-time payment to the Company in connection with the selection of such target in the high single digit millions. In addition, on a target-by-target basis, if Bayer elects to exercise its option to expand its rights with respect to such target to develop and commercialize non-radiopharmaceutical compounds directed to such target, Bayer will be required to pay to the Company, for each such target program for which it exercises such option, either a one-time option fee payment or quarterly payments of specified installment amounts for a specified maximum time period during which the Company is performing research activities, with the aggregate amounts receivable by the Company ranging from the high single digit millions in the case of the one-time option fee payment, to the low single digit millions in the case of the quarterly installments, in each case where the Company is performing specified research activities following the exercise of the option. Additionally, for each collaboration program, Bayer will reimburse the Company for certain expenses incurred in connection with specified research and discovery activities performed by a contract research organization (“CRO”).

On a target-by-target basis for the up to three targets, if Bayer elects to progress one or more candidate compounds into further development, Bayer will be required to pay a candidate selection fee for the first such compound progressed by Bayer directed to such target that incorporates a radionuclide, and for the first such compound directed to such target that does not incorporate a radionuclide (and for which Bayer has not paid the one-time option fee payment for non-radiopharmaceutical compounds), ranging from high single-digit millions to the mid single-digit millions. On a target-by-target basis, if Bayer successfully conducts clinical development and achieves regulatory approval for compounds arising from the collaboration directed to such target in two indications, Bayer will be required to pay to the Company development and regulatory/first commercial sale milestones of up to £178.3 million for the first product directed to the applicable target to achieve such milestones (whether radiopharmaceutical or non-radiopharmaceutical), or £534.9 million across all three potential target programs. In addition, if Bayer successfully commercializes products arising from the collaboration, Bayer will be required to pay to the Company, on a product-by-product basis, tiered royalties on net sales of products by Bayer, its affiliates or sublicensees at percentages ranging from the mid-single digits to the very low double digits, subject to standard reductions and offsets in certain circumstances, and a royalty floor. If Bayer commercializes diagnostic products directed to a target, royalties will be payable on such diagnostic products at a specified reduced percentage of the rates for therapeutic products. Royalties will be payable under the Bayer Collaboration Agreement on a product-by-product and country-by-country basis, commencing on the first commercial sale of each product, until the latest of (a) the expiration of the last valid claim of certain patents licensed by the Company to Bayer, (b) a specified number of years following first commercial sale of such product, and (c) expiration of all data and regulatory exclusivity for such product in the applicable country. On a target-by-target basis, Bayer will also owe the Company tiered sales milestones based on the achievement of specified levels of net sales of therapeutic products directed to such target totaling up to £194.5 million in the aggregate per target, or £583.5 million across all three potential target programs, and on diagnostic products directed to such target at a low double digit percentage of the therapeutic product milestones.

The Bayer Collaboration Agreement will remain in force on a product-by-product and country-by-country basis, unless earlier terminated by either party, until the expiration of the obligation for Bayer to make royalty payments to the Company for such product in such country, and will terminate in its entirety on the expiration of all such royalty

terms in all countries. Either party may terminate the agreement upon 90 days' written notice for the other party's uncured material breach (or 20 business days in the case of non-payment by Bayer), subject to extension of such cure period in certain circumstances, or upon the other party's insolvency. In addition, the Company has the right to terminate in the case of a patent challenge by or on behalf of Bayer (or any of its affiliates or sublicensees). In addition, Bayer may terminate the Bayer Collaboration Agreement (i) in its entirety or with respect to any product, collaboration program or target for any reason upon 60 or 90 days' written notice to the Company (depending on whether such termination is prior to or following first commercial sale of a licensed product). The closing of the Bayer Collaboration Agreement was subject to the clearance of the transaction under the U.K. National Security and Investment Act 2021, which occurred on June 22, 2023 (the "Effective Date").

#### *Accounting Analysis*

At inception of the Bayer Collaboration Agreement, the Company identified the following performance obligations:

- (i) Two combined performance obligations comprised of the license and the related research and development services during the research term associated with radiopharmaceutical compounds for the first and second targets;
- (ii) A material right associated with certain limited substitution rights with respect to either the first or second target;
- (iii) Two material rights associated with the option to progress radiopharmaceutical candidates directed to the first and second targets into further development;
- (iv) Two material rights associated with the options to generate, develop, and commercialize non-radiopharmaceutical compounds for each of the first and second targets, for which each option includes an underlying option for research and development services and an option to progress non-radiopharmaceutical candidates directed to the first and second targets into further development; and
- (v) A material right related to the option to expand the collaboration to include a third target, which upon exercise includes research and development services during the research term associated with radiopharmaceutical compounds directed to the third target, as well as underlying options for: certain limited substitution rights; an option to progress a radiopharmaceutical candidate directed to the third target into further development; and an option to generate, develop, and commercialize non-radiopharmaceutical compounds directed to the third target, inclusive of an underlying option for research and development services and an option to progress a non-radiopharmaceutical candidate into further development.

The Company's participation in the joint research committee was assessed as immaterial in the context of the contract.

The Company concluded that the license granted at contract inception is not distinct from the research and development services as Bayer cannot obtain the benefit of the license without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as they relate to constrained peptide technology that is not available in the marketplace. As a result, for each target, the license has been combined with the research and development services into a single performance obligation which is the combined performance obligation comprised of the license and related research and development services.

In assessing whether the various options under the Bayer Collaboration Agreement represent material rights, the Company considered the additional consideration the Company would be entitled to upon option exercise and the standalone selling price of the underlying goods and services. For the material rights identified above, the Company concluded that each of the options provided Bayer with a discount that it otherwise would not have received.

The transaction price was initially determined to be \$47.5 million, consisting of the \$45.0 million upfront fee and an estimated \$2.5 million for the reimbursement of certain external CRO costs. The Company utilized the expected value method to determine the amount of variable consideration to be received. Additional payments to the Company upon Bayer’s exercise of options are excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the exercise of an option. The estimated \$2.5 million in variable consideration was first allocated entirely to the first and second target combined performance obligations as the terms of the variable consideration relate specifically to the Company’s efforts in satisfying the performance obligations and allocating the variable consideration entirely to those performance obligations is consistent with the allocation objective in Accounting Standards Codification (“ASC”) Topic 606, *Revenue from Contracts with Customers*, or ASC 606. The remaining transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the combined performance obligations for the first and second targets were based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin for what would be expected to be realized under similar contracts. The estimated standalone selling prices for the material rights were determined based on the fees that Bayer would pay to exercise the options, the estimated value of the underlying goods and services, and the probability that Bayer would exercise the options. Based on the relative standalone selling prices, the allocation of the transaction price to the separate performance obligations is as follows (in thousands):

<b>Performance Obligations</b>	<b>Allocation of Transaction Price</b>
Two combined performance obligations related to the licenses and research and development services associated with radiopharmaceutical compounds directed to the first and second targets	\$ 14,976
Material right associated with limited substitution rights for either the first or second target	1,527
Two material rights associated with the option to progress radiopharmaceutical candidates directed to the first and second targets into further development	14,691
Two material rights associated with the option to progress a non-radiopharmaceutical compound directed to the first and second targets	8,703
Material right for the option to expand the collaboration to include a third target and the underlying additional option rights	7,603
	<b>\$ 47,500</b>

The Company will recognize revenue related to amounts allocated to the first and second target combined performance obligations as the underlying services are performed using a proportional performance model over the period of service using input-based measurements of full-time equivalent efforts and external costs incurred to date as a percentage of total expected full-time equivalent efforts and external costs, which best reflects the progress towards satisfaction of the performance obligations. The amounts allocated to the material rights are recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the respective option. The first and second target combined performance obligations are expected to be satisfied over a period of approximately four years and the remaining material rights are expected to be exercised or expire within approximately seven years from contract inception.

During the three and nine months ended September 30, 2023, the Company recognized revenue of \$0.4 million and \$0.4 million, respectively, in connection with the Bayer Collaboration Agreement. The Company did not recognize revenue during the three and nine months ended September 30, 2022 in connection with the Bayer Collaboration Agreement. As of September 30, 2023 and December 31, 2022, the Company recorded deferred revenue of \$42.5 million and zero, respectively, in connection with the Bayer Collaboration Agreement.

#### **Novartis Collaboration Agreement**

On March 27, 2023, the Company and Novartis entered into a collaboration and license agreement (the “Novartis Collaboration Agreement”), pursuant to which the parties will perform research and discovery activities under a mutually agreed upon research plan during a research term of up to a specified number of years per target program to generate compounds incorporating optimized *Bicycle* constructs directed to two specified targets, under the oversight of a joint steering committee. The Company granted Novartis a non-exclusive, worldwide, royalty-free, sublicensable

(subject to certain restrictions) license under the Company's intellectual property solely for Novartis to perform its research activities under each collaboration program during the research term (the "Novartis Research License"). For each collaboration program, Novartis may elect to progress compounds arising from activities under the research programs ("Licensed Compounds") into further preclinical development of potential products directed to the target of such collaboration program. At a specified point, the Company will grant Novartis an exclusive, royalty-bearing, sublicensable, license under certain of the Company's intellectual property to develop, manufacture, and commercialize such Licensed Compound, subject to certain limitations. Novartis also has certain limited substitution rights for each target, and Novartis may extend the initial research term by one year by electing to make an additional payment. On a target-by-target basis, if Novartis elects to progress development candidates directed to such target into further clinical development, Novartis will be required to use commercially reasonable efforts to develop and seek regulatory approval in certain major markets for products containing Licensed Compounds directed to the applicable target.

Novartis agreed to pay a nonrefundable upfront payment to the Company of \$50.0 million, which was received in April 2023. During the research term, upon achievement of a specified discovery milestone for the first target program, Novartis will make a one-time payment to the Company in the low single digit millions. On a target-by-target basis, if Novartis elects to progress one or more candidate compounds into further development and obtain an exclusive license for commercialization, Novartis will be required to pay a candidate selection fee for the first such Licensed Compound progressed by Novartis that incorporates a radionuclide, and for the first such Licensed Compound that does not incorporate a radionuclide, in each case in the mid-teen millions. Upon declaring a candidate, Novartis will be responsible for all future development, manufacturing, and commercialization activities. On a target-by-target basis, Novartis will be required to pay to the Company additional development and regulatory/first commercial sale milestones of up to \$210.0 million for each of the first radionuclide product and non-radionuclide product directed to the applicable target upon the achievement of specified milestones, or \$840.0 million in the aggregate if Novartis successfully achieves all such milestone events for both a radionuclide and a non-radionuclide product in each of the targets. In addition, the Company is eligible to receive tiered sales milestones based on the achievement of specified levels of net sales of such products totaling up to \$200.0 million in the aggregate per product, or \$800.0 million in the aggregate if Novartis successfully commercializes both a radionuclide and a non-radionuclide product in each of the target programs. In addition, (i) the Company is eligible to receive, on a therapeutic product-by-therapeutic product basis, tiered royalties on net sales of products by Novartis, its affiliates or sublicensees at percentages ranging from the high single digits to the very low double digits, subject to standard reductions and offsets in certain circumstances, and a royalty floor, and (ii) the Company is eligible to receive low single digit royalties on net sales of diagnostic products on a diagnostic product-by-diagnostic product basis and a low single digit percentage of sublicensing income on diagnostic products. Royalties will be payable under the Novartis Collaboration Agreement on a product-by-product and country-by-country basis, commencing on the first commercial sale of each product in a country, until the latest of (a) the expiration of the last valid claim of certain patents licensed by Company to Novartis, (b) a specified number of years following first commercial sale of such product, and (c) expiration of all data and regulatory exclusivity for such product in the applicable country.

The Novartis Collaboration Agreement will remain in force on a product-by-product and country-by-country basis, unless earlier terminated by either party, until the expiration of the obligation for Novartis to make royalty payments to Company for such product in such country, and will terminate in its entirety on the expiration of all such royalty payment obligations in all countries. Either party may terminate the agreement upon 60 days' written notice for the other party's uncured material breach, or upon the other party's insolvency. In addition, Novartis may terminate the Collaboration Agreement (i) in its entirety or on a product-by-product or target-by-target basis for any reason upon 90 days' written notice to Company, and (ii) on a target-by-target basis on 30 days' written notice if Novartis determines that a safety or regulatory issue exists which would have a material adverse effect on the development, manufacture, or commercialization of any product with respect to a given target. The Company may terminate the Novartis Collaboration Agreement, (a) on a target-by-target basis upon 30 days' prior written notice if Novartis has not yet declared a development candidate for such target by the sixth anniversary of the commencement of research activities for such target and (b) if Novartis or any of its affiliates or sublicensees challenges the validity or enforceability of any of the patents in the Company's licensed intellectual property.

*Accounting Analysis*

Upon the execution of the Novartis Collaboration Agreement, the Company identified the following performance obligations:

- (i) Two combined performance obligations comprised of the Novartis Research License and the related research and development services during the research term for the first and second targets;
- (ii) Two material rights associated with certain limited substitution rights with respect to the first and second targets;
- (iii) Two material rights associated with the option to progress development candidates that incorporate a radionuclide with respect to the first and second target; and
- (iv) Two material rights associated with the option to progress development candidates that do not incorporate a radionuclide with respect to the first and second target.

The Company concluded that certain rights that require the payment of additional consideration, which approximates the standalone selling of the underlying services to be provided, do not provide the customer with a material right and therefore, are not considered as performance obligations at the inception of the arrangement. The Company's participation in the joint steering committee was assessed as immaterial in the context of the contract.

The Company has concluded that the Novartis Research License is not distinct from the research and development services as Novartis cannot obtain the benefit of the research license without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as they relate to constrained peptide technology that is not available in the marketplace. As a result, for each target, the research license has been combined with the research and development services into a single performance obligation.

In assessing whether the various options under the Novartis Collaboration Agreement represent material rights, the Company considered the additional consideration the Company would be entitled to upon option exercise and the standalone selling price of the underlying goods and services. For the material rights identified above the Company concluded that each of the options provided Novartis with a discount that it otherwise would not have received.

The total transaction price was initially determined to be \$50.0 million, consisting of the \$50.0 million upfront fee. The Company utilizes the most likely amount method to determine the amount of variable consideration to be received. Variable consideration for development milestones not subject to option exercises was fully constrained as a result of the uncertainty regarding whether any of the milestones will be achieved. Additional consideration to be paid to the Company upon the exercise of options by Novartis is excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the exercise of an option.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the combined performance obligations for each of the targets were based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin for what would be expected to be realized under similar contracts. The estimated standalone selling prices for the material rights were determined based on the fees Novartis would pay to exercise the options, the estimated value of the underlying goods and services, and the probability that Novartis would exercise the options. Based on the relative standalone selling prices, the allocation of the transaction price to the separate performance obligations is as follows (in thousands):

<b>Performance Obligations</b>	<b>Allocation of Transaction Price</b>
Two combined performance obligations for the first and second targets	\$ 18,008
Two material rights associated with limited substitution rights	2,466
Two material rights associated with options to progress development candidates incorporating radionuclides	19,684
Two material rights associated with options to progress development candidates not incorporating radionuclides	9,842
	<b>\$ 50,000</b>

The Company will recognize revenue related to amounts allocated to the first and second target combined performance obligations as the underlying services are performed using a proportional performance model over the period of service using input-based measurements of total full-time equivalent efforts and external costs incurred to date as a percentage of total full-time equivalent efforts and expected external costs, which best reflects the progress towards satisfaction of the performance obligations. The amounts allocated to the material rights are recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the respective option. The first and second target combined performance obligations are expected to be satisfied over a period of approximately three years and the remaining material rights are expected to be exercised or expire within approximately six years from contract execution.

During the three and nine months ended September 30, 2023, the Company recognized revenue of \$0.8 million and \$0.8 million, respectively, in connection with the Novartis Collaboration Agreement. The Company did not recognize revenue during the three and nine months ended September 30, 2022 in connection with the Novartis Collaboration Agreement. As of September 30, 2023 and December 31, 2022, the Company recorded deferred revenue of \$49.1 million and zero, respectively, in connection with the Novartis Collaboration Agreement.

### ***Ionis Agreements***

#### *Ionis Evaluation and Option Agreement*

On December 31, 2020 (the "Effective Date"), the Company entered into an Evaluation and Option Agreement (the "Evaluation and Option Agreement") with Ionis. Under the terms of the Evaluation and Option Agreement, the Company agreed to transfer *Bicycles* (the "Option Materials") to Ionis in order to evaluate a particular application of the Company's technology platform for a period of up to four months (the "Evaluation Period"). Ionis paid the Company a non-refundable \$3.0 million option fee in January 2021.

At any point during the term of the agreement and continuing through 30 days after the expiration of the Evaluation Period, Ionis had the option (the "Ionis Option") to obtain an exclusive license to the Company's intellectual property for the purpose of continued research, development, manufacture and commercialization of products within a particular application of the Company's platform technology. The upfront payment of \$3.0 million was fully creditable against the upfront payment to be paid upon the execution of a license agreement.

The Company concluded that the only performance obligation was a material right for the option to obtain an exclusive license. All other promises under the Evaluation and Option Agreement were immaterial in the context of the contract. The Company accounted for the \$3.0 million payment as deferred revenue as of December 31, 2020. On July

9, 2021, the Ionis Option was exercised upon the parties' entry into a collaboration and license agreement as contemplated by the Evaluation and Option Agreement. The Company determined that the Ionis Option exercise constituted a continuation of the existing arrangement. Therefore, the \$3.0 million in deferred revenue under the Evaluation and Option Agreement was included in the transaction price of the collaboration and license agreement.

#### *Ionis Collaboration Agreement*

Following the exercise by Ionis of the Ionis Option granted pursuant to the Evaluation and Option Agreement, on July 9, 2021, the Company and Ionis entered into a collaboration and license agreement (the "Ionis Collaboration Agreement"). Pursuant to the Ionis Collaboration Agreement, the Company granted to Ionis a worldwide exclusive license under the Company's relevant technology to research, develop, manufacture and commercialize products incorporating *Bicycle* peptides directed to the protein coded by the gene TFRC1 (transferrin receptor) ("*TfR1 Bicycles*") intended for the delivery of oligonucleotide compounds directed to targets selected by Ionis for diagnostic, therapeutic, prophylactic and preventative uses in humans. Ionis will maintain exclusivity to all available targets unless it fails to achieve specified development diligence milestone deadlines. If Ionis fails to achieve one or more development diligence milestone deadlines, the Company has the right to limit exclusivity to certain specific collaboration targets, subject to the payment by Ionis of a low-single-digit million dollar amount per target as specified in the Ionis Collaboration Agreement. Each party will be responsible for optimization of such *TfR1 Bicycles* and other research and discovery activities related to *TfR1 Bicycles*, as specified by a research plan, and thereafter Ionis will be responsible for all future research, development, manufacture and commercialization activities. The Company will perform research and discovery activities including a baseline level of effort for a period of three years for no additional consideration. The parties will negotiate a commercially reasonable rate if additional research activities are agreed to be performed. For certain research and discovery activities that the Company is responsible for performing, the Company may use the assistance of a contract research organization ("CRO"). The Company has retained certain rights, including the right to use *TfR1 Bicycles* for all non-oligonucleotide therapeutic purposes.

The activities under the Ionis Collaboration Agreement are governed by a joint steering committee ("JSC") with an equal number of representatives from the Company and Ionis. The JSC will oversee the performance of the research and development activities. Upon first commercial sales of a licensed product, the JSC will have no further responsibilities or authority under the Ionis Collaboration Agreement.

Under the Ionis Collaboration Agreement, Ionis made a non-refundable upfront payment of \$31.0 million in addition to the \$3.0 million already paid under the Option and Evaluation Agreement. Additionally, Ionis is obligated to reimburse the Company on a pass-through basis for expenses incurred in connection with research and discovery activities performed by a CRO. If Ionis is at risk of failing to achieve a specified development diligence milestone deadline, it can make up to three separate payments of a mid-single-digit million dollar amount to extend the development diligence milestone deadlines. On a collaboration target-by-collaboration target basis, Ionis will be required to make a low-single-digit million dollar payment upon acceptance of an investigational new drug application ("IND") for the first product directed to such collaboration target (provided that Ionis will have a high single-digit million dollar credit to be applied towards the IND acceptance fee for four collaboration targets, or for exclusivity payments for certain targets if specified development diligence milestones deadlines are not achieved), and Ionis will be required to make milestone payments upon the achievement of specified development and regulatory milestones of up to a low double-digit million dollar amount per collaboration target. In addition, the Company is eligible to receive up to a low double-digit million dollar amount in cumulative sales milestone payments. The Company is also entitled to receive tiered royalty payments on net sales at percentages in the low single digits, subject to certain standard reductions and offsets. Royalties will be payable, on a product-by-product and country-by-country basis, until the latest of the expiration of specified licensed patents covering such product in such country, ten years from first commercial sale of such product in such country, or expiration of marketing exclusivity for such product in such country.

In December 2021, the Company and Ionis entered into an amendment to the Ionis Collaboration Agreement (the "Ionis Amendment"). Ionis paid the Company \$1.6 million and the Company agreed to perform additional research services utilizing its proprietary phage screening technology to identify and optimize new product candidates that target the *TfR1* receptor. The Company will perform the additional research services for an initial six-month period, which was extended in August 2022 for an additional three months, in exchange for consideration of \$0.8 million. In October 2022,

Ionis exercised an option it had for the Company to perform additional research services for an additional six months in exchange for the remaining consideration of \$0.8 million. In April 2023, the Company and Ionis entered into the third amendment to the Ionis Collaboration Agreement (the “Third Ionis Amendment”). Ionis paid the Company \$0.8 million and the Company agreed to perform additional research services to continue to evaluate and optimize the new product candidates that target the TfR1 receptor. The Company will perform the additional research services for a period of one year in exchange for consideration of \$0.8 million.

Either party may terminate the Ionis Collaboration Agreement for the uncured material breach of the other party or in the case of insolvency. Ionis may terminate the Ionis Collaboration Agreement for convenience on specified notice periods depending on the development stage of the applicable target, either in its entirety or on a target-by-target basis.

#### *Ionis Share Purchase Agreement*

Concurrently with the execution of the Ionis Collaboration Agreement on July 9, 2021, the Company entered into a share purchase agreement (the “Ionis Share Purchase Agreement”) with Ionis, pursuant to which Ionis purchased 282,485 of the Company’s ordinary shares (the “Ionis Shares”) at a price per share of \$38.94, for an aggregate purchase price of approximately \$11.0 million.

The Share Purchase Agreement also provided that, subject to limited exceptions, Ionis could not sell any of the Ionis Shares until July 2022.

The Company determined the fair value of the Ionis Shares to be \$7.6 million, based on the closing price of the Company’s ADSs of \$31.11 per ADS on the date of the Ionis Share Purchase Agreement, less a discount for lack of marketability associated with resale restrictions applicable to the Ionis Shares, which was recorded as a component of shareholders’ equity. The Company concluded that the premium paid by Ionis under the Ionis Share Purchase Agreement represents additional consideration for the goods and services to be provided under the Ionis Collaboration Agreement. As such, the total premium of \$3.4 million was included in the transaction price under the Ionis Collaboration Agreement.

#### *Accounting analysis*

Upon execution of the Ionis Collaboration Agreement, the Company identified the following promises in the arrangement: i) a worldwide exclusive license to research, develop, manufacture and commercialize products incorporating TfR1 *Bicycles* intended for the delivery of oligonucleotide compounds directed to targets selected by Ionis for diagnostic, therapeutic, prophylactic and preventative uses in humans; ii) research and discovery activities to customize and optimize such TfR1 *Bicycles*; iii) four material rights associated with options to obtain credits to be applied towards the IND acceptance fee for four collaboration targets.

The Company’s participation in the JSC was deemed immaterial in the context of the contract. The Company has concluded that the exclusive license to research, develop, manufacture and commercialize products is not distinct from the research and development services as Ionis cannot obtain the intended benefit of the license without the Company performing the agreed upon research and discovery services, including the optimization of such TfR1 *Bicycles*. The services incorporate proprietary technology, unique skills and specialized expertise to optimize *Bicycles* that are not available in the marketplace. As a result, the exclusive license to research, develop, manufacture and commercialize products has been combined with the research and discovery activities into a single performance obligation. The Company concluded that the low-single-digit million dollar payments upon acceptance of an IND (and payment to extend the exclusive license to research, develop, manufacture and commercialize a product candidate for certain specific collaboration targets if Ionis fails to achieve specified development diligence milestone deadlines) is a customer option, as Ionis has the contractual right to choose to make the payment in exchange for the continued exclusive right to research, develop, manufacture and commercialize the product candidate, and the Company is not presently obligated to provide, and does not have a right to consideration, for the additional goods or services prior to Ionis’s exercise of the option. In assessing whether the options under the Ionis Collaboration Agreement represent material rights, the Company considered the additional consideration the Company would be entitled to upon the option exercise and the standalone selling price of the underlying goods and services. For the material rights identified above,

the Company concluded that each of the options to obtain credits provided Ionis with a discount that it otherwise would not have received without entering into the Ionis Collaboration Agreement.

The total transaction price was initially determined to be \$38.0 million, consisting of the \$31.0 million up front payment, the \$3.0 million payment under the Option and Evaluation Agreement that was credited against the total upfront payment payable pursuant to the Ionis Collaboration Agreement, the \$3.4 million premium paid under the Ionis Share Purchase Agreement, and an estimated \$0.6 million for the reimbursement of CRO costs. Additional variable consideration including development diligence milestone deadline extension payments, development and regulatory milestone payments, sales milestone payments and royalty payments was fully constrained as a result of the uncertainty regarding whether any of the milestones will be achieved.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling price of the Ionis combined licenses and research and discovery performance obligation was based on the nature of the licenses to be delivered, as well as the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin for what would be expected to be realized under similar contracts. The estimated standalone selling price for the material rights was determined based on the estimated value of the underlying goods and services, and the probability that Ionis would exercise the option. Based on the relative standalone selling price, the allocation of the transaction price to the separate performance obligations is as follows (in thousands):

<b>Performance Obligations</b>	<b>Allocation of Transaction Price</b>
Combined licenses and research and discovery performance obligation	\$ 34,100
Four material rights associated with credits for IND Acceptance fees	3,900
	<b>\$ 38,000</b>

The Company is recognizing revenue related to amounts allocated to the combined licenses and research and discovery performance obligation using a proportional performance model over the period of service using input-based measurements including total full-time equivalent effort and CRO costs incurred to date as a percentage of total full-time equivalent effort and CRO costs expected, which best reflects the progress towards satisfaction of the performance obligation. The amount allocated to the material rights is recorded as deferred revenue and the Company commences revenue recognition upon exercise of or upon expiry of the respective option. The Company anticipates that the combined licenses and research and discovery performance obligation will be satisfied over a period of three years and anticipates the material rights may be exercisable or may expire after approximately four years from contract execution.

The Company concluded that the Ionis Amendment will be accounted for as a separate contract, as the services are distinct from the Ionis Collaboration Agreement, and the price of the contract increased by an amount of consideration that reflects the Company's standalone selling price. The Company concluded that the option does not contain a material right. The Company recognized the \$0.8 million associated with the services in the initial six-month period as revenue as the underlying services were performed using a proportional performance model over the period of service using input-based measurements of total full time equivalent efforts and external costs incurred to date as a percentage of total expected full time equivalent efforts and expected external costs, which best reflects the progress towards satisfaction of the performance obligation. As the option to perform additional research services for an additional six months does not contain a material right, the Company accounted for Ionis' exercise of the option in October 2022 as a separate contract. The Company recognized the \$0.8 million associated with the services for the additional six-month period as revenue as the underlying services were performed using a proportional performance model over the period of service using input-based measurements of total full time equivalent efforts and external costs incurred to date as a percentage of total expected full time equivalent efforts and expected external costs, which best reflects the progress towards satisfaction of the performance obligation.

The Company concluded that the Third Ionis Amendment will be accounted for as a contract modification to the separate contract under the Ionis Amendment, as the services are not distinct from the services provided under the Ionis Amendment. The Company is recognizing the \$0.8 million associated with the services for the additional one-year period as revenue as the underlying services are performed using a proportional performance model over the period of

service using input-based measurements of total full time equivalent efforts and external costs incurred to date as a percentage of total expected full time equivalent efforts and expected external costs, which best reflects the progress towards satisfaction of the performance obligation.

For the three and nine months ended September 30, 2023, the Company recognized revenue of \$2.8 million and \$8.1 million, respectively, and for the three and nine months ended September 30, 2022, the Company recognized revenue of \$2.2 million and \$6.8 million, respectively. As of September 30, 2023, and December 31, 2022, the Company recorded deferred revenue of \$14.5 million and \$21.5 million, respectively, in connection with the Ionis Collaboration Agreement, Ionis Amendments, and Ionis Evaluation and Option Agreement.

### **Genentech Collaboration Agreement**

On February 21, 2020, the Company entered into a Discovery Collaboration and License Agreement, as amended from time to time, with Genentech (the “Genentech Collaboration Agreement”). The collaboration is focused on the discovery and development of *Bicycle* peptides directed to biological targets selected by Genentech and aimed at developing up to four potential development candidates against multiple immuno-oncology targets suitable for Genentech to advance into further development and commercialization.

Under the terms of the Genentech Collaboration Agreement, the Company received a \$30.0 million upfront, non-refundable payment. The initial discovery and optimization activities are focused on utilizing the Company’s phage screening technology to identify product candidates aimed at two immuno-oncology targets (“Genentech Collaboration Programs”), which may also include additional discovery and optimization of *Bicycles* as targeting elements for each Genentech Collaboration Program (each a “Targeting Arm”). Genentech also had the option to nominate up to two additional immuno-oncology targets (each, an “Expansion Option”) as additional Genentech Collaboration Programs, which may also include an additional Targeting Arm for each Expansion Option. Genentech exercised the Expansion Options in October 2021 and June 2022, respectively. Genentech paid to the Company an expansion fee of \$10.0 million for each Expansion Option. Genentech also has rights, under certain limited circumstances, to select an alternative target to be the subject of a Genentech Collaboration Program, in some cases subject to payment of an additional target selection fee.

If Genentech elects for the Company to perform discovery and optimization services for certain Targeting Arms, the Company will be entitled to receive an additional advance payment for the additional research services. Genentech exercised its right to select a Targeting Arm for one of the initial Genentech Collaboration Programs at the inception of the arrangement, and for the first Expansion Option in October 2021, which entitled the Company to additional payments of \$1.0 million each. If a Targeting Arm achieves specified criteria in accordance with the research plan, Genentech will be required to pay a further specified amount in the low single digit millions for each such Targeting Arm as consideration for the additional services to be provided.

The Company granted to Genentech a non-exclusive research license under the Company’s intellectual property solely to enable Genentech to perform any activities under the agreement. The activities under the Genentech Collaboration Agreement are governed by a joint research committee (“JRC”) with representatives from each of the Company and Genentech. The JRC will oversee, review and recommend direction of each Genentech Collaboration Program, achievement of development criteria, and variations of or modifications to the research plans.

After the Company performs the initial discovery and optimization activities in accordance with an agreed research plan and achieves specified criteria, Genentech will have the option to have the Company perform initial pre-clinical development and optimization activities in exchange for an additional specified milestone payment in the mid-single digit millions for each Genentech Collaboration Program (the “LSR Go Option”). Upon completion of such initial pre-clinical development and optimization activities for each Genentech Collaboration Program, Genentech will have the option to obtain an exclusive license to exploit any compound developed under such Genentech Collaboration Program in exchange for an additional specified payment in the mid to high single digit millions for each of the initial two Genentech Collaboration Programs and each of the two Expansion Option Genentech Collaboration Programs (the “Dev Go Option”).

On a Genentech Collaboration Program by Genentech Collaboration Program basis, if Genentech elects to obtain exclusive development and commercialization rights and pays the applicable LSR Go Option and Dev Go Option fees, Genentech will be required to make milestone payments to the Company upon the achievement of specified development, regulatory, and initial commercialization milestones for products arising from each collaboration program, totaling up to \$200.0 million. Specifically, the Company is eligible for additional development milestones totaling up to \$65.0 million, as well as regulatory milestones of up to \$135.0 million for each collaboration program. In addition, the Company is also eligible to receive up to \$200.0 million in sales milestone payments on a Genentech Collaboration Program-by-Genentech Collaboration Program basis. In addition, to the extent any of the product candidates covered by the licenses conveyed to Genentech are commercialized, the Company would be entitled to receive tiered royalty payments on net sales at percentages ranging from the mid-single to low double-digits, subject to certain standard reductions and offsets. Royalties will be payable, on a product by product and country by country basis, until the later of the expiration of specified licensed patents covering such product in such country, or ten years from first commercial sale of such product in such country.

*Accounting analysis*

Upon the execution of the Genentech Collaboration Agreement, the Company has identified the following performance obligations:

- (i) Research license, and the related research and development and preclinical services through LSR Go for a first Genentech Collaboration Program (Genentech Collaboration Program #1);
- (ii) Research license, and the related research and development and preclinical services through LSR Go for a second Genentech Collaboration Program with a specified Targeting Arm (Genentech Collaboration Program #2);
- (iii) Material right associated with an option to a specified Targeting Arm for Genentech Collaboration Program #1;
- (iv) Two material rights associated with the LSR Go Option for Genentech Collaboration Program #1 and Genentech Collaboration Program #2, which includes research services to be provided through the Dev Go Option and an option to receive an exclusive license;
- (v) Material rights associated with certain limited substitution rights with respect to a limited number of collaboration targets;
- (vi) Two material rights related to each Genentech Expansion Option, which upon exercise include the services for an additional immuno-oncology target through the LSR Go Option, an LSR Go Option which includes the services to be provided through the Dev Go Option and an option to receive an exclusive license, limited substitution rights, and an option to select a specified Targeting Arm.

The Company concluded that certain substitution rights that require the payment of additional consideration, which approximate the standalone selling price of the underlying services to be provided, do not provide the customer with a material right and therefore, are not considered as performance obligations and are accounted for as separate contracts upon exercise, if ever. The Company's participation in the JRC was assessed as immaterial in the context of the contract.

The Company has concluded that the research license is not distinct from the research and development services as Genentech cannot obtain the benefit of the research license without the Company performing the research and development services. The services incorporate proprietary technology and unique skills and specialized expertise, particularly as it relates to constrained peptide technology that is not available in the marketplace. As a result, for each research program, the research license has been combined with the research and development services into a single performance obligation. In addition, the Company concluded that the Dev Go Option is not distinct or separately

exercisable from the LSR Go Option, as the customer cannot benefit from the Dev Go Option unless and until the LSR Go Option is exercised.

In assessing whether the various options under the Genentech Collaboration Agreement represent material rights, the Company considered the additional consideration the Company would be entitled to upon the option exercise, the standalone selling price of the underlying goods, services, and additional options. For the material rights identified above the Company concluded that each of the options provided Genentech with a discount that it otherwise would not have received.

The total transaction price was initially determined to be \$31.0 million, consisting of the \$30.0 million upfront fee and the additional \$1.0 million for Genentech's selection of a new Targeting Arm at inception. The Company utilizes the most likely amount method to determine the amount of research and development funding to be received. Additional consideration to be paid to the Company upon the exercise of options by Genentech and subsequent milestones are excluded from the transaction price as they relate to option fees and milestones that can only be achieved subsequent to the exercise of an option. In addition, other variable consideration for development milestones not subject to option exercises was fully constrained, as a result of the uncertainty regarding whether any of the milestones will be achieved. In March 2021, the Company achieved specified criteria in accordance with the research plan under the Genentech Collaboration agreement and therefore updated its estimate of the variable consideration to include an additional \$2.0 million, that is no longer constrained. The arrangement consideration was increased to \$33.0 million.

The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. The estimated standalone selling prices for the Genentech Collaboration Programs was based on the nature of the services to be performed and estimates of the associated effort and costs of the services, adjusted for a reasonable profit margin for what would be expected to be realized under similar contracts. The estimated standalone selling price for the material rights was determined based on the fees Genentech would pay to exercise the options, the estimated value of the underlying goods and services, and the probability that Genentech would exercise the option and any underlying options. Based on the relative standalone selling price, the initial allocation of the transaction price to the separate performance obligations is as follows (in thousands):

<b>Performance Obligations</b>	<b>Allocation of Transaction Price</b>
Genentech Collaboration Program #1 Performance Obligation	\$ 4,019
Genentech Collaboration Program #2 Performance Obligation	8,037
Specified Targeting Arm Material Right Arm for Genentech Collaboration Program #1	352
Two material rights associated with the LSR Go Option for Collaboration Programs #1 and #2	12,400
Material rights associated with limited substitution rights	1,187
Two material rights for Expansion Options	7,005
	<b>\$ 33,000</b>

The Company recognizes revenue related to amounts allocated to the Genentech Collaboration Program #1 and #2 Performance Obligations as the underlying services are performed using a proportional performance model over the period of service using input-based measurements of total full-time equivalent efforts and external costs incurred to date as a percentage of total full-time equivalent efforts and external costs expected, which best reflects the progress towards satisfaction of the performance obligation. The amount allocated to the material rights is recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the respective option. The Company anticipates that the Genentech Collaboration Performance Program #1 and #2 obligations will be performed over a period of approximately two to three years, and the material rights will be exercised or expire within approximately four years from contract execution. In June 2023, Genentech terminated Genentech Collaboration Program #1 and revenue of \$6.0 million was recognized during the nine months ended September 30, 2023 related to the expiration of the material right associated with the LSR Go Option for Collaboration Program #1.

In October 2021 and June 2022, respectively, Genentech exercised the first and second Expansion Options to add additional Genentech Collaboration Programs (Genentech Collaboration Program #3 and Genentech Collaboration Program #4) and paid to the Company an expansion fee of \$10.0 million for each option. For the first Expansion Option, Genentech also elected for the Company to perform discovery and optimization services for a Targeting Arm, and the Company received an additional payment of \$1.0 million for additional research services. The Company exercised judgment and concluded that the exercise of each Expansion Option, including the option to a specified Targeting Arm for the first Expansion Option, is accounted for as a continuation of an existing contract as the customer decided to purchase additional goods and services contemplated in the original contract. For the first Expansion Option, the additional arrangement consideration of \$11.0 million received upon the option exercises and the \$3.5 million originally allocated to the first Expansion Option material right is allocated to the underlying goods and services associated with the first Expansion Option on the same basis as the initial allocation of the Genentech Collaboration Agreement. In December 2022, the Targeting Arm associated with the first Expansion Option achieved specified criteria in accordance with the research plan under the Genentech Collaboration Agreement and therefore the Company updated its estimate of variable consideration to include an additional \$2.0 million, that is no longer constrained. The Company allocated the additional \$2.0 million entirely to the Genentech Collaboration Program #3 and Targeting Arm services as the terms of the variable consideration relate specifically to the Company's efforts in satisfying the performance obligation and allocating the variable consideration entirely to the performance obligation is consistent with the allocation objective in ASC 606. For the second Expansion Option, the additional arrangement consideration of \$10.0 million received pursuant to the option exercise together with the \$3.5 million originally allocated to the second Expansion Option material right is allocated to the underlying goods and services associated with the second Expansion option on the same basis as the initial allocation of the Genentech Collaboration Agreement. The Company recognizes the \$8.4 million allocated to the Genentech Collaboration Program #3 and Targeting Arm services and \$5.3 million allocated to the Genentech Collaboration Program #4 services as the underlying services are performed using a proportional performance model over the period of service of approximately two to three years for each program using input-based measurements of total full-time equivalent efforts and external costs incurred to date as a percentage of total full-time equivalent efforts and external costs expected, which best reflects the progress towards satisfaction of the performance obligations. The amount allocated to the material rights associated with an LSR Go Options for Genentech Collaboration Program #3 and Genentech Collaboration #4 of \$7.4 million and \$7.4 million, respectively, limited substitution material rights of \$0.7 million and \$0.7 million, respectively, and the material right associated with the option to select a Targeting Arm for Genentech Collaboration #4 of \$0.1 million, are recorded as deferred revenue and the Company will commence revenue recognition upon exercise or expiry of each respective option which is expected to be within approximately four years of the Expansion Option exercise. Other variable consideration for development milestones not subject to option exercises was fully constrained as a result of the uncertainty regarding whether any of the milestones will be achieved.

During the three and nine months ended September 30, 2023, the Company recognized revenue of \$1.4 million and \$11.1 million, respectively, and during the three and nine months ended September 30, 2022, the Company recognized revenue of \$0.8 million and \$3.1 million, respectively. As of September 30, 2023 and December 31, 2022, the Company recorded \$28.7 million and \$39.3 million, respectively, of deferred revenue in connection with the Genentech Collaboration Agreement.

#### ***AstraZeneca Collaboration Agreement***

In November 2016, the Company entered into a Research Collaboration Agreement (the "AstraZeneca Collaboration Agreement") with AstraZeneca. The collaboration activities initially focused on two targets within respiratory, cardiovascular and metabolic disease, for which collaboration activities were terminated by AstraZeneca in October 2020 and March 2021, respectively. In May 2018, AstraZeneca made an irrevocable election to exercise an option to nominate four additional targets ("Additional Four Target Option"). As a result, AstraZeneca was entitled to obtain research and development services from the Company with respect to *Bicycle* peptides that bind to up to four additional targets, along with license rights to those selected targets, in exchange for an option fee of \$5.0 million.

Upon the execution of the Additional Four Target Option, the Company identified the following five performance obligations: (i) Research license and the related research and development services during the Bicycle Research Term for the third target (the "Target Three Research License and Related Services"); (ii) Material right associated with the development and exploitation license option for the third target ("Target Three Material Right"); (iii)

Material right associated with the research services option, including the underlying development and exploitation license option for the fourth target (“Target Four Material Right”); (iv) Material right associated with the research services option, including the underlying development and exploitation license option for the fifth target (“Target Five Material Right”); and (v) Material right associated with the research services option, including the underlying development and exploitation license option for the sixth target (“Target Six Material Right”). The total transaction price was initially determined to be \$5.7 million, consisting of the \$5.0 million option exercise fee and research and development funding of an estimated \$0.7 million. The transaction price was allocated to the performance obligations based on the relative estimated standalone selling prices of each performance obligation. In June 2019, the transaction was increased to \$6.3 million for additional research and development funding received.

The Company recognized revenue related to amounts allocated to the Target Three Research License and Related Services as the underlying services were performed using a proportional performance model over the period of service using input-based measurements of total full-time equivalent effort incurred to date as a percentage of total full-time equivalent effort expected, which best reflected the progress towards satisfaction of the performance obligation. The amount allocated to the material rights was recorded as deferred revenue and the Company commenced revenue recognition upon exercise of or upon expiry of the option. In October 2020, August 2021, and June 2022, AstraZeneca terminated the collaboration activities related to the third target, sixth and fifth targets, respectively, and the deferred revenue related to the associated material rights of \$1.5 million, \$1.2 million, and \$1.1 million, respectively, was recognized. In April 2023, AstraZeneca terminated the collaboration activities related to the fourth target and the deferred revenue related to the associated material right of \$1.2 million was recognized during the nine months ended September 30, 2023. As of September 30, 2023, there are no research programs remaining under the AstraZeneca Collaboration Agreement.

For the three and nine months ended September 30, 2023, the Company recognized revenue of zero and \$1.2 million, respectively, and for the three and nine months ended September 30, 2022, the Company recognized no revenue and \$1.2 million, respectively, in connection with the AstraZeneca Collaboration Agreement. As of September 30, 2023, and December 31, 2022, the Company recorded zero and \$1.1 million, respectively, of deferred revenue in connection with the AstraZeneca Collaboration Agreement.

### Summary of Contract Assets and Liabilities

The following table presents changes in the balances of the Company's contract assets and liabilities (in thousands):

	Beginning Balance January 1, 2023	Additions	Deductions	Impact of Exchange Rates	Ending Balance September 30, 2023
<b>Contract liabilities:</b>					
Deferred revenue					
Bayer collaboration deferred revenue	\$ —	\$ 45,000	\$ (434)	\$ (2,045)	\$ 42,521
Novartis collaboration deferred revenue	—	50,000	(772)	(178)	49,050
Ionis collaboration deferred revenue	21,489	870	(8,123)	227	14,463
Genentech collaboration deferred revenue	39,308	—	(11,112)	542	28,738
AstraZeneca collaboration deferred revenue	1,076	—	(1,204)	128	—
<b>Total deferred revenue</b>	<b>\$ 61,873</b>	<b>\$ 95,870</b>	<b>\$ (21,645)</b>	<b>\$ (1,326)</b>	<b>\$ 134,772</b>

	Beginning Balance January 1, 2022	Additions	Deductions	Impact of Exchange Rates	Ending Balance December 31, 2022
<b>Contract liabilities:</b>					
Deferred revenue					
Ionis collaboration deferred revenue	\$ 34,115	\$ 99	\$ (9,347)	\$ (3,378)	\$ 21,489
Genentech collaboration deferred revenue	34,436	12,000	(3,565)	(3,563)	39,308
DDF collaboration deferred revenue	428	—	(386)	(42)	—
AstraZeneca collaboration deferred revenue	2,361	—	(1,165)	(120)	1,076
<b>Total deferred revenue</b>	<b>\$ 71,340</b>	<b>\$ 12,099</b>	<b>\$ (14,463)</b>	<b>\$ (7,103)</b>	<b>\$ 61,873</b>

Contract assets represent research and development services which have been performed but have not yet been billed, and are reduced when they are subsequently billed. There were no contract assets at September 30, 2023 or December 31, 2022.

As of September 30, 2023, the Bayer, Novartis, Ionis, and Genentech deferred revenue balances include \$31.0 million, \$31.9 million, \$3.5 million, and \$20.9 million, respectively, allocated to material rights that will commence revenue recognition when the respective option is exercised or when the option expires.

During the three and nine months ended September 30, 2023 and 2022, the Company recognized the following revenues as a result of changes in the contract asset and the contract liability balances in the respective periods (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
<b>Revenue recognized in the period from:</b>				
Revenue recognized based on proportional performance	\$ 5,006	\$ 3,040	\$ 13,829	\$ 10,072
Revenue recognized based on expiration of material rights	346	—	7,816	1,206
<b>Total</b>	<b>\$ 5,352</b>	<b>\$ 3,040</b>	<b>\$ 21,645</b>	<b>\$ 11,278</b>

*Cancer Research UK*

*BT1718*

On December 13, 2016, the Company entered into a Clinical Trial and License Agreement with Cancer Research Technology Limited (“CRTL”), a wholly owned subsidiary of Cancer Research UK that Cancer Research UK’s commercial activities operate through, and Cancer Research UK (the “Cancer Research UK Agreement”). Pursuant to the Cancer Research UK Agreement, as amended in March 2017 and June 2018, Cancer Research UK’s Centre for Drug Development will sponsor and fund a Phase I/IIa clinical trial for BT1718, a *Bicycle Toxin Conjugate*, in patients with advanced solid tumors.

Cancer Research UK is responsible for designing, preparing, carrying out and sponsoring the clinical trial at its cost. The Company is responsible for supplying agreed quantities of GMP materials for the trial, the supply of which has been completed. In the event that additional quantities are needed, the Company will provide Cancer Research UK with all reasonable assistance to complete the arrangements necessary for the generation and supply of such additional GMP materials, but Cancer Research UK will be responsible for supplying and paying for such additional quantities of GMP materials.

The Company granted Cancer Research UK a license to its intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial. The Company retains the right to continue the development of BT1718 during the clinical trial. Upon the completion of the Phase I/IIa clinical trial, the Company has the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and the Company decides to abandon development of all products that deliver cytotoxic payloads to the MT1 target antigen, the Company will assign or grant to CRTL an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case the Company will receive tiered royalties of 70% to 90% of the net revenue depending on the stage of development when the license is granted). The Cancer Research UK Agreement contains additional future milestone payments upon the achievement of development and regulatory milestones, payable in cash and shares, with an aggregate total value of \$50.9 million, as well as royalty payments based on a single digit percentage on net sales of products developed.

The Cancer Research UK Agreement can be terminated by either party upon an insolvency event, material breach of the terms of the contract, or upon a change in control (and the new controlling entity develops, sells or manufactures tobacco products or generates the majority of its profits from tobacco products or is an affiliate of such party). Cancer Research UK may also terminate the arrangement for safety reasons or if it determines that the objectives of the clinical trial will not be met. The Company was obligated to reimburse Cancer Research UK for certain costs if the Cancer Research UK agreement was terminated by Cancer Research UK prior to the completion of the dose escalation (Phase I) part of the clinical trial for an insolvency event of, or material breach by, the Company or upon termination for safety reasons or if Cancer Research UK determined that the objectives of the clinical trial would not be met, however, these reimbursement obligations expired unexercised upon the completion of the Phase I portion of the clinical trial in 2020. If the Company is subject to a change in control and the new controlling entity develops, sells or manufactures tobacco products or generates the majority of its profits from tobacco products or is an affiliate of such party prior to the last cycle of treatment under the Phase IIa clinical trial, the Company will reimburse Cancer Research UK in full for all costs paid or committed in connection with the clinical trial and no further license payments, where applicable, shall be due. In such case, Cancer Research UK will not be obliged to grant a license to the Company in respect of the results of the clinical trial and the Company will assign or grant to CRTL an exclusive license to develop and commercialize the product without CRTL being required to make any payment to the Company.

The Company concluded that the costs incurred by Cancer Research UK is a liability in accordance with ASC 730, *Research and Development*, as certain payments are not based solely on the results of the research and development having future economic benefit. As such, the Company recorded a liability of \$4.1 million and \$3.6 million at September 30, 2023 and December 31, 2022, respectively, which is recorded in other long-term liabilities in the condensed consolidated balance sheets. The liability is recorded as incremental research and development expense in the condensed consolidated statements of operations and comprehensive loss.

## BT7401

In December 2019, the Company entered into a clinical trial and license agreement with Cancer Research Technology Limited and Cancer Research UK. Pursuant to the agreement, Cancer Research UK's Centre for Drug Development will fund and sponsor development of BT7401, a multivalent *Bicycle* CD137 agonist, from current preclinical studies through the completion of a Phase IIa trial in patients with advanced solid tumors.

The Company granted to Cancer Research UK a license to the Company's intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial and all necessary preclinical activities to support the trial. The Company retains the right to continue the development of BT7401 during the clinical trial. Upon the completion of the Phase I/IIa clinical trial, the Company has the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and the Company decides to abandon development of all products that contain BT7401 or all the pharmaceutically active parts of BT7401, CRTL may elect to receive an exclusive license to develop and commercialize the product on a revenue sharing basis (in which case the Company will receive tiered royalties of 55% to 80% of the net revenue depending on the stage of development when the license is granted) less certain costs, as defined by the agreement. The BT7401 Cancer Research UK agreement contains additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash, with an aggregate total value of up to \$60.3 million for each licensed product, as well as royalty payments based on a single digit percentage on net sales of products developed, and sublicense royalties to the Cancer Research UK in the low double digit percentage of sublicense income depending on the stage of development when the license is granted.

The BT7401 Cancer Research UK agreement can be terminated by either party upon an insolvency event, material breach of the terms of the contract, or upon a change in control (and the new controlling entity develops, sells or manufactures tobacco products or generates the majority of its profits from tobacco products or is an affiliate of such party), or upon written notice by Cancer Research UK prior to the last cycle of treatment has been completed under the clinical trial. If the trial is terminated by the Company prior to the filing of a clinical trial authorization, or by Cancer Research UK for an insolvency event or a material breach by the Company prior to the start of a clinical trial, the Company will reimburse Cancer Research UK for certain costs paid or committed prior to the start of the clinical trial. In such case where the Company is subject to a change of control and the new controlling entity develops, sells or manufactures tobacco products or generates the majority of its profits from tobacco products or is an affiliate of such party, Cancer Research UK will not be obliged to grant a license to the Company in respect of the results of the clinical trial and CRTL may elect to receive an exclusive license to develop and commercialize the product without CRTL being required to make any payment to the Company. The Company concluded that the BT7401 Cancer Research UK arrangement does not represent a liability in accordance with ASC 730, *Research and Development*, as the payments are based solely on the results of the research and development having future economic benefit and risk of repayment is substantive and genuine, and as such there was no accounting impact for the three and nine months ended September 30, 2023.

## 10. Income taxes

During the three and nine months ended September 30, 2023 the Company recorded an income tax provision of \$2.3 million and \$1.1 million, respectively, and during the three and nine months ended September 30, 2022, the Company recorded an income tax benefit of \$0.2 million and \$1.1 million, respectively. The Company is subject to United Kingdom corporate taxation. Due to the nature of its business, the Company has generated losses since inception and has therefore not paid United Kingdom corporation tax. The provision for (benefit from) income taxes included in the condensed consolidated statements of operations and comprehensive loss represents the tax impact from operating activities in the United States, which has generated taxable income based on intercompany service arrangements. Deferred tax assets benefitted in the United States do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement.

Starting in 2022, amendments to Section 174 of the Internal Revenue Code of 1986, as amended ("IRC"), eliminated the option to immediately deduct research and development expenditures in the tax year that such costs are

incurred. In accordance with the amendments, beginning on January 1, 2022, and continuing until the end of the second quarter of 2023, these research and development costs were capitalized by the Company and amortized over either a five- or 15-year period, depending on the location of the activities performed. In the third quarter of 2023, the Company completed an assessment, inclusive of an external tax analysis, and concluded that it is not required to capitalize certain research and development expenses incurred by its U.S. subsidiary associated with contractual research services performed on behalf of its U.K. subsidiary pursuant to an intercompany service arrangement because its U.S. subsidiary does not retain any ownership or rights in the underlying intellectual property resulting from the research services. The change in estimate upon the completion of this analysis resulted in an income tax provision of \$2.4 million during the three months ended September 30, 2023. The Company's income tax benefit recognized during the three and nine months ended September 30, 2022 is mainly the result of deferred tax assets benefitted in the U.S. that do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement.

The Company regularly assesses its ability to realize its deferred tax assets. Assessing the realization of deferred tax assets requires significant judgment. In determining whether its deferred tax assets are more likely than not realizable, the Company evaluated all available positive and negative evidence, and weighed the evidence based on its objectivity. After consideration of the evidence, including the Company's history of cumulative net losses in the U.K., the Company has concluded that it is more likely than not that the Company will not realize the benefits of its U.K. deferred tax assets and accordingly the Company has provided a valuation allowance for the full amount of the net deferred tax assets in the U.K. The Company has considered the Company's history of cumulative net profits in the U.S., estimated future taxable income and concluded that it is more likely than not that the Company will realize the benefits of its U.S. deferred tax assets and has not provided a valuation allowance against the net deferred tax assets in the U.S. The Company recorded a valuation allowance against all of its U.K. deferred tax assets as of September 30, 2023 and December 31, 2022.

The Company intends to continue to maintain a full valuation allowance on its U.K. deferred tax assets until there is sufficient evidence to support the reversal of all or some portion of these allowances. The release of the valuation allowance would result in the recognition of certain deferred tax assets and an increase to the benefit from income taxes for the period the release is recorded. However, the exact timing and amount of the valuation allowance release are subject to change on the basis of the level of profitability that the Company is able to actually achieve.

The provision for (benefit from) income taxes recorded in the condensed consolidated statements of operations differs from amounts that would result from applying the statutory tax rates to income before taxes primarily because of certain permanent expenses that were not deductible, U.K., federal and state research and development credits, as well as the application of valuation allowances against the U.K. deferred tax assets.

## **11. Commitments and contingencies**

### *Leases*

In January 2023, the Company entered into a lease agreement for office and laboratory space in Cambridge, Massachusetts. The lease has a contractual period of approximately three years, which, subject to certain conditions, may be extended for an additional two years at the Company's option. The Company concluded that the lease term is three years, representing the non-cancelable lease period, as it is not reasonably certain that the lease will be extended. The annual rent is approximately \$2.1 million in the first year of the lease and increases annually with the last year of the lease having annual rent of approximately \$2.3 million. The annual rent is payable monthly in advance following a two-month rent-free period. In connection with the lease agreement, the Company has delivered to the landlord a security deposit in the form of a letter of credit of approximately \$0.5 million. The Company initially recorded a right of use asset and lease liability of approximately \$5.8 million, respectively, at the lease commencement date, based on the present value of future lease payments, discounted at 9.0%, the Company's estimated incremental borrowing rate at the commencement of the lease, over the lease term. Rent expense is recognized on a straight-line basis over the lease term, including the two month rent-free period.

On December 6, 2021, the Company entered into a lease of new office and laboratory space in Cambridge, United Kingdom. The lease has a contractual period of 10 years, but may be cancelled by the Company on the fifth

anniversary of the lease commencement date. The lease term is five years, representing the non-cancelable lease period, as it is not reasonably certain that the lease will not be cancelled. The Company has a contractual right to renew the lease for a further ten-year period, which also may be cancelled after five years. The annual rent is approximately \$3.0 million, payable quarterly in advance beginning in June 2022, following a six-month period of free rent. There was no deposit paid in conjunction with the lease. The Company recorded a right of use asset of approximately \$11.6 million and a lease liability of approximately \$11.1 million at the lease commencement date, based on the present value of future lease payments, discounted at 6.9%, the Company's estimated incremental borrowing rate at the commencement of the lease, over the lease term. Rent expense is recognized on a straight-line basis over the five year lease term, including the six month rent-free period.

In October 2017, the Company entered into a lease agreement for office and laboratory space in Building 900, Babraham Research Campus, Cambridge, U.K., which was renewed in December 2021 for five years through December 2026. The annual rent for the lease was approximately \$0.6 million. Service charges were also payable based on floor area and are estimated to be approximately \$0.2 million per year. In April 2023, the Company entered into a deed of surrender related to the lease, pursuant to which the lease was terminated effective immediately. As a result of the deed, the Company derecognized the lease liability and right of use asset associated with the lease. The Company also paid termination-related fees of \$0.3 million in connection with the deed, which were recorded as a loss on lease termination and are included in operating expenses in the condensed consolidated statements of operations and comprehensive loss for the nine months ended September 30, 2023.

In September 2017, Bicycle Therapeutics Inc. entered into a lease agreement for office and laboratory space in Lexington, Massachusetts, which commenced on January 1, 2018. In March 2022, Bicycle Therapeutics Inc. notified the landlord of its intent to exercise its option to extend the lease, originally set to expire on December 31, 2022, for a successive period through December 31, 2027. The successive period was not included in the original lease term as it was not reasonably certain that the option would be exercised. In March 2022, the Company accounted for the lease extension as a modification of the existing lease and remeasured the right of use asset and lease liability by calculating the present value of lease payments, discounted at 7.0%, the Company's incremental borrowing rate, over the new lease term. In May 2022, the lease was extended. The payments for the extended lease are approximately \$0.2 million remaining through December 31, 2022, \$0.7 million in 2023, and increases annually pursuant to an escalation clause with the last year of the lease term having a per annum fixed rent obligation of \$0.8 million. In conjunction with the lease agreement, Bicycle Therapeutics Inc. paid a security deposit of \$0.2 million as well as prepaid rent of \$0.1 million for the first month of the third, fourth, and fifth year of the lease.

The components of the Company's lease expense, which are recorded as a component of research and development expenses and general and administrative expenses in the condensed consolidated statement of operations and comprehensive loss are as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Operating lease cost	\$ 1,364	\$ 924	\$ 4,057	\$ 2,866
Variable lease cost	566	410	2,017	1,005
Total lease cost	<u>\$ 1,930</u>	<u>\$ 1,334</u>	<u>\$ 6,074</u>	<u>\$ 3,871</u>

The weighted average remaining operating lease term was 3.2 years and 4.5 years as of September 30, 2023 and 2022, respectively, and the weighted average discount rate was 7.94% and 7.03% as of September 30, 2023 and 2022, respectively.

The following table summarizes the maturities of the Company's operating lease liabilities as of September 30, 2023 (in thousands):

<u>Year Ending December 31,</u>	
2023	1,394
2024	5,654
2025	5,740
2026	3,271
2027	821
Present value adjustment	(1,796)
Total lease liabilities	15,084
Less: current lease liabilities	(4,661)
Long term lease liabilities	<u>\$ 10,423</u>

The Company has entered into various agreements with contract research organizations to provide clinical trial services, contract manufacturing organizations to provide clinical trial materials and with vendors for preclinical research studies, synthetic chemistry and other services for operating purposes. These payments are not included in the table of operating lease payments above since the contracts are generally cancelable at any time upon less than 90 days' prior written notice. The Company is not contractually able to terminate for convenience and avoid any and all future obligations to these vendors. In some cases, we are contractually obligated to make certain minimum payments to the vendors, based on the timing of the termination notification and the exact terms of the agreement.

The Company's arrangements with CRUK provide for additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash and shares, with an aggregate total value of \$111.2 million, as well as royalty payments based on a single digit percentage on net sales of products developed. In addition, the Company has a separate agreement with a third party that provides for additional future milestone payments by the Company upon the achievement of specified development, regulatory and commercial milestones, with an aggregate total value of \$92.4 million. The Company also has a separate agreement with a third party that provides for future milestone payments by the Company upon the achievement of specified regulatory, development, commercial, and sales-based milestones, with an aggregate total, on a product-by-product basis, of \$1.3 million. These additional milestone payments are contingent upon future events. As of September 30, 2023, the Company was unable to estimate the timing or likelihood of achieving any of these milestones.

#### *Legal proceedings*

From time to time, the Company or its subsidiaries may become involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. The Company is currently not subject to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of ASC 450, *Contingencies*.

#### *Founder royalty arrangements*

At the time BicycleRD Limited was organized, BicycleRD Limited entered into a royalty agreement with its founders and initial investors (the "Founder Royalty Agreement"). Pursuant to the Founder Royalty Agreement, as amended, the Company will pay a royalty rate in the low single digit percentages on net product sales under the collaborations with Oxurion and AstraZeneca to its founders and initial investors, for a period of 10 years from the first commercial sale on a country-by-country basis. No royalties have been earned or paid under the Founder Royalty Agreement, as amended, to date.

#### *Indemnification obligations*

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses

arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has indemnification obligations towards members of its board of directors and officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification arrangements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnification obligations. The Company is not aware of any claims under indemnification arrangements, and therefore it has not accrued any liabilities related to such obligations in its condensed consolidated financial statements as of September 30, 2023, and December 31, 2022.

## 12. Net loss per share

Basic and diluted net loss per share was calculated as follows (in thousands, except share and per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
<b>Numerator:</b>				
Net loss	\$ (49,898)	\$ (28,347)	\$ (131,565)	\$ (82,739)
<b>Denominator:</b>				
Weighted average ordinary shares outstanding, basic and diluted	39,576,467	29,676,021	33,291,701	29,643,502
Net loss per share, basic and diluted	\$ (1.26)	\$ (0.96)	\$ (3.95)	\$ (2.79)

The Company's potentially dilutive securities, which are options to purchase ordinary shares and restricted share units for ordinary shares, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of ordinary shares outstanding, which includes both ordinary shares and non-voting ordinary shares, used to calculate both basic and diluted net loss per share is the same. The Company excluded the following potentially dilutive ordinary shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	September 30,	
	2023	2022
Restricted ordinary shares	335,104	187,725
Options to purchase ordinary shares	7,312,020	5,784,581
	<u>7,647,124</u>	<u>5,972,306</u>

## 13. Related party transactions

The Company has entered into the Founder Royalty Agreement, as amended, with its founders and initial investors (Note 11). No royalties have been earned or paid under the Founder Royalty Agreement, as amended, to date.

The Chairman of the Company's board of directors is associated with Stone Sunny Isles Inc. and Stone Atlanta Estates LLC, the successor-in-interest to Stone Sunny Isles Inc., which provided consultancy services to the Company totaling \$49,000 and \$0.2 million during the three and nine months ended September 30, 2023, respectively, and \$43,000 and \$0.2 million during the three and nine months ended September 30, 2022, respectively.

#### 14. Geographic information

The Company operates in two geographic regions: the United States and the United Kingdom. Information about the Company's long-lived assets, including operating lease right-of-use assets, held in different geographic regions is presented in the table below (in thousands):

	<u>September 30,</u> <u>2023</u>	<u>December 31,</u> <u>2022</u>
United States	\$ 8,817	\$ 4,466
United Kingdom	21,379	28,302
	<u>\$ 30,196</u>	<u>\$ 32,768</u>

The Company's collaboration revenues are attributed to the operations of the Company in the United Kingdom.

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

*You should read this discussion and analysis of our financial condition and consolidated results of operations together with our unaudited condensed consolidated financial statements and the related notes appearing elsewhere in this Quarterly Report on Form 10-Q and our audited financial statements and related notes for the year ended December 31, 2022, included in our Annual Report on Form 10-K for the year ended December 31, 2022, or the 2022 Annual Report, which was filed with the Securities and Exchange Commission, or SEC, on February 28, 2023. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including statements of our plans, objectives, expectations and intentions, contain 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 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. Please also see the section titled “Forward-Looking Statements.”*

### Overview

We are a clinical-stage biopharmaceutical company developing a novel class of medicines, which we refer to as *Bicycles*, for diseases that are underserved by existing therapeutics. *Bicycles* are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making *Bicycles* attractive candidates for drug development. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic, or PK, properties of a small molecule. The relatively large surface area presented by *Bicycles* allow targets to be drugged that have historically been intractable to non-biological approaches. *Bicycles* are excreted by the kidney rather than the liver and have shown no signs of immunogenicity to date.

We have a novel and proprietary phage display screening platform which we use to identify *Bicycles* in an efficient manner. The platform initially displays linear peptides on the surface of engineered bacteriophages, or phages, before “on-phage” cyclization with a range of small molecule scaffolds which can confer differentiated physicochemical and structural properties. Our platform encodes quadrillions of potential *Bicycles* which can be screened to identify molecules for optimization to potential product candidates. We have used this powerful screening technology to identify our current portfolio of candidates in oncology and intend to use it in conjunction with our collaborators to seek to develop additional future candidates across a range of other disease areas.

Our product candidates, BT8009, BT5528, and BT1718, are each a *Bicycle*<sup>®</sup> Toxin Conjugate, or BTC<sup>™</sup>. These *Bicycles* are chemically attached to a toxin that when administered is cleaved from the *Bicycle* and kills the tumor cells. We are evaluating BT8009, a BTC targeting Nectin-4, in a company-sponsored Phase I/II clinical trial and BT5528, a BTC targeting Ephrin type A receptor 2, or EphA2, in a company-sponsored Phase I/II clinical trial. In addition, BT1718 is being developed to target tumors that express Membrane Type 1 matrix metalloproteinase, or MT1 MMP, and is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial sponsored and fully funded by the Cancer Research UK Centre for Drug Development, or Cancer Research UK. In addition, our other product candidates, BT7480 and BT7455, are each a *Bicycle* tumor-targeted immune cell agonist<sup>®</sup>, or *Bicycle* TICA<sup>™</sup>. A *Bicycle* TICA links immune cell receptor binding *Bicycles* to tumor antigen binding *Bicycles*. We are evaluating BT7480, a *Bicycle* TICA targeting Nectin-4 and agonizing CD137, in a company-sponsored Phase I/II clinical trial, and we are conducting IND-enabling studies for BT7455, an EphA2/CD137 *Bicycle* TICA. Our discovery pipeline in oncology includes *Bicycle*-based systemic immune cell agonists and *Bicycle* TICAs.

In February 2023, results from the completed dose escalation portion of the Phase I/II clinical trial of BT8009 were presented at the 2023 ASCO Genitourinary (GU) Cancers Symposium. BT8009 demonstrated anti-tumor activity in heavily pre-treated urothelial, lung and breast cancer patients with signs of differentiation compared to antibody-based approaches. We announced that we dosed our first patient in the Phase II expansion portion of the clinical trial and established recommended Phase II doses of 5 mg/m<sup>2</sup> weekly and 7.5 mg/m<sup>2</sup> administered two-weeks on, one-week off over a 21-day cycle in November 2022. Enrollment in the clinical trial remains ongoing. In January 2023, we announced that the FDA has granted Fast Track Designation, or FTD, to our BT8009 monotherapy for the treatment of adult patients with previously treated locally advanced or metastatic urothelial cancer. FTD is intended to facilitate and expedite development and review of new drugs to address unmet medical need in the treatment of a serious or life-

threatening condition. In September 2023, we announced that we have aligned with the FDA on the design of a Phase II/III registrational trial for BT8009, called Duravelo-2, allowing for potential accelerated approval in untreated and previously treated metastatic urothelial cancer. In addition, in October 2023, we announced that BT8009 has been selected to participate in the Chemistry, Manufacturing and Controls (CMC) Development and Readiness Pilot Program recently launched by the FDA to facilitate CMC development for therapies with expedited clinical development timeframes based on the anticipated clinical benefits of earlier patient access to the therapy.

Beyond our wholly owned oncology portfolio, we are collaborating with biopharmaceutical companies and organizations in additional therapeutic areas in which we believe our proprietary *Bicycle* screening platform can identify therapies to treat diseases with significant unmet medical need.

## Financial Overview

Since our inception, we have devoted substantially all of our resources to developing our *Bicycle* platform and our product candidates, BT8009, BT5528, BT1718, BT7480, BT7455 and BT7401, conducting research and development of our product candidates and preclinical programs, raising capital and providing general and administrative support for our operations. To date, we have financed our operations primarily with proceeds from the sale of our ordinary shares, American Depositary Shares, or ADSs, non-voting ordinary shares, and convertible preferred shares, proceeds received from upfront payments, research and development payments, and development milestone payments from our collaboration arrangements with Bayer Consumer Care AG, or Bayer, Novartis Pharma AG, or Novartis, Ionis Pharmaceuticals, Inc., or Ionis, Genentech Inc., or Genentech, the Dementia Discovery Fund, or DDF, Sanofi (formerly Bioverativ Inc.), AstraZeneca AB, or AstraZeneca and Oxurion NV, or Oxurion; and borrowings pursuant to our Loan and Security Agreement, as amended, or the Loan Agreement with Hercules Capital, Inc., or Hercules. From our inception in 2009 through September 30, 2023, we have received gross proceeds of \$830.1 million from the sale of ADSs, ordinary shares, non-voting ordinary shares, and convertible preferred shares; and \$233.1 million of cash payments under our collaboration revenue arrangements, including \$45.0 million from Bayer, \$50.0 million from Novartis, \$47.5 million from Ionis, \$56.0 million from Genentech, \$10.3 million from AstraZeneca, and \$6.6 million from Oxurion; and borrowings of \$30.0 million pursuant to our Loan Agreement with Hercules. We do not have any products approved for sale and have not generated any revenue from product sales.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were \$49.9 million and \$131.6 million for the three and nine months ended September 30, 2023, respectively. As of September 30, 2023, we had an accumulated deficit of \$462.7 million. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future.

We anticipate that our expenses and capital requirements will increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates and, if any product candidates are approved, pursue the commercialization of such product candidates by building internal sales and marketing capabilities. We expect that our expenses and capital requirements will increase substantially if and as we:

- continue our development of our product candidates, including conducting future clinical trials of BT8009, BT5528, BT7480 and BT1718;
- progress the preclinical and clinical development of BT7455 and BT7401;
- seek to identify and develop additional product candidates;
- develop the necessary processes, controls and manufacturing data to obtain marketing approval for our product candidates and to support manufacturing to commercial scale;

- develop, maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- hire and retain additional personnel, such as non-clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, commercial and scientific personnel;
- acquire or in-license other products and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base, including adding equipment and infrastructure to support our research and development; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs and any future commercialization efforts.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain marketing approval for one or more of our product candidates, which we expect will take many years and is subject to significant uncertainty. We have no commercial-scale manufacturing facilities of our own, and all of our manufacturing activities have been and are planned to be contracted out to third parties. Additionally, we currently utilize third-party contract research organizations, or CROs, to carry out our clinical development activities. If we seek to obtain marketing approval for any of our product candidates from which we obtain promising results in clinical development, we expect to incur significant commercialization expenses as we prepare for product sales, marketing, manufacturing, and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances, charitable and governmental grants, monetization transactions or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more of our product candidates. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of September 30, 2023, we had cash and cash equivalents of \$572.1 million. We believe that our existing cash will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of filing of this Quarterly Report on Form 10-Q. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our available capital resources sooner than we expect. See “— Liquidity and Capital Resources” and “Capital Resources and Funding Requirements.”

## **Components of Our Results of Operations**

### ***Collaboration Revenues***

To date, we have not generated any revenue from product sales and we do not expect to generate any revenue from product sales for the foreseeable future. Our revenue primarily consists of collaboration revenue under our arrangements with our collaboration partners, including amounts that are recognized related to upfront payments, milestone payments and option exercise payments, and amounts due to us for research and development services. In the future, revenue may include additional milestone payments and option exercise payments, and royalties on any net

product sales under our collaborations. We expect that any revenue we generate will fluctuate from period to period as a result of the timing and amount of license, research and development services, milestone and other payments.

## **Expenses**

### *Research and Development Expenses*

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

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

Research and development costs are expensed as incurred. Costs for certain activities are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our condensed consolidated financial statements as prepaid expenses or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

U.K. research and development tax credits and government grant funding are recorded as an offset to research and development expenses. See “— Provision For (Benefit From) Income Taxes.”

Our direct external research and development expenses are tracked on a program-by-program basis and consist of costs, such as fees paid to consultants, contractors and contract manufacturing organizations, or CMOs, in connection with our preclinical and clinical development activities. Costs incurred after a product candidate has been designated and that are directly related to the product candidate are included in direct research and development expenses for that program. Costs incurred prior to designating a product candidate are included in other discovery and platform related expense. We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified.

In December 2016, we entered into a Clinical Trial and License Agreement with Cancer Research Technology Limited, or CRTL and Cancer Research UK, pursuant to which the Cancer Research UK Centre for Drug Development is sponsoring and funding a Phase I/IIa clinical trial for our product candidate, BT1718, in patients with advanced solid tumors. Cancer Research UK has designed and prepared and is carrying out and sponsoring the clinical trial at its own cost. Upon the completion of the Phase I/IIa clinical trial, we have the right to obtain a license to the results of the clinical trial upon the payment of a milestone, in cash and ordinary shares, with a combined value in the mid six digit dollar amount. If such license is not acquired, or if it is acquired and the license is terminated and we decide to abandon development of all products that deliver cytotoxic payloads to the MT1 target antigen, CRTL may elect to receive an assignment and exclusive license to develop and commercialize the product on a revenue sharing basis (in which case

we will receive tiered royalties of 70% to 90% of the net revenue depending on the stage of development when the license is granted is less certain costs, as defined in the agreement). The Cancer Research UK Agreement contains additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash and shares, with an aggregate total value of \$50.9 million, as well as royalty payments based on a single digit percentage on net sales of products developed. The Cancer Research UK Agreement can be terminated by either party upon an insolvency event, material breach of the terms of the contract, upon a change in control involving a tobacco related entity, and in certain other specified circumstances, and includes provisions that require the repayment of costs to Cancer Research UK upon certain termination events. The costs incurred by Cancer Research UK are recorded as a liability in accordance with ASC 730, *Research and Development* as the payments are not based solely on the results of the research and development having future economic benefit. The accrual of the liability is recorded as incremental research and development expense in the condensed consolidated statements of operations and comprehensive loss. Upon the completion of the Phase IIa part of the clinical trial, we expect research and development expenses to increase significantly as we expect to fund the continued development of BT1718, as well as incur additional development milestone payments.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future as a result of our expanded portfolio of product candidates and as we: (i) continue the clinical development and seek to obtain marketing approval for our product candidates, including BT8009, BT5528, BT7480 and BT1718; (ii) initiate clinical trials for our product candidates, including BT7455; and (iii) build our in-house process development and analytical capabilities and continue to discover and develop additional product candidates.

The successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates. This is due to the numerous risks and uncertainties associated with developing products, including the uncertainty of:

- completing research and preclinical and clinical development of our product candidates, including conducting future clinical trials of BT8009, BT5528, BT7480 and BT1718;
- progressing the preclinical and clinical development of BT7455 and BT7401;
- establishing an appropriate safety profile with IND-enabling studies to advance our preclinical programs into clinical development;
- identifying new product candidates to add to our development pipeline;
- successful enrollment in, and the initiation and completion of clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with others;
- establishing commercial manufacturing capabilities or making arrangements with third party manufacturers;
- the development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials;

- addressing any competing technological and market developments, as well as any changes in governmental regulations;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations under such arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how, as well as obtaining and maintaining regulatory exclusivity for our product candidates;
- continued acceptable safety profile of the drugs following approval; and
- attracting, hiring and retaining qualified personnel.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, the FDA, EMA or another regulatory authority may require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or we may experience significant trial delays due to patient enrollment or other reasons in which case we would be required to expend significant additional financial resources and time on the completion of clinical development. In addition, we may obtain unexpected results from our clinical trials and we may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. Identifying potential product candidates and conducting preclinical testing 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 marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Moreover, if adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity for our product candidates in the EU.

#### *General and Administrative Expenses*

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, auditing, tax and consulting services, insurance, travel and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

Foreign currency transactions in currencies different from the applicable functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the remeasurement at period-end exchange rates in foreign currencies are recorded in general and administrative expense in the condensed consolidated statement of operations and comprehensive loss. As such, our operating expenses may be impacted by future changes in exchange rates. See “Quantitative and Qualitative Disclosures About Market Risks” for further discussion.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development and potential commercialization of our portfolio of product candidates. We also expect to continue to incur increased expenses associated with being a public company including costs of accounting, audit, information systems, legal, intellectual property, regulatory and tax compliance services, director and officer insurance and investor and public relations.

### **Other Income (Expense), net**

#### *Interest Income*

Interest income consists primarily of interest earned on our cash held in operating accounts and our cash equivalents.

#### *Interest Expense*

Interest expense consists primarily of interest expense for financing arrangements. As of September 30, 2023, we have borrowings of \$30.0 million outstanding pursuant to our Loan Agreement with Hercules.

### **Provision For (Benefit From) Income Taxes**

We are subject to corporate taxation in the United States and the United Kingdom. We have generated losses since inception and have therefore not paid U.K. corporation tax. The provision for (benefit from) income taxes included in the condensed consolidated statements of operations and comprehensive loss represents the tax impact from operating activities in the U.S., which has generated taxable income based on intercompany service arrangements.

The research and development tax credit received in the United Kingdom is recorded as a reduction to research and development expenses. The U.K. research and development tax credit, as described below, is fully refundable to us after surrendering tax losses and is not dependent on current or future taxable income. As a result, we have recorded the entire benefit from the U.K. research and development tax credit as a reduction to research and development expenses and is not reflected as part of the income tax provision. If, in the future, any U.K. research and development tax credits generated are needed to offset a corporate income tax liability in the United Kingdom, that portion would be recorded as a benefit within the income tax provision and any refundable portion not dependent on taxable income would continue to be recorded as a reduction to research and development expenses.

As a company that carries out extensive research and development activities, we seek to benefit from one of two U.K. research and development tax credit cash rebate regimes: The Small and Medium-sized Enterprises R&D Tax Relief program, or SME Program, and the Research and Development Expenditure Credit program, or RDEC Program. Qualifying expenditures largely comprise employment costs for research staff, consumables, expenses incurred under agreements with third parties that conduct research and development, preclinical activities, clinical activities and manufacturing on our behalf and certain internal overhead costs incurred as part of research projects.

Based on criteria established by U.K. law, a portion of expenditures being carried out in relation to our pipeline research and development, clinical trials management and manufacturing development activities were eligible for the SME Program for the year ended December 31, 2022. Under the SME Program, the trading losses that arise from our qualifying R&D activities can be surrendered for a cash rebate of up to 33.35% of qualifying expenditure incurred prior to April 1, 2023, and up to 18.6% of qualifying expenditure incurred thereafter. Moreover, if adopted in the form proposed, recent legislation proposed by the U.K. government may increase the cash rebate in future periods up to 26.97% if we qualify as “R&D intensive” for an accounting period (broadly, a loss making SME whose qualifying R&D expenditures for an accounting period represents 40% or more of its total expenditure for that accounting period).

Further amendments to the U.K. R&D tax credit regime have also recently been proposed that may (unless limited exceptions apply) introduce restrictions on the tax relief that can be claimed for expenditures incurred on sub-contracted R&D activities or externally provided workers, where such sub-contracted activities are not carried out in the U.K. or such workers are not subject to U.K. payroll taxes. These amendments are expected to take effect from April 1, 2024. In addition, the U.K. Government is currently considering a proposal to merge the SME Program and the RDEC Program into a single scheme with effect from April 2024; if such proposal is implemented, it may be the case that we are no longer able to make claims in respect of sub-contracted R&D activities, and that different (and potentially lower) caps are imposed on the amount of tax relief that we can claim. These and other potential future changes to the U.K. research and development tax relief programs may impact the extent to which we can make claims.

In addition, the payable credit claims under the SME Program in excess of £20,000 are subject to a cap, by reference to, broadly, of three times the total PAYE and NIC liability paid by the Company, unless an exception applies. That exception requires the Company to be creating, taking steps to create, or managing intellectual property, as well as having qualifying research and development expenditure in respect of connected parties which does not exceed 15% of the total amount claimed.

Unsurrendered U.K. losses may be carried forward indefinitely to be offset against future taxable profits, subject to numerous utilization criteria and restrictions. The amount that can be offset each year is limited to £5.0 million plus an incremental 50% of U.K. taxable profits.

Value Added Tax, or VAT, is broadly charged on all taxable supplies of goods and services by VAT-registered businesses. Under current rates, an amount of 20% of the value, as determined for VAT purposes, of the goods or services supplied is added to all sales invoices and is payable to HM Revenue & Customs, or HMRC. Similarly, VAT paid on purchase invoices is generally reclaimable from HMRC and is included as a component of prepaid and other current assets in our condensed consolidated balance sheets.

## Results of Operations

### Comparison of the Three Months Ended September 30, 2023 and 2022

The following table summarizes our results of operations for the three months ended September 30, 2023 and 2022:

	Three Months Ended September 30,		Change
	2023	2022 (in thousands)	
Collaboration revenues	\$ 5,352	\$ 3,040	\$ 2,312
Operating expenses:			
Research and development	39,868	22,752	17,116
General and administrative	16,281	10,047	6,234
Total operating expenses	56,149	32,799	23,350
Loss from operations	(50,797)	(29,759)	(21,038)
Other income (expense):			
Interest income	3,985	1,991	1,994
Interest expense	(814)	(817)	3
Total other income (expense), net	3,171	1,174	1,997
Net loss before income tax provision	(47,626)	(28,585)	(19,041)
Provision for (benefit from) income taxes	2,272	(238)	2,510
Net loss	\$ (49,898)	\$ (28,347)	\$ (21,551)

### Collaboration Revenues

Collaboration revenues increased by \$2.3 million in the three months ended September 30, 2023 compared to the three months ended September 30, 2022, primarily due to increases of \$0.7 million from our collaboration with Novartis entered into in March 2023, \$0.4 million from our collaboration with Bayer entered into in May 2023, \$0.6 million from our collaboration with Ionis and \$0.6 million from our collaboration with Genentech.

### Research and Development Expenses

The table below summarizes our research and development expenses for the period:

	<b>Three Months Ended September 30,</b>		<b>Change</b>
	<b>2023</b>	<b>2022</b> (in thousands)	
BT8009 (Nectin-4)	\$ 11,806	\$ 2,757	\$ 9,049
BT5528 (EphA2)	2,149	3,460	(1,311)
BT1718 (MT1)	147	142	5
<i>Bicycle</i> tumor-targeted immune cell agonists	4,717	3,790	927
Other discovery and platform related expense	9,464	6,504	2,960
Employee and contractor related expenses	11,793	8,275	3,518
Share-based compensation	3,357	2,637	720
Facility expenses	1,697	1,339	358
Research and development incentives and government grants	(5,262)	(6,152)	890
Total research and development expenses	<u>\$ 39,868</u>	<u>\$ 22,752</u>	<u>\$ 17,116</u>

Research and development expenses increased by \$17.1 million in the three months ended September 30, 2023 compared to the three months ended September 30, 2022, due primarily to an increase of \$11.6 million in direct program spend, primarily associated with increases in clinical program expenses for BT8009 due to the ongoing Phase II expansion portion of the Phase I/II clinical trial, increases in *Bicycle* TICA program development expenses and increases in other discovery and platform related expenses including costs of our collaboration agreements, offset by decreases in clinical program expenses for BT5528, as well as increases of \$3.5 million in employee and contractor related expenses attributable to increased headcount, and \$0.7 million of incremental share-based compensation expense associated with equity grants issued since the same period in the prior year. In addition, research and development expenses increased by \$0.9 million as a result of a decrease in the U.K. research and development tax credit reimbursement rate for qualifying expenditures incurred after April 1, 2023.

We begin to separately track program expenses at candidate nomination, at which point we accumulate all direct external program costs to support that program to date. Through September 30, 2023, we have incurred approximately \$57.1 million, \$38.1 million, and \$15.4 million of direct external expenses for the development of the BT8009, BT5528, and BT1718, respectively, since their candidate nominations, and an aggregate of \$38.4 million of direct external expenses for the development of the two named *Bicycle* TICA candidates since their nominations.

### General and Administrative Expenses

The table below summarizes our general and administrative expenses for the period:

	<b>Three Months Ended September 30,</b>		<b>Change</b>
	<b>2023</b>	<b>2022</b> (in thousands)	
Personnel-related costs	\$ 5,172	\$ 3,266	\$ 1,906
Professional and consulting fees	4,278	1,960	2,318
Other general and administration costs	2,044	2,290	(246)
Share-based compensation	4,073	2,731	1,342
Effect of foreign exchange rates	714	(200)	914
Total general and administrative expenses	<u>\$ 16,281</u>	<u>\$ 10,047</u>	<u>\$ 6,234</u>

General and administrative expenses increased by \$6.2 million in the three months ended September 30, 2023 compared to the three months ended September 30, 2022. This increase is primarily due to an increase of \$2.3 million in professional and consulting fees that is primarily related to increased legal and consulting fees, an increase of \$1.9 million in personnel-related costs as a result of increased headcount, an increase of \$1.3 million in share-based

compensation expense primarily associated with equity grants issued since the same period in the prior year, and a \$0.9 million unfavorable impact of foreign exchange rates.

*Other Income (Expense), net*

Other income (expense), net increased by \$2.0 million in the three months ended September 30, 2023 compared to the three months ended September 30, 2022, primarily due to an increase of \$2.0 million in interest income related to higher interest rates and higher average interest-bearing cash and cash equivalents balances period over period.

*Provision For (Benefit From) Income Taxes*

The provision for income taxes of \$2.3 million for the three months ended September 30, 2023 is primarily associated with a change in estimate that certain research and development expenses incurred by our U.S. subsidiary pursuant to an intercompany service arrangement are not required to be capitalized under IRC Section 174 because our U.S. subsidiary does not retain any ownership or rights in the underlying intellectual property resulting from the research activities. The benefit from income taxes of \$0.2 million for the three months ended September 30, 2022 is mainly the result of deferred tax assets benefitted in the U.S. that do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement.

**Comparison of the Nine Months Ended September 30, 2023 and 2022**

The following table summarizes our results of operations for the nine months ended September 30, 2023 and 2022:

	<b>Nine Months Ended September 30,</b>		<b>Change</b>
	<b>2023</b>	<b>2022</b> (in thousands)	
Collaboration revenues	\$ 21,645	\$ 11,278	\$ 10,367
Operating expenses:			
Research and development	111,799	56,890	54,909
General and administrative	45,557	38,830	6,727
Total operating expenses	157,356	95,720	61,636
Loss from operations	(135,711)	(84,442)	(51,269)
Other income (expense):			
Interest income	7,726	3,117	4,609
Interest expense	(2,443)	(2,518)	75
Total other income (expense), net	5,283	599	4,684
Net loss before income tax provision	(130,428)	(83,843)	(46,585)
Provision for (benefit from) income taxes	1,137	(1,104)	2,241
Net loss	\$ (131,565)	\$ (82,739)	\$ (48,826)

*Collaboration Revenues*

Collaboration revenues increased by \$10.4 million in the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022, primarily due to increases of \$8.0 million from our collaboration with Genentech which was primarily a result of the recognition of \$6.0 million due to the expiration of a material right upon the termination of Genentech Collaboration Program #1 during the three months ended June 30, 2023 as well as an increase in revenue recognized associated with proportional performance, \$1.4 million from our collaboration with Ionis which was primarily a result of an increase in revenue recognized associated with proportional performance, \$0.8 million from our collaboration with Novartis entered into in March 2023 and \$0.4 million from our collaboration with Bayer entered into in May 2023.

### Research and Development Expenses

The table below summarizes our research and development expenses for the period:

	<b>Nine Months Ended September 30,</b>		<b>Change</b>
	<b>2023</b>	<b>2022</b> (in thousands)	
BT8009 (Nectin-4)	\$ 27,271	\$ 6,390	\$ 20,881
BT5528 (EphA2)	7,677	7,406	271
BT1718 (MT1)	461	490	(29)
<i>Bicycle</i> tumor-targeted immune cell agonists	15,828	8,488	7,340
Other discovery and platform related expense	26,658	15,598	11,060
Employee and contractor related expenses	33,955	21,025	12,930
Share-based compensation	11,941	7,643	4,298
Facility expenses	6,461	3,689	2,772
Research and development incentives and government grants	(18,453)	(13,839)	(4,614)
Total research and development expenses	<u>\$ 111,799</u>	<u>\$ 56,890</u>	<u>\$ 54,909</u>

Research and development expenses increased by \$54.9 million in the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022, due primarily to an increase in clinical program expenses associated with the ongoing Phase I/II clinical trials for BT8009 and *Bicycle* TICAs, and increased other discovery and platform related expenses including the costs associated with our collaboration agreements, as well as increases of \$12.9 million in employee and contractor related expenses attributable to increased headcount, \$4.3 million of incremental share-based compensation expense primarily associated with equity grants issued since the same period in the prior year, and \$2.8 million in facilities-related expenses primarily associated with our U.K. lease entered into in December 2021 as well as our U.S. lease entered into in January 2023. These increases were offset by \$4.6 million of incremental research and development incentives, including U.K. research and development tax credit reimbursements due to the corresponding increase in qualifying research and development spending which is offset by a decrease in the U.K. research and development tax credit reimbursement rate for qualifying expenditures incurred after April 1, 2023.

### General and Administrative Expenses

The table below summarizes our general and administrative expenses for the period:

	<b>Nine Months Ended September 30,</b>		<b>Change</b>
	<b>2023</b>	<b>2022</b> (in thousands)	
Personnel-related costs	\$ 13,688	\$ 10,158	\$ 3,530
Professional and consulting fees	11,470	7,958	3,512
Other general and administration costs	6,898	6,525	373
Share-based compensation	12,724	13,596	(872)
Effect of foreign exchange rates	777	593	184
Total general and administrative expenses	<u>\$ 45,557</u>	<u>\$ 38,830</u>	<u>\$ 6,727</u>

General and administrative expenses increased by \$6.7 million in the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022. This increase is primarily due to a \$3.5 million increase in personnel-related costs primarily due to increased headcount as well as an increase in professional and consulting fees of \$3.5 million that was primarily related to increased legal and consulting fees. These increases were offset by a decrease of \$0.9 million in share-based compensation expense primarily associated with certain equity grants issued to our non-employee directors in January 2022 that were fully vested on the date of grant.

*Other Income (Expense), net*

Other income (expense), net increased by \$4.7 million in the nine months ended September 30, 2023 compared to the nine months ended September 30, 2022, primarily due to an increase of \$4.6 million in interest income related to higher interest rates and higher average interest-bearing cash and cash equivalents balances period over period.

*Provision For (Benefit From) Income Taxes*

The provision for income taxes of \$1.1 million for the nine months ended September 30, 2023 is primarily associated with a change in estimate that certain research and development expenses incurred by our U.S. subsidiary pursuant to an intercompany service arrangement are not required to be capitalized under IRC Section 174 because our U.S. subsidiary does not retain any ownership or rights in the underlying intellectual property resulting from the research activities, offset by the impact of deferred tax assets benefited in the U.S. that do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement. The benefit from income taxes of \$1.1 million for the nine months ended September 30, 2022, is mainly the result of deferred tax assets benefited in the U.S. that do not have a valuation allowance against them because of profits that will be generated by an intercompany service agreement.

**Liquidity and Capital Resources**

*Liquidity*

From our inception through September 30, 2023, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. We do not expect to generate significant revenue from sales of any products for several years, if at all.

To date, we have financed our operations primarily with proceeds from the sale of our ADSs, ordinary shares, non-voting ordinary shares, and convertible preferred shares; proceeds received from upfront payments, payments for research and development services, and development milestone payments pursuant to collaboration agreements; and borrowings pursuant to our Loan Agreement with Hercules.

On July 17, 2023, we completed an underwritten public offering of our securities, pursuant to which we issued and sold 6,117,648 ADSs, representing the same number of ordinary shares, nominal value £0.01 per share, which included 1,411,764 ADSs sold upon the underwriters' full exercise of their option to purchase additional ADSs, and 4,705,882 non-voting ordinary shares, nominal value £0.01 per share, at a public offering price of \$21.25 per ADS or non-voting ordinary share, respectively. The transaction resulted in gross proceeds to us of \$230.0 million, and after deducting underwriting discounts, commissions, and offering expenses of \$14.9 million, net proceeds to us of approximately \$215.1 million.

On June 5, 2020, we entered into a Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. and Oppenheimer & Co. Inc. (the "Sales Agents") with respect to an ATM program pursuant to which we may offer and sell through the Sales Agents, from time to time at our sole discretion, ADSs, each ADS representing one ordinary share. During the three and nine months ended September 30, 2023, we issued and sold 941,176 and 1,561,176 ADSs, respectively, representing the same number of ordinary shares, for gross proceeds of \$20.0 million and \$35.3 million, respectively, resulting in net proceeds of \$19.4 million and \$34.2 million, respectively, after deducting sales commissions and offering expenses of \$0.6 million and \$1.1 million, respectively.

### Cash Flows

The following table summarizes our cash flows for each of the periods presented:

	Nine Months Ended September 30,	
	2023	2022
	(in thousands)	
Net cash used in operating activities	\$ (13,340)	\$ (55,802)
Net cash used in investing activities	(2,878)	(17,539)
Net cash provided by financing activities	249,641	804
Effect of exchange rate changes on cash	57	(4,674)
Net increase (decrease) in cash, cash equivalents and restricted cash	<u>\$ 233,480</u>	<u>\$ (77,211)</u>

### Operating Activities

Net cash used in operating activities for the nine months ended September 30, 2023 was \$13.3 million as compared to \$55.8 million for the nine months ended September 30, 2022. The decrease in cash used in operations of \$42.5 million is primarily due to an increase in net loss of \$48.8 million as described in the Results of Operations above as well as a net increase in non-cash expenses, including a change of \$6.2 million in deferred income tax provision (benefit), an increase of \$3.4 million in share-based compensation expense and an increase of \$2.6 million in depreciation and amortization. These impacts were offset by an increase in cash flows from changes in our operating assets and liabilities of \$79.1 million. The increase in cash flows from changes in operating assets and liabilities was primarily driven by increases resulting from changes in deferred revenue of \$75.2 million primarily driven by upfront payments received from our collaboration agreements with Bayer and Novartis, research and development incentives receivable of \$5.3 million, accounts receivable of \$2.1 million and accrued expenses and other current liabilities of \$0.6 million, offset by decreases resulting from changes in prepaid expenses and other current assets of \$2.5 million and accounts payable of \$1.1 million.

### Investing Activities

During the nine months ended September 30, 2023 and 2022, we used \$2.9 million and \$17.5 million, respectively, of cash in investing activities for purchases of property and equipment, consisting primarily of leasehold improvements and laboratory equipment. The decrease in cash used in investing activities of \$14.7 million is primarily due to purchases of property and equipment associated with our U.K. lease during the nine months ended September 30, 2022.

### Financing Activities

During the nine months ended September 30, 2023, net cash provided by financing activities was \$249.6 million, primarily consisting of net proceeds of \$215.1 million from the underwritten public offering in July 2023 and \$34.2 million from our ATM program.

During the nine months ended September 30, 2022, net cash provided by financing activities was \$0.8 million, primarily consisting of net proceeds from the exercise of share options.

### Loan Agreement with Hercules

Our Loan Agreement, as amended from time to time, with Hercules as agent, consisting of (i) outstanding term loans of \$30.0 million and (ii) subject customary conditions, additional term loans of up to an aggregate of \$45.0 million, which are available through December 31, 2024, but have not yet been drawn. Borrowings under the Loan Agreement bear interest at an annual rate equal to the prime rate as reported in the Wall Street Journal plus 4.55%, with a minimum annual rate of at least 8.05%, capped at a rate no greater than 9.05%. The interest-only period ends on April 1, 2025. We may prepay all or any portion greater than \$5.0 million of the outstanding borrowings, subject to a prepayment premium equal to 1.5% prior to December 31, 2023, or 1% thereafter. The Loan Agreement also provides for an end of term

charge, payable upon maturity or the repayment of obligations under the Loan Agreement, equal to 5.0% of the principal amount repaid. In connection with the Loan Agreement, we granted Hercules a security interest in substantially all of our personal property and other assets, other than our intellectual property. In addition, the Loan Agreement contains customary affirmative and restrictive covenants and representations and warranties, as well as customary events of default. For additional information on the Loan Agreement, see Note 6. Long-term debt of our condensed consolidated financial statements.

### **Capital Resources and Funding Requirements**

Our material cash requirements include expenses associated with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates and as we:

- continue our development of our product candidates, including continuing current clinical trials and conducting future clinical trials of BT8009, BT5528, BT7480 and BT1718;
- progress the preclinical and clinical development of BT7455 and BT7401;
- seek to identify and develop additional product candidates;
- develop the necessary processes, controls and manufacturing data to seek to obtain marketing approval for our product candidates and to support manufacturing of product to commercial scale;
- develop, maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials, if any;
- hire and retain additional personnel, such as non-clinical, clinical, pharmacovigilance, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, medical affairs, finance, commercial and scientific personnel;
- acquire or in-license other products and technologies;
- expand our infrastructure and facilities to accommodate our growing employee base, including adding equipment and infrastructure to support our research and development; and
- add operational, financial and management information systems and personnel, including personnel to support our research and development programs, and any future commercialization efforts.

If we obtain marketing approval for any product candidate that we identify and develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, and distribution are not the responsibility of our collaboration partners.

The following table summarizes our material contractual obligations as of September 30, 2023, and the effects that such obligations are expected to have on our liquidity and cash flows in future periods. For additional information, see Note 11. Commitments and contingencies of our condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

	Payments due by period			
	Total	Less than 1 year	1 to 3 years	3 years to 5 years
	(in thousands)			
Operating lease commitments <sup>(1)</sup>	\$ 16,880	\$ 5,633	\$ 10,228	\$ 1,019
Debt obligations <sup>(2)</sup>	35,978	2,534	33,444	—
<b>Total</b>	<b>\$ 52,858</b>	<b>\$ 8,167</b>	<b>\$ 43,672</b>	<b>\$ 1,019</b>

- (1) Amounts reflect minimum payments due for our office and laboratory space leases. We have one office and laboratory lease in Cambridge, U.K. under an operating lease with a lease term through December 2026. We have two office and laboratory leases in Massachusetts, U.S.A. under operating leases with lease terms through March 2026 and December 2027.
- (2) Amounts in table reflect the contractually required principal, interest, and the final payments under the Loan Agreement with Hercules as of September 30, 2023.

In the ordinary course of business, we enter into various agreements with contract research organizations to provide clinical trial services, with contract manufacturing organizations to provide clinical trial materials, and with vendors for preclinical research studies, synthetic chemistry and other services for operating purposes. These payments are not included in the table above since the contracts are generally cancelable with advanced written notice, generally with a notice period of 90 days or less. From the time of notice until termination, we are contractually obligated to make certain minimum payments to the vendors, based on the timing of the notification and the exact terms of the agreement.

Our arrangements with CRUK provide for additional future milestone payments upon the achievement of development, regulatory and commercial milestones, payable in cash and shares, with an aggregate total value of \$111.2 million, as well as royalty payments based on a single digit percentage on net sales of products developed. In addition, we have a separate agreement with a third party which provides for additional future milestone payments by us upon the achievement of specified development, regulatory and commercial milestones, with an aggregate total value of \$92.4 million. We also have a separate agreement with a third party that provides for future milestone payments by us upon the achievement of specified regulatory, development, commercial, and sales-based milestones, with an aggregate total, on a product-by-product basis, of \$1.3 million. We have not included future payments under this agreement in the table of contractual obligations above since these obligations are contingent upon future events. As of September 30, 2023, we were unable to estimate the timing or likelihood of achieving these milestones.

As of September 30, 2023, we had cash and cash equivalents of \$572.1 million. We expect that our existing cash will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of filing of this Quarterly Report on Form 10-Q.

We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of product candidates and programs, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- our ability to raise capital in light of the impacts of the unfavorable global economic and political conditions;

- the scope, progress, results, and costs of drug discovery, preclinical development, laboratory testing, and clinical trials for the product candidates we may develop;
- our ability to enroll clinical trials in a timely manner and to quickly resolve any delays or clinical holds that may be imposed on our development programs;
- the costs associated with our manufacturing process development and evaluation of third-party manufacturers and suppliers;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of preparing and submitting marketing approvals for any of our product candidates that successfully complete clinical trials, and the costs of maintaining marketing authorization and related regulatory compliance for any products for which we obtain marketing approval;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive marketing approval;
- the terms of our current and any future license agreements and collaborations; and the extent to which we acquire or in-license other product candidates, technologies and intellectual property.
- the success of our ongoing or future collaborations;
- our ability to establish and maintain additional collaborations on favorable terms, if at all; and
- the costs of operating as a public company.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, monetization transactions, government contracts or other strategic transactions. To the extent that we raise additional capital through the sale of equity, ownership interests of existing holders of our ADSs and ordinary shares will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our ADSs or ordinary shares. If we raise additional funds through collaboration agreements, strategic alliances, licensing arrangements, monetization transactions, or marketing and distribution arrangements, 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 or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves. Future debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt. Any debt or equity financing that we raise may contain terms that are not favorable to us or our shareholders.

There have been significant disruptions to global financial markets that have contributed to a general global economic slowdown. The resulting high inflation rates may materially affect our business and corresponding financial position and cash flows. Inflationary factors, such as increases in the cost of our clinical trial materials and supplies, interest rates and overhead costs may adversely affect our operating results. Rising interest rates also present a recent challenge impacting the U.S. economy and could make it more difficult for us to obtain traditional financing on acceptable terms, if at all, in the future. Additionally, the general consensus among economists suggests that we should expect a higher recession risk to continue over the next year, which, together with the foregoing, could result in further economic uncertainty and volatility in the capital markets in the near term, and could negatively affect our operations. Furthermore, such economic conditions have produced downward pressure on share prices. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience

increases in the near future (especially if inflation rates remain high or begin to rise again) on our operating costs, including our labor costs and research and development costs, due to supply chain constraints, consequences associated with geopolitical conflicts such as the ongoing wars in Ukraine and Israel, worsening global macroeconomic conditions, and employee availability and wage increases, which may result in additional stress on our working capital resources. 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 future commercialization efforts.

### **Critical Accounting Estimates**

Our management’s discussion and analysis of financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of our condensed consolidated financial statements and related disclosures requires us to make estimates, assumptions and judgments that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We base our estimates on historical experience, known trends and events and various other factors that we believe are 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. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

Our critical accounting policies are described under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Estimates” in our 2022 Annual Report, which was filed with the SEC on February 28, 2023. If actual results or events differ materially from the estimates, judgments and assumptions used by us in applying these policies, our reported financial condition and results of operations could be materially affected. Other than as disclosed in Note 2 to the condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, there have been no significant changes to our critical accounting estimates from those described in our 2022 Annual Report.

### **Item 3. Quantitative and Qualitative Disclosure About Market Risk**

#### *Interest Rate Sensitivity*

As of September 30, 2023, we had cash and cash equivalents of \$572.1 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.K. and U.S. bank interest rates. Our surplus cash has been placed in interest-bearing savings accounts, 30-day term deposits and money market funds. We have not entered into investments for trading or speculative purposes. Due to the conservative nature of our investment portfolio, which is predicated on capital preservation of investments with short-term maturities, we do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

We are subject to interest rate risk in connection with our borrowings under our credit facility with Hercules, which were \$30.0 million as of September 30, 2023. Our outstanding indebtedness with Hercules bears interest at an annual rate equal to the *Wall Street Journal* prime rate plus 4.55%, with a minimum annual rate of at least 8.05%, capped at a rate no greater than 9.05%. As of September 30, 2023, our outstanding indebtedness with Hercules bears interest at 9.05%. We currently do not engage in any interest rate hedging activity, and we have no intention to do so in the foreseeable future. Based on the current interest rate of the term loan and the scheduled payments thereunder, we do not believe a 1.0% increase in interest rates would have a material impact on our financial condition or results of operations.

#### *Foreign Currency Exchange Risk*

The functional currency is the currency of the primary economic environment in which an entity’s operations are conducted. The functional currency of Bicycle Therapeutics plc and Bicycle Therapeutics Inc. is the United States Dollar, or USD. The functional currency of Bicycle Therapeutics plc’s wholly owned non-U.S. subsidiaries, BicycleTx

Limited and BicycleRD Limited, is the British Pound Sterling, and the condensed consolidated financial statements are presented in USD. The functional currency of our subsidiaries is the same as the local currency.

Monetary assets and liabilities denominated in currencies other than the functional currency are remeasured into the functional currency at rates of exchange prevailing at the balance sheet dates. Non-monetary assets and liabilities denominated in foreign currencies are remeasured into the functional currency at the exchange rates prevailing at the date of the transaction. Exchange gains or losses arising from foreign currency transactions are included in the determination of net loss for the respective periods. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included in general and administrative expense in the condensed consolidated statements of operations and comprehensive loss as incurred. We recorded foreign exchange losses of \$0.7 million and \$0.8 million for the three and nine months ended September 30, 2023, respectively. We recorded foreign exchange a foreign exchange gain of \$0.2 million for the three months ended September 30, 2022, and a foreign exchange loss of \$0.6 million for the nine months ended September 30, 2022.

For financial reporting purposes, our condensed consolidated financial statements have been translated into USD. We translate the assets and liabilities of BicycleTx Limited and BicycleRD Limited into USD at the exchange rate in effect on the balance sheet date. Revenues and expenses are translated at the average exchange rate in effect during the period and shareholders' equity amounts are translated based on historical exchange rates as of the date of each transaction. Translation adjustments are not included in determining net loss but are included in our foreign exchange adjustment included in the condensed consolidated statements of shareholders' equity as a component of accumulated other comprehensive income (loss).

We do not currently engage in currency hedging activities in order to reduce our currency exposure, but we may begin to do so in the future.

#### **Item 4. Controls and Procedures**

##### **Evaluation of Disclosure Controls and Procedures**

As required by Rule 13a-15(d) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation of the internal control over financial reporting to determine whether any changes occurred during the period covered by this Quarterly Report on Form 10-Q that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. Based on the evaluation of our disclosure controls and procedures at September 30, 2023, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

##### **Changes in Internal Control over Financial Reporting.**

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended September 30, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## **PART II - OTHER INFORMATION**

#### **Item 1. Legal Proceedings.**

From time to time, we may become involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. We are not currently subject to any material legal proceedings.

## Item 1A. Risk Factors.

*Our operations and financial results are subject to various risks and uncertainties, including those described below. The following information about these risks and uncertainties, together with the other information appearing elsewhere in this Quarterly Report on Form 10-Q, and our 2022 Annual Report on Form 10-K, filed with the Securities and Exchange Commission, or SEC, on February 28, 2023, including our consolidated financial statements and related notes thereto, should be carefully considered before a decision to invest in our American Depositary Shares, or ADSs. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. Additional risks that are currently unknown to us or that we currently believe to be immaterial may also impair our business. In these circumstances, the market price of our ADSs could decline and holders of our ADSs may lose all or part of their investment. We cannot provide assurance that any of the events discussed below will not occur.*

### Summary of Selected Risk Factors

Our business is subject to numerous risks and uncertainties, of which you should be aware before making a decision to invest in our ADSs. These risks and uncertainties include, among others, the following:

- We have a history of significant operating losses and expect to incur significant and increasing losses for the foreseeable future, and we may never achieve or maintain profitability.
- We may need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.
- Raising additional capital may cause dilution to our existing shareholders or holders of our ADSs, restrict our operations or cause us to relinquish valuable rights.
- Our failure to comply with the covenants or payment obligations under our existing term loan facility with Hercules Capital, Inc., or Hercules, could result in an event of default, which may result in increased interest charges, acceleration of our repayment obligations or other actions by Hercules, any of which could negatively impact our business, financial condition and results of operations.
- We are substantially dependent on the success of our internal development programs and of our product candidates from our *Bicycle*<sup>®</sup> Toxin Conjugate, or BTC<sup>™</sup>, and *Bicycle* tumor-targeted immune cell agonist<sup>®</sup>, or *Bicycle* TICA<sup>™</sup>, programs, which may not successfully complete clinical trials, receive regulatory approval or be successfully commercialized.
- We are at an early stage in our development efforts, and our product candidates and those of our collaborators represent a new category of medicines and may be subject to heightened regulatory scrutiny until they are established as a therapeutic modality.
- We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.
- Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.
- Our current or future product candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs, or IND, that could halt their clinical development, prevent their marketing approval, limit their commercial potential or result in significant negative consequences.

- We may be delayed or not be successful in our efforts to identify or discover additional product candidates.
- 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.
- We may seek designations for our product candidates with the U.S. Food and Drug Administration, or FDA, and other comparable regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, but there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any collaborators, will obtain marketing approval to commercialize a product candidate.
- The market opportunities for any current or future product candidate we develop, if and when approved may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed, and may be small.
- Even if we receive marketing approval of a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products, if approved.
- We face significant competition and if our competitors develop and market products that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.
- The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, payors and others in the medical community.
- The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for any of our product candidates, could limit our ability to market those products and decrease our ability to generate revenue.
- Healthcare legislative reform measures may have a negative impact on our business and results of operations.
- We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, and other adverse business consequences.
- We rely on third parties, including independent clinical investigators and clinical research organizations, or CROs, to conduct and sponsor some of the clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.

- We intend to rely on third parties to manufacture product candidates, which increases the risk that we will not have sufficient quantities of such product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- If we are unable to obtain and maintain patent and other intellectual property protection for our products and product candidates, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products and product candidates may be adversely affected.
- 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.
- The market price of our ADSs is highly volatile, and holders of our ADSs may not be able to resell their ADSs at or above the price at which they purchased their ADSs.
- As a company based outside of the United States, we are subject to economic, political, regulatory and other risks associated with international operations.

### **Risks Related to Our Financial Position and Need for Additional Capital**

***We have a history of significant operating losses and expect to incur significant and increasing losses for the foreseeable future, and we may never achieve or maintain profitability.***

We do not expect to generate revenue or profitability that is necessary to finance our operations in the short term. Since inception, we have incurred recurring losses, including net losses of \$131.6 million and \$82.7 million for the nine months ended September 30, 2023 and 2022, respectively. As of September 30, 2023, the Company had an accumulated deficit of \$462.7 million. To date, we have not commercialized any products or generated any revenues from the sale of products, and absent the realization of sufficient revenues from product sales, we may never attain profitability in the future. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders' equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials with respect to our BTC and *Bicycle* TICA programs and our other pipeline programs;
- initiate and continue research, preclinical and clinical development efforts for any future product candidates;
- seek to discover and develop additional product candidates and further expand our clinical product pipeline;
- seek marketing and regulatory approvals for any product candidates that successfully complete clinical trials;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;

- expand our research and development infrastructure, including hiring and retaining additional personnel, such as clinical, quality control and scientific personnel;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize products for which we obtain marketing approval, if any;
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development.

Our ability to become and remain profitable depends on our ability to generate revenue. Generating product revenue will depend on our or any of our collaborators' ability to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. Successful commercialization will require achievement of key milestones, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, and if or when we might achieve profitability. We and any collaborators may never succeed in these activities and, even if we do, or any collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our revenue to date has been primarily generated from our research collaborations with Bayer Consumer Care AG, or Bayer, Novartis Pharma AG, or Novartis, Ionis Pharmaceuticals, Inc., or Ionis, Genentech Inc., or Genentech, Dementia Discovery Fund, or DDF, Sanofi (formerly Bioverativ Inc.), AstraZeneca AB, or AstraZeneca, and Oxurion NV, or Oxurion. There can be no assurance that we will generate revenue from our collaborations in the future.

Our failure to become and remain profitable would depress the market price of our ADSs and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to suffer losses, investors may not receive any return on their investment and may lose their entire investment.

***Our limited operating history may make it difficult for holders of our ADSs or ordinary shares to evaluate the success of our business to date and to assess our future viability.***

Our business commenced operations in 2009. Our operations to date have been limited to financing and staffing our company, developing our technology, conducting preclinical research and early-stage clinical trials for our product candidates and pursuing strategic collaborations to advance our product candidates. We have not yet demonstrated an ability to successfully conduct late-stage clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, any current or prospective holder of our ADSs or ordinary shares should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions made about our future success or viability may not be as accurate as they would be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control and reliance should not be made upon the results of any quarterly or annual periods as indications of future operating performance.

***We may need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.***

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and preclinical development efforts for and seek marketing approval for, our current product candidates or any future product candidates. In addition, if we obtain marketing approval for any of our product candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a collaborator. Furthermore, we expect to incur significant ongoing costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We will be required to expend significant funds in order to advance the development of the product candidates in our pipeline, as well as other product candidates we may seek to develop. In addition, while we may seek one or more collaborators for future development of our product candidates, we may not be able to enter into a collaboration for any of our product candidates for such indications on suitable terms, on a timely basis or at all. In any event, our existing cash will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash and cash equivalents of \$572.1 million as of September 30, 2023, will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of filing of this Quarterly Report on Form 10-Q. Our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, our current and future product candidates;
- our ability to enter into, and the terms and timing of, any collaborations, licensing or other arrangements;
- our ability to identify one or more future product candidates for our pipeline;
- the number of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of our current and future product candidates;

- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights including enforcing and defending intellectual property related claims; and
- the costs of operating as a public company.

While the long-term economic impact of either the COVID-19 pandemic or the ongoing geopolitical conflicts is difficult to assess or predict, each of these events has caused significant disruptions to the global financial markets and contributed to a general global economic slowdown. Furthermore, inflation rates, particularly in the United States and the United Kingdom, have increased recently to levels not seen in decades. Increased inflation may result in increased operating costs (including labor costs) and may affect our operating budgets. In addition, the U.S. Federal Reserve has raised, and may further raise, interest rates in response to concerns about inflation. Increases in interest rates, especially if coupled with reduced government spending and volatility in financial markets and the global banking system, may further increase economic uncertainty and heighten these risks. On March 10, 2023, in addition to the failure of SVB UK, its parent company, Silicon Valley Bank, also failed, and Signature Bank failed on March 12, 2023. Although the U.K. and U.S. governments both took steps to guarantee all depositors at these banks, there is no guarantee that these governments or any other government would guarantee depositors in the event of further bank closures, and continued instability in the global banking system may adversely impact our business and financial condition. If the disruptions, instability and slowdown deepen or persist, we may not be able to access our cash as needed or to raise additional capital on favorable terms, or at all, which could in the future negatively affect our financial condition and our ability to pursue our business strategy.

***Raising additional capital may cause dilution to our existing shareholders or holders of our ADSs, restrict our operations or cause us to relinquish valuable rights.***

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances, licensing arrangements or monetization transactions. To the extent that we raise additional capital through the sale of equity, convertible debt securities or other equity-based derivative securities, the ownership interest of existing holders of our ADSs or ordinary shares will be diluted and the terms may include liquidation or other preferences that adversely affect existing holders' rights. Any indebtedness we incur would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our ADSs to decline and existing shareholders may not agree with our financing plans or the terms of such financings. If we raise additional funds through strategic partnerships and alliances, licensing arrangements or monetization transactions with third parties, we may have to relinquish valuable rights to our technologies, or our product candidates, or grant licenses on terms unfavorable to us. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds 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.

***Our failure to comply with the covenants or payment obligations under our existing term loan facility with Hercules could result in an event of default, which may result in increased interest charges, acceleration of our repayment obligations or other actions by Hercules, any of which could negatively impact our business, financial condition and results of operations.***

We are party to a secured term loan facility with Hercules. As of September 30, 2023, our outstanding borrowings under this facility totaled \$30.0 million. In connection with the Loan and Security Agreement, as amended, with Hercules, or the Loan Agreement, we granted Hercules a security interest in substantially all of our personal property and other assets, other than our intellectual property. The Loan Agreement contains customary affirmative and restrictive covenants and representations and warranties, including a covenant against the occurrence of a change in

control (as defined by the Loan Agreement), financial reporting obligations, and certain limitations on indebtedness, liens (including a negative pledge on intellectual property and other assets), investments, distributions (including dividends), collateral, investments, transfers, mergers or acquisitions, taxes, corporate changes, and deposit accounts. The Loan Agreement also includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, the occurrence of certain events that could reasonably be expected to have a material adverse effect as set forth in the Loan Agreement, cross acceleration to third-party indebtedness and certain events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, a default interest rate of an additional 5.0% may be applied to the outstanding principal and interest payments due, and Hercules may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement, including proceeding against the collateral securing such indebtedness. Such increased interest charges, accelerated repayment, proceedings against the collateral or other actions may have a negative impact on our business, financial condition and results of operations.

***Our existing and any future indebtedness may limit our cash flow available to invest in the ongoing needs of our business.***

As of September 30, 2023, we had \$30.0 million of borrowings outstanding under the Loan Agreement with Hercules with an interest rate that is capped at 9.05%. We could also in the future incur additional indebtedness pursuant to additional loan agreements.

Our debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate cash flow from operations or cash on hand to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and funds from external sources. Nonetheless, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing or any future debt facility. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under the Loan Agreement or any future loan agreements we may enter into could result in an event of default and acceleration of amounts due. If an event of default occurs and the lenders accelerate the amounts due under such loan agreements, we may not be able to make accelerated payments, and such lenders could seek to enforce security interests in the collateral securing such indebtedness.

**Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates**

***We are substantially dependent on the success of our internal development programs and of our product candidates from our BTC™ and Bicycle TICA™ programs, which may not successfully complete clinical trials, receive regulatory approval or be successfully commercialized.***

Our future success will depend heavily on the success of our internal development programs and of product candidates from our BTC and Bicycle TICA programs.

Within our BTC programs, we are evaluating BT8009, a BTC that targets Nectin-4 and carries a monomethyl auristatin E, or MMAE, cytotoxin payload, in a company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and preliminary clinical activity in patients with Nectin-4 expressing advanced malignancies and have aligned with the FDA on the design of a Phase II/III registrational trial, and BT5528, a BTC that targets Ephrin type-A receptor 2, or EphA2 and carries a MMAE cytotoxin payload, in an ongoing, company-sponsored Phase I/II clinical trial to assess safety, pharmacokinetics and preliminary clinical activity in patients with advanced malignancies associated with EphA2 expression. In addition, BT1718, a BTC designed to target tumors that express MT1-MMP, is being investigated for safety, tolerability and efficacy in an ongoing Phase I/IIa clinical trial sponsored and fully funded by the Cancer Research UK Centre for Drug Development, or Cancer Research UK. Upon the completion of the Phase I/IIa clinical trial for BT1718, we have the right to obtain a license to the results of the clinical trial from Cancer Research UK upon the payment of a milestone, in cash and ordinary shares with a combined value in a mid-six digit dollar amount. If we do not exercise our right to obtain a license to the results of the clinical trial or we fail to obtain a license, our ability to continue development of BT1718 would be negatively impacted. We are also evaluating BT7480, which is a *Bicycle* TICA targeting Nectin-4 and agonizing CD137, in a company-sponsored Phase I/II clinical trial to assess the safety and tolerability of BT7480, and to determine a recommended Phase II dose. There can be no assurance our BTCs or *Bicycle* TICAs will ever demonstrate evidence of safety or effectiveness for any use or receive regulatory approval in the United States, the European Union, or any other country in any indication. Even if clinical trials show positive results, there can be no assurance that the FDA in the United States, or the European Commission, whose decision is based on a recommendation from the European Medicines Agency, or EMA, in Europe or similar regulatory authorities will approve our BTCs or any of our other product candidates for any given indication for several potential reasons, including the failure to follow Good Clinical Practice, or GCP, a negative assessment of the risks and benefits, insufficient product quality control and standardization, failure to have Good Manufacturing Practices, or GMP, compliant manufacturing facilities, or the failure to agree with regulatory authorities on clinical endpoints.

Our ability to successfully commercialize our BTCs, *Bicycle* TICAs, and our other product candidates will depend on, among other things, our ability to:

- successfully complete preclinical studies and clinical trials, which may be delayed;
- receive regulatory approvals from the FDA, the European Commission based on a recommendation from the EMA and other similar regulatory authorities;
- establish and maintain collaborations with third parties for the development and/or commercialization of our product candidates, or otherwise build and maintain strong development, sales, distribution and marketing capabilities that are sufficient to develop products and launch commercial sales of any approved products;
- obtain coverage and adequate reimbursement from payors such as government health care systems and insurance companies and achieve commercially attractive levels of pricing;
- secure acceptance of our product candidates from physicians, health care payors, patients and the medical community;
- produce, through a validated process, in manufacturing facilities inspected and approved by regulatory authorities, including the FDA, sufficiently large quantities of our product candidates to permit successful commercialization;
- manage our spending as expenses increase due to clinical trials and commercialization; and
- obtain and enforce sufficient intellectual property rights for any approved products and product candidates and maintain freedom to operate for such products with respect to the intellectual property rights of third parties.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a new drug application, or NDA, to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market our product candidates, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot provide assurance that our product candidates will be successfully developed or commercialized. If we are unable to develop, or obtain regulatory approval for, or, if approved, to successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business. Moreover, if adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity for our product candidates in the EU.

***We are at an early stage in our development efforts, and our product candidates and those of our collaborators represent a new category of medicines and may be subject to heightened regulatory scrutiny until they are established as a therapeutic modality.***

*Bicycles* are fully synthetic short peptides constrained to form two loops which stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making *Bicycles* attractive candidates for drug development. *Bicycles* are a unique therapeutic modality combining the pharmacology usually associated with a biologic with the manufacturing and pharmacokinetic, or PK, properties of a small molecule. Our product candidates may not demonstrate in patients any or all of the pharmacological benefits we believe they may possess. We have not yet succeeded and may never succeed in demonstrating efficacy and safety for these or any other product candidates in clinical trials or in obtaining marketing approval thereafter.

Regulatory authorities have limited experience with *Bicycles* and may require evidence of safety and efficacy that goes beyond what we and our collaborators have included in our development plans. In such a case, development of *Bicycle* product candidates may be more costly or time-consuming than expected, and our candidate products and those of our collaboration partners may not prove to be viable.

If we are unsuccessful in our development efforts, we may not be able to advance the development of our product candidates, commercialize products, raise capital, expand our business or continue our operations.

***Our product candidates and those of our collaborators will need to undergo preclinical and clinical trials that are time consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If preclinical or clinical trials of our or their product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA, the EMA and any other comparable regulatory authority, additional costs may be incurred or delays experienced in completing, the development of these product candidates, or their development may be abandoned.***

The FDA in the United States, the European Commission based on a recommendation from the EMA, or other European regulatory authorities, in the European Union and the European Economic Area, or EEA, and any other comparable regulatory authorities in other jurisdictions must approve new product candidates before they can be marketed, promoted or sold in those territories. We have not previously submitted an NDA to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. We must provide these regulatory authorities with data from preclinical studies and clinical trials that demonstrate that our product candidates are safe and effective for a specific indication before they can be approved for commercial distribution. We cannot be certain that our clinical trials for our product candidates will be successful or that any of our other product candidates will receive approval from the FDA, the European Commission based on a recommendation from the EMA or any other comparable regulatory authority.

Preclinical studies and clinical trials are long, expensive and unpredictable processes that can be subject to extensive delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. It may take several years and require significant expenditures to complete the preclinical studies and clinical trials necessary to commercialize a product candidate, and delays or failure are inherently unpredictable and can occur at any stage. New or ongoing public health crises may also impact our and our collaboration partners' abilities to activate trial sites or enroll patients in clinical trials or to otherwise advance those clinical trials. Interruptions resulting from such

crises may reduce our, or our collaboration partners', abilities to administer the investigational product to enrolled patients, present difficulties for enrolled patients to adhere to protocol-mandated visits and laboratory/diagnostic testing, increase the possibility of patient dropouts, or impact our, and our suppliers', abilities to provide investigational product to trial sites, all of which could negatively impact the data we are able to obtain from our clinical trials and complicate regulatory review.

We may also be required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we contemplate, which may lead to us incurring additional unplanned costs or result in delays in clinical development. In addition, we may be required to redesign or otherwise modify our plans with respect to an ongoing or planned clinical trial, and changing the design of a clinical trial can be expensive and time consuming. An unfavorable outcome in one or more trials would be a major setback for our product candidates and for us. An unfavorable outcome in one or more trials may require us to delay, reduce the scope of or eliminate one or more product development programs, which could have a material adverse effect on our business, financial position, results of operations and future growth prospects.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval for our product candidates. The FDA, EMA or any other comparable regulatory authority may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

In connection with clinical trials of our product candidates, we face a number of risks, including risks that:

- a product candidate is ineffective, inferior or a rigorous comparison cannot be made to existing approved products for the same indications;
- a product candidate causes or is associated with unacceptable toxicity or has unacceptable side effects;
- patients may die or suffer adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results may not confirm the positive results of earlier trials;
- the results may not meet the level of statistical significance required by the FDA, the EMA or other relevant regulatory agencies to establish the safety and efficacy of our product candidates for continued trial or marketing approval; and
- our collaborators may be unable or unwilling to perform under their contracts.

Furthermore, we sometimes estimate for planning purposes the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, the receipt of marketing approval or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions, which may cause the timing of achievement of the milestones to vary considerably from our estimates. If we fail to achieve milestones in the timeframes we expect, the commercialization of our product candidates may be delayed, we may not be entitled to receive certain contractual payments, which could have a material adverse effect on our business, financial position, results of operations and future growth prospects.

***We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.***

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate as well as the completion of required follow-up periods. Patients may be unwilling to participate in our clinical trials because of negative publicity from adverse events related to novel therapeutic approaches, competitive clinical trials for similar patient populations, the existence of current treatments or for other reasons. Enrollment risks are heightened with respect to certain indications that we may target for one or more of our product candidates that may be rare diseases, which may limit the pool of patients that may be enrolled in our planned clinical trials. The timeline for recruiting patients, conducting trials and obtaining regulatory approval of our product candidates may be delayed, which could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with the required or desired characteristics, to complete our clinical trials in a timely manner. For example, due to the nature of the indications that we are initially targeting, patients with advanced disease progression may not be suitable candidates for treatment with our product candidates and may be ineligible for enrollment in our clinical trials. Therefore, early diagnosis in patients with our target diseases is critical to our success. Patient enrollment and trial completion is affected by factors including the:

- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- eligibility and exclusion criteria;
- safety profile, to date, of the product candidate under study;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of our approach to treatment of diseases;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- degree of progression of the subject's disease at the time of enrollment;
- proximity and availability of clinical trial sites for prospective subjects;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

In addition, clinical testing of BT8009, BT5528, BT7480 and BT1718 is currently taking place outside of the United States. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with academic partners or contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;
- the absence in some countries of established groups with sufficient regulatory expertise for review of protocols related to our novel approach;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

***Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.***

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and preliminary or interim results of clinical trials do not necessarily predict success in the results of completed clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. For example, our company-sponsored Phase I/II clinical trials of BT8009, BT5528 and BT7480 and the Phase I/IIa trial of BT1718 being conducted by Cancer Research UK are ongoing, and the interim results of these trials, including specific patient responses we have observed and disclosed, may not be replicated in the completed data sets or in future trials at global clinical trial sites in a later stage clinical trial conducted by us or our collaborators. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. While we have aligned with the FDA on the design of a Phase II/III registrational trial for BT8009, we otherwise have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval.

Preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, our ability to enroll trial participants, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

***Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics could harm our drug development strategy.***

We may employ companion diagnostics to help us more accurately identify patients within a particular subset, both during our clinical trials and in connection with the commercialization of our product candidates that we are developing or may in the future develop. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate regulatory approval prior to commercialization. We do not develop companion diagnostics internally and thus we will be dependent on the sustained cooperation and

effort of our third-party collaborators in developing and obtaining approval for these companion diagnostics. There can be no guarantees that we will successfully find a suitable collaborator to develop companion diagnostics. We and our collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, our collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community or difficulties obtaining insurance coverage and reimbursement from private insurance or government payors. If such companion diagnostics fail to gain market acceptance, our ability to derive revenues from sales of any products, if approved, will be adversely affected. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

***Our current or future product candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could halt their clinical development, prevent their marketing approval, limit their commercial potential or result in significant negative consequences.***

Undesirable or clinically unmanageable side effects could occur and cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. If unacceptable side effect profiles arise, or side effects beyond those identified to date develop or worsen, as we continue development of our current or future product candidates, we, the FDA or comparable foreign regulatory authorities, the Institutional Review Boards, or IRBs, or independent ethics committees at the institutions in which our studies are conducted, or Safety Review Committees could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial, cause delays in ongoing clinical trials, or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We may be required to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

Four of our product candidates are currently undergoing safety testing in the form of Phase I/IIa or Phase I/II clinical trials. None of our products have completed this testing to date. While our current and future product candidates will undergo safety testing to the extent possible and, where applicable, under such conditions discussed with regulatory authorities, not all adverse effects of drugs can be predicted or anticipated. Unforeseen side effects could arise either during clinical development or, if such side effects are rarer, after our products have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. So far, we have not demonstrated, and we cannot predict if ongoing or future clinical trials will demonstrate, that BT8009, BT5528, BT7480, BT1718 or any other of our product candidates are safe in humans.

Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less

effective than previously believed or causes undesirable side effects that were not previously identified, any of the following consequences could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any collaborators, may need to recall the product, or be required to change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning or a contraindication;
- we, or any collaborators, may be required to create a medication guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

If any of our current or future product candidates fail to demonstrate safety and efficacy in clinical trials or do not gain marketing approval, we will not be able to generate revenue and our business will be harmed. Any of these events could harm our business and operations, and could negatively impact the price of our ADSs.

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

Although we intend to utilize our *Bicycle* screening platform to explore other therapeutic opportunities in addition to the product candidates that we are currently developing, we may fail to identify other product candidates for clinical development for a number of reasons. For example, our research methodology may not be successful in identifying potential product candidates or those we identify may be shown to have harmful side effects or other characteristics that make them unmarketable or unlikely to receive regulatory approval. A key part of our strategy is to utilize our screening technology to identify product candidates to pursue in clinical development. Such product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development. If we fail to identify and develop additional potential product candidates, we may be unable to grow our business and our results of operations could be materially harmed.

***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 intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may 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 product candidates. If we do not accurately evaluate the

commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

***We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.***

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- the impairment of our business reputation;
- the withdrawal of clinical trial participants;
- substantial monetary awards to patients or other claimants;
- costs due to related litigation;
- the distraction of management's attention from our primary business;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage each time we commercialize an additional product; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our ADS price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Patients with the diseases targeted by certain of our product candidates, such as our lead indications in oncology, are often already in severe and advanced stages of disease and have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations.

***We may seek designations for our product candidates with the FDA and other comparable regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, but there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.***

The FDA and other comparable regulatory authorities offer certain designations for product candidates that are intended to encourage the research and development of pharmaceutical products addressing conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. There can be no assurance that we will successfully obtain such designation for any of our other product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Breakthrough Therapy Designation for one or more of our product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, if preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA are also eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

We may also seek Fast Track Designation for some of our product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track Designation does not provide assurance of ultimate FDA approval. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

***We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.***

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, in particular if such product candidate has received a Breakthrough Therapy Designation, the FDA may decide not to grant it. Moreover, a priority review designation does not result in expedited development and does not necessarily result in expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared

to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

***Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not mean that we will be successful in obtaining marketing approval of our current and future product candidates in other jurisdictions.***

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction, while a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. We do not have experience in obtaining reimbursement or pricing approvals in international markets.

Obtaining marketing approvals and compliance with regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries outside of the United States. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

***The withdrawal of the United Kingdom from the European Union, commonly referred to as “Brexit,” may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.***

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. A trade and cooperation agreement, or the Trade and Cooperation Agreement, which outlines the future trading relationship between the United Kingdom and the European Union, was agreed upon in December 2020 and formally entered into force on May 1, 2021.

The potential impact on our results of operations and liquidity resulting from Brexit remains unclear. The actual effects of Brexit will depend upon many factors and significant uncertainty remains.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from European Union directives and regulations, Brexit has had, and will continue to have, a material impact on the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. For example, Great Britain is no longer covered by the centralized procedures for obtaining European Union-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our product candidates in Great Britain. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the United Kingdom and the European Union, there may be additional non-tariff costs to such trade which did not exist

prior to the end of the transition period until December 31, 2020. Further, should the United Kingdom diverge from the European Union from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could, therefore, both now and in the future, face significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the European Union.

Brexit may influence the attractiveness of the United Kingdom as a place to conduct clinical trials. The European Union's regulatory environment for clinical trials has been harmonized as part of the Clinical Trials Regulation, which entered into application on January 31, 2022. The Medicines & Healthcare products Regulatory Agency, or MHRA, has conducted a consultation on proposed revisions to U.K. clinical trials legislation, but it is currently unclear as to what extent the United Kingdom will seek to align its regulations with the European Union. Failure of the United Kingdom to closely align its regulations with the European Union may have an effect on the cost of conducting clinical trials in the United Kingdom as opposed to other countries and/or make it harder to seek a marketing authorization for our product candidates on the basis of clinical trials conducted in the United Kingdom. Pursuant to the Regulation, clinical trial data arising from a clinical trial site in a country outside of the EEA that is used in applications for clinical trial approval in the European Union must adhere to standards that are equivalent to those found in the Regulation. In the short term, there will be few changes to clinical trials that only have sites in the United Kingdom. The MHRA has confirmed that the sponsor of a clinical trial can be based in the EEA for an initial period following Brexit. Further investigational medicinal products can be supplied directly from the European Union/EEA to either a trial site or a distribution hub in Great Britain. Such products will require oversight by the holder of a U.K. Manufacturing and Import Authorisation but do not currently require recertification. The United Kingdom is now a "third country" for the purpose of clinical trials that have sites in the EEA. For such trials the sponsor/legal representative must be based in the EEA, and the trial must be registered on the EU Clinical Trials Register (including data on sites outside of the EEA).

#### **Risks Related to Commercialization of Our Product Candidates and Other Regulatory Compliance Matters**

***Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any collaborators, will obtain marketing approval to commercialize a product candidate.***

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that our product candidates are not 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. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product

candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. It is possible that we could experience delays in the timing of our interactions with regulatory authorities due to absenteeism by governmental employees, inability to conduct planned physical inspections related to regulatory approval, or the diversion of regulatory authority efforts, which could delay anticipated approval decisions and otherwise delay or limit our ability to make planned regulatory submissions or obtain new product approvals. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Any marketing approval we ultimately obtain, if any, may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or other regulatory authority. The FDA or other regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or other 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 other 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.

In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, regulatory agencies may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. Regulators may approve a product candidate for a smaller patient population, a different drug formulation or a different manufacturing process, than we are seeking. If we are unable to obtain necessary regulatory approvals, or more limited regulatory approvals than we expect, our business, prospects, financial condition and results of operations may suffer.

Any delay in obtaining or failure to obtain required approvals could negatively impact our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact the price of our ADSs.

***We currently have no marketing, sales or distribution infrastructure with respect to our product candidates. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates.***

We currently have no marketing, sales or distribution capabilities and have limited sales or marketing experience within our organization. If one or more of our product candidates is approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize that product candidate, or to outsource this function to a third party. There are risks involved with either establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services.

Recruiting and training an internal commercial organization is expensive and time consuming and could delay any product launch. Some or all of these costs may be incurred in advance of any approval of any of our product candidates. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States or other target market that is sufficient in size or has adequate expertise in the medical markets that we intend to target.

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

- the inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product that we may develop;
- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

***The market opportunities for any current or future product candidate we develop, if and when approved, may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed, and may be small.***

Cancer therapies are sometimes characterized as first-line, second-line, third-line or later-line therapies, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, surgery, radiation therapy, immunotherapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. We may initially seek approval of BT8009, BT5528, BT7480, BT1718 and any other product candidates we develop as a therapy for patients who have received one or more prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first-line therapy, but there is no guarantee that product candidates we develop, even if approved, would be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

The number of patients who have the cancers we are targeting may turn out to be lower than expected. Additionally, the potentially addressable patient population for our current programs or future product candidates may be limited, if and when approved. Even if we obtain significant market share for any product candidate, if and when approved, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications, including use as first- or second-line therapy.

***Even if we receive marketing approval of a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products, if approved.***

Any marketing approvals that we receive for any current or future product candidate may be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval, or contain requirements for potentially costly post-market testing and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval of any product candidate, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If the FDA or a comparable foreign regulatory authority approves a product candidate, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import and export and record keeping for the product candidate will be subject to extensive and ongoing regulatory requirements. These requirements include, among others, submissions of safety and other post-marketing information

and reports, registration, as well as continued compliance with current Good Manufacturing Practice, or cGMP, and Good Clinical Practice, or GCP, for any clinical trials that we conduct post-approval, and prohibitions on the promotion of an approved product for uses not included in the product's approved labeling. 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 may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict manufacturer's communications on the subject of off-label use of their products.

Later discovery of previously unknown problems with any approved candidate, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the labeling, distribution, marketing or manufacturing of the product, withdrawal of the product from the market, or product recalls;
- untitled and warning letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications we filed or suspension or revocation of license approvals;
- requirements to conduct post-marketing studies or clinical trials;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- product seizure or detention, or refusal to permit the import or export of the product; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval of a product. 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.

***We face significant competition and if our competitors develop and market products that are more effective, safer or less expensive than the product candidates we develop, our commercial opportunities will be negatively impacted.***

The life sciences industry is highly competitive. We are currently developing therapeutics that will compete, if approved, with other products and therapies that currently exist, are being developed or will in the future be developed, some of which we may not currently be aware.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities and other research institutions. Many of our competitors have significantly greater financial, manufacturing, marketing, product development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative

arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing approval or discovering, developing and commercializing products in our field before we do.

There are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. These treatments consist both of small molecule drug products, such as traditional chemotherapy, as well as novel immunotherapies. For example, a number of multinational companies as well as large biotechnology companies, are developing programs for the targets that we are exploring for our BTC programs, including Seagen, Inc, which has a marketed Nectin-4 antibody-drug conjugate. Furthermore, many companies are developing programs for CD137 or CD137 bi-specific antibodies or antibody fragments.

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 effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain FDA, European or other 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. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness.

Smaller and other early-stage companies may also prove to be significant competitors. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. In addition, the biopharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render our product candidates obsolete, less competitive or not economical.

***The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, payors and others in the medical community.***

We have never commercialized a product, and even if we obtain any regulatory approval for our product candidates, the commercial success of our product candidates will depend in part on the medical community, patients, and payors accepting products based on our *Bicycle* peptides in general, and our product candidates in particular, as effective, safe and cost-effective. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

The degree of market acceptance of these product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the potential efficacy and potential advantages over alternative treatments;
- the frequency and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the frequency and severity of any side effects resulting from follow-up requirements for the administration of our product candidates;
- the relative convenience and ease of administration;

- 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 and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and adequate reimbursement.

Even if a product candidate displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product, if approved for commercial sale, will not be known until after it is launched. Our efforts to educate the medical community and payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors, particularly due to the novelty of our *Bicycle* approach. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable.

***If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.***

We currently focus our research and product development on treatments for oncology indications and our product candidates are designed to target specific tumor antigens. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. Patient identification efforts also influence the ability to address a patient population. If efforts in patient identification are unsuccessful or less impactful than anticipated, we may not address the entirety of the opportunity we are seeking.

In addition, the tumor antigens that our product candidates target may not be expressed as broadly as we anticipate. Further, if companion diagnostics are not developed alongside our product candidates, testing patients for the tumor antigens may not be possible, which would hamper our ability to identify patients who could benefit from treatment with our product candidates.

As a result, the number of patients we are able to identify in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to access, all of which would adversely affect our business, financial condition, results of operations and prospects.

***The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for any of our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

We expect the cost of our product candidates to be substantial, when and if they achieve market approval. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by private payors, such as private health coverage insurers, health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health care programs, such as Medicare and Medicaid. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize our product candidates, even if approved. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to coverage and reimbursement for novel products such as ours, as there is no body of established practices and precedents for these new products. 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: (1) a covered benefit under its health plan; (2) safe, effective and medically necessary; (3) appropriate for the specific patient; (4) cost-effective; and (5) neither experimental nor investigational. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Because our product candidates may have a higher cost of goods than conventional therapies, and may require long-term follow-up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

We or our collaborators will be required to obtain coverage and reimbursement for companion diagnostic tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. There is significant uncertainty regarding our and our collaborators' ability to obtain coverage and adequate reimbursement for any companion diagnostic test for the same reasons applicable to our product candidates.

Outside the United States, certain countries, including a number of member states of the European Union, set prices and reimbursement for pharmaceutical products, or medicinal products, as they are commonly referred to in the European Union. These countries have broad discretion in setting prices and we cannot be sure that such prices and reimbursement will be acceptable to us or our collaborators. If the regulatory authorities in these jurisdictions set prices or reimbursement levels that are not commercially attractive for us or our collaborators, our revenues from sales by us or our collaborators, and the potential profitability of our drug products, in those countries would be negatively affected. An increasing number of countries are taking initiatives to attempt to reduce large budget deficits by focusing cost-cutting efforts on pharmaceuticals for their state-run health care systems. These international price control efforts have impacted all regions of the world, but have been most drastic in the European Union. Additionally, some countries require approval of the sale price of a product before it can be lawfully marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we, or any collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. As a result, we might obtain marketing approval for a product in a particular country, but then may experience delays in the reimbursement approval of our product or be subject to price regulations that would delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country.

Moreover, efforts by governments and payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate reimbursement for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug practices. Specifically, there have

been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug 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 drugs. 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 drugs and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

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

***If the FDA or comparable foreign regulatory authorities approve generic versions of any of our product candidates that receive marketing approval, or such authorities do not grant such products appropriate periods of data exclusivity before approving generic versions of such products, the sales of such products could be adversely affected.***

Once an NDA is approved, the product covered thereby becomes a “reference-listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning, in part, that it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product, and the price of the branded product may be lowered.

The FDA may not accept for review or approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. It is unclear whether the FDA will treat the active ingredients in our product candidates as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for our products in the Orange Book. Three year exclusivity is given to a non-NCE drug if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the NDA. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

***We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws health information privacy and security laws, and other health care laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our prescribers, customers and purchasers, subject to

various U.S. federal and state fraud and abuse laws and regulations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, or Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. “Remuneration” has been interpreted broadly to include anything of value. A person or entity does not need to have actual knowledge of the Anti-Kickback Statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA, or federal civil money penalties. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- the U.S. federal civil and criminal false claims laws, including the FCA, and civil monetary penalty law, which impose criminal and civil penalties against individuals or entities for, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; knowingly making, using or causing to be made or used, a false statement of record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government. 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. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the beneficiary inducement provisions of the civil monetary penalty law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the Anti-Kickback Statute, 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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their respective business associates, individuals and entities that perform services on their behalf that involve the use or disclosure of individually identifiable health information and their subcontractors that

use disclose or otherwise process individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information;

- the U.S. federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- U.S. federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and
- U.S. federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we are subject to U.S. state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the Anti-Kickback Statute and FCA, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America’s Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. There are ambiguities as to what is required to comply with these state requirements, and if we fail to comply with an applicable state law requirement we could be subject to significant penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. For further information concerning the data privacy and security laws we may be subject to and our processing of personal data, see the risk factor titled *“We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenues or profits, and other adverse business consequences.”*

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our current and future business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. If our operations, including our arrangements with physicians and other healthcare providers, some of whom receive share options as compensation for services provided, are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, imprisonment, exclusion from participation in federal and state healthcare programs (such as Medicare and Medicaid), additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and imprisonment, any of which could adversely affect our ability to operate our business and our financial results. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management’s attention from

the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

***Healthcare legislative reform measures may have a negative impact on our business and results of operations.***

In the United States and some foreign jurisdictions, there have been, and continue to be, 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. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products, (iv) restriction on coverage, reimbursement, and pricing for our products, (v) transparency reporting obligations regarding transfers of value to health care professionals or (vi) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect our business, financial condition and results of operations.

Among policy makers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, created a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

There have been executive, judicial and Congressional challenges to certain aspects of ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or the IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket costs and creating a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA and the Consolidated Appropriations Act of 2023, will remain in effect through 2032 unless additional Congressional action is taken. 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. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including

hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries, Presidential executive orders and proposed federal and state legislation designed to, among other things, bring more transparency to drug 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 drugs. At the federal level, in July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at prescription drugs. In response to Biden’s executive order, on September 9, 2021, the U.S. Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (i) allows HHS to negotiate the price of certain high-expenditure drugs and biologics covered under Medicare, and subjects drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law, and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions will take effect progressively starting in 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. It is currently unclear how the IRA will be effectuated but it is likely to have a significant impact on the pharmaceutical industry. Further, in response to the Biden administration’s October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Similarly, individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation, administrative or executive action. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

***We are subject to the U.K. Bribery Act 2010, or the Bribery Act, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.***

Our operations are subject to anti-corruption laws, including the Bribery Act, the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us, our employees and our intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us

from committing a bribery offense. We and our commercial partners operate in a number of jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by the United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

***We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, and other adverse business consequences.***

In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, processing) personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, and sensitive third-party data. Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws. For example, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information. Additionally, various U.S. states, including California, Virginia and Colorado, have passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. These developments may further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely.

Outside of the U.S., an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, the European Union's General Data Protection Regulation, or EU GDPR, and the United Kingdom's GDPR, or UK GDPR, impose strict requirements for processing personal data. For example, under the EU GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

In the ordinary course of business, we transfer personal data from the United Kingdom (UK) to the United States or other countries. The UK has enacted laws requiring data to be localized or limiting the transfer of personal data

to the United States and other countries whose privacy laws it believes are inadequate. Although there are currently various mechanisms that may be used to transfer personal data from the UK to the United States in compliance with law, such as the UK data transfer agreement, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the UK to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors, and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups.

In addition to data privacy and security laws, we are also bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful.

We may publish privacy policies, marketing materials, and other statements, regarding data privacy and security. If these policies, materials, or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflicting among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy or security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data; and orders to destroy or not use personal data. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; inability to process personal data or operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

***Our activities subject us to various laws relating to foreign investment and the export of certain technologies, and our failure to comply with these laws or adequately monitor the compliance of our suppliers and others we do business with could subject us to substantial fines, penalties and even injunctions, the imposition of which on us could have a material adverse effect on the success of our business.***

We are subject to laws that regulate certain transactions and access to technology. In the U.S., these laws include section 721 of the Defense Production Act of 1950, as amended by the Foreign Investment Risk Review Modernization Act of 2018, and the regulations at 31 C.F.R. Parts 800 and 801, as amended, administered by the Committee on Foreign Investment in the United States; and the Export Control Reform Act of 2018, which is being implemented in part through Commerce Department rulemakings to impose new export control restrictions on “emerging and foundational technologies” yet to be fully identified. Application of these laws, including as they are implemented through regulations being developed, may negatively impact our business in various ways, including by restricting our access to capital and markets; limiting the collaborations we may pursue; regulating the export our products, services, and technology from the United States and abroad; increasing our costs and the time necessary to obtain required authorizations and to ensure compliance; and threatening monetary fines and other penalties if we do not.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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 or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

#### **Risks Related to Our Business and Our International Operations**

***As a company based outside of the United States, we are subject to economic, political, regulatory and other risks associated with international operations.***

As a company based in the United Kingdom, our business is subject to risks associated with conducting business outside of the United States. Many of our suppliers and clinical trial relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements for product approvals;
- differing jurisdictions could present different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations, including, without limitation, restrictive regulations such as the EU GDPR and UK GDPR governing the use, processing, and cross-border transfer of personal data;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates of the pound sterling, U.S. dollar, euro and currency controls;

- changes in a specific country’s or region’s political or economic environment, including the implications of the recent decision of the United Kingdom to withdraw from the European Union;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- differing reimbursement regimes and price controls in certain non-U.S. markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad, including, for example, the variable tax treatment in different jurisdictions of options granted under our share option schemes or equity incentive plans;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- litigation or administrative actions resulting from claims against us by current or former employees or consultants individually or as part of class actions, including claims of wrongful terminations, discrimination, misclassification or other violations of labor law or other alleged conduct;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, natural disasters, including earthquakes, typhoons, floods and fires, or public health crises.

Any or all of these factors could have a material adverse impact on our business, financial condition and results of operations. Moreover, global instability increased after Russia invaded Ukraine in February 2022. In response to the invasion, North Atlantic Treaty Organization, or NATO, has deployed additional military forces to Eastern Europe, including to Lithuania, and the United Kingdom, the European Union and the United States implemented certain sanctions against Russia. The invasion of Ukraine and the retaliatory measures that have been taken, or could be taken in the future, by the United States, NATO, and other countries have created global security concerns that could result in a regional conflict and otherwise have a lasting impact on regional and global economies, any or all of which could disrupt our supply chain and increase the costs associated with or otherwise adversely affect our ability to conduct ongoing and future clinical trials of our product candidates. In addition, the conflict has had significant ramifications on global financial markets, which may adversely impact our ability to raise capital in the future on favorable terms or at all.

***Cyber-attacks or other failures in telecommunications or information technology systems and deficiency in our, or those of third parties upon which we rely, cybersecurity could result in information theft, data corruption and significant disruption of our business operations.***

In the ordinary course of business, we and the third parties upon which we rely, may collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, processing) proprietary, confidential, and sensitive data, including personal data (such as health-related data), intellectual property, and trade secrets (collectively, sensitive information). Cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer “hackers,” threat actors, “hacktivists,” organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors.

Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to conduct our research and development programs and our clinical trials. We and the third parties upon which we rely may be subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, and other similar threats. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, loss of sensitive data and income, reputational harm, and diversion of funds. Remote work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers, and devices outside of our premises or network, including working at home, while in transit and in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

In addition, our reliance on third-party service providers, including those located in China, could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We may rely on third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, encryption and authentication technology, employee email, content delivery to customers, CROs for managing clinical trial data, and other functions. We also rely on third-party service providers to manufacture our product candidates and provide other products, services, parts, or otherwise operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, the liability of such third party may be limited such that any award may be insufficient to cover our damages, or we may be unable to recover any such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our services. We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and sensitive information.

Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class-action claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause customers to stop using our services, deter new customers from using our services, and negatively impact our ability to grow and operate our business. Our contracts may not

contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

***Social media platforms and artificial intelligence-based platforms present new risks and challenges to our business.***

As social media continues to expand, it also presents us with new risks and challenges. Social media is increasingly being used to communicate information about us, our programs and the diseases our therapeutics are being developed to treat. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations or other consequences. Further, the accidental or intentional disclosure of non-public information by our workforce or others through media channels could lead to information loss. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us, our products, or our product candidates on any social media platform. The nature of social media prevents us from having real-time control over postings about us on social media. We may not be able to reverse damage to our reputation from negative publicity or adverse information posted on social media platforms or similar mediums. If any of these events were to occur or we otherwise fail to comply with application regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business including quick and irreversible damage to our reputation, brand image and goodwill. Additionally, artificial intelligence, or AI, based platforms are increasingly being used in the biopharmaceutical industry. While we have undertaken measures to restrict the internal use of public AI platforms, their use by people, including our vendors, suppliers and contractors, with access to our proprietary and confidential information, including trade secrets, may continue to increase and may lead to the release of such information, which may negatively impact our company, including our ability to realize the benefit of our intellectual property.

***Exchange rate fluctuations may materially affect our results of operations and financial condition.***

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, may adversely affect us. Although we are based in the United Kingdom, we source research and development, manufacturing, consulting and other services from the United States, European Union and Asia that are billed in U.S. dollars. Further, potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the price of our ADSs may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the euro, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place. Any fluctuation in the exchange rate of these foreign currencies may negatively impact our business, financial condition and operating results. Global economic events have and may continue to significantly impact local economies and the foreign exchange markets, which may increase the risks associated with sales denominated in foreign currencies.

**Risks Related to Our Dependence on Third Parties**

***For certain product candidates, we depend, or will depend, on development and commercialization collaborators to develop and conduct clinical trials with, obtain regulatory approvals for, and if approved, market and sell product candidates. If such collaborators fail to perform as expected, the potential for us to generate future revenue from such product candidates would be significantly reduced and our business would be harmed.***

For certain products candidates, we depend, or will depend, on our development and commercial collaborators to develop, conduct clinical trials of, and, if approved, commercialize product candidates.

Under our collaborations with Genentech, Ionis, Novartis, Bayer and Oxurion, we are responsible for identifying and optimizing *Bicycle* peptides related to collaboration targets and our collaborators are responsible for further development and product commercialization after we complete the defined research screening and compound

optimization. In addition, Cancer Research UK is sponsoring and funding a Phase I/IIa clinical trial of BT1718, in patients with advanced solid tumors, and will sponsor and fund development of BT7401 from current preclinical studies through the completion of a Phase IIa trial in patients with advanced solid tumors. We depend on these collaborators to develop and, where applicable, commercialize products based on *Bicycle* peptides, and the success of their efforts directly impacts the milestones and royalties we will receive. We cannot provide assurance that our collaborators will be successful in or that they will devote sufficient resources to the development or commercialization of their products. If our current or future collaboration and commercialization partners do not perform in the manner we expect or fail to fulfill their responsibilities in a timely manner, or at all, if our agreements with them terminate or if the quality or accuracy of the clinical data they obtain is compromised, the clinical development, regulatory approval and commercialization efforts related to their and our product candidates and products could be delayed or terminated and it could become necessary for us to assume the responsibility at our own expense for the clinical development of such product candidates.

Our current collaborations and any future collaborations that we enter into are subject to numerous risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to the collaborations;
- collaborators may not perform their obligations as expected or fail to fulfill their responsibilities in a timely manner, or at all;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay preclinical studies or clinical trials, provide insufficient funding for clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our shareholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- the collaborations may not result in product candidates to develop and/or preclinical studies or clinical trials conducted as part of the collaborations may not be successful;
- product candidates developed with collaborators may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to stop commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;
- public health crises and other adverse global economic events could materially affect our operations as well as causing significant disruption in the operations and business of our collaborators and the third-party

manufacturers, CROs and other service providers that we and/or our collaborators conduct business with; and

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation.

In addition, certain collaboration and commercialization agreements provide our collaborators with rights to terminate such agreements, which rights may or may not be subject to conditions, and which rights, if exercised, would adversely affect our product development efforts and could make it difficult for us to attract new collaborators. In that event, we would likely be required to limit the size and scope of efforts for the development and commercialization of such product candidates or products; we would likely be required to seek additional financing to fund further development or identify alternative strategic collaborations; our potential to generate future revenue from royalties and milestone payments from such product candidates or products would be significantly reduced, delayed or eliminated; and it could have an adverse effect on our business and future growth prospects. Our rights to recover tangible and intangible assets and intellectual property rights needed to advance a product candidate or product after termination of a collaboration may be limited by contract, and we may not be able to advance a program post-termination.

***If conflicts arise with our development and commercialization collaborators or licensors, they may act in their own self-interest, which may be adverse to the interests of our company.***

We may in the future experience disagreements with our development and commercialization collaborators or licensors. Conflicts may arise in our collaboration and license arrangements with third parties due to one or more of the following:

- disputes with respect to milestone, royalty and other payments that are believed due under the applicable agreements;
- disagreements with respect to the ownership of intellectual property rights or scope of licenses;
- disagreements with respect to the scope of any reporting obligations;
- unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities, or to permit public disclosure of these activities; and
- disputes with respect to a collaborator's or our development or commercialization efforts with respect to our products and product candidates.

For example, we were previously involved in litigation with Pepscan Systems B.V., and its affiliates, or Pepscan, related to a non-exclusive patent license agreement that our subsidiary, BicycleRD Limited, or BicycleRD, entered into with Pepscan in 2009.

Conflicts with our development and commercialization collaborators or licensors could materially adversely affect our business, financial condition or results of operations and future growth prospects. If we are unable to prevail against these challenges, our intellectual property estate may be materially harmed, which would impair our ability to establish competitive barriers to entry in the form of intellectual property protections.

***We rely on third parties, including independent clinical investigators and CROs, to conduct and sponsor some of the clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.***

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators, academic partners, regulatory affairs consultants and third-party CROs, to conduct our preclinical studies

and clinical trials, including in some instances sponsoring such clinical trials, and to engage with regulatory authorities and monitor and manage data for our ongoing preclinical and clinical programs. For example, Cancer Research UK currently sponsors and funds the Phase I/IIa clinical trial of BT1718 in patients with advanced solid tumors. We also utilize CROs to perform toxicology studies related to our preclinical activities. While we will have agreements governing the activities of such third parties, we will control only certain aspects of their activities and have limited influence over their actual performance. Given the breadth of clinical therapeutic areas for which we believe *Bicycles* may have utility, we intend to continue to rely on external service providers rather than build internal expertise.

Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

We remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and 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 products in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we fail to exercise adequate oversight over any of our academic partners or CROs or if we or any of our academic partners or CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon a regulatory inspection of us, our academic partners or our CROs or other third parties performing services in connection with our clinical trials, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under applicable CGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, 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 may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, with respect to investigator-sponsored trials that are being or may be conducted, we do not control the design or conduct of these trials, and it is possible that the FDA or EMA will not view these investigator-sponsored trials as providing adequate support for future clinical trials or market approval, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials, manufacturing issues, safety concerns or other trial results. We expect that such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including the ability to obtain a license to obtain access to use and reference the data, including for our own regulatory submissions, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have

gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. Additionally, the FDA or EMA may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or EMA may require us to obtain and submit additional preclinical, manufacturing, or clinical data.

***We intend to rely on third parties to manufacture product candidates, which increases the risk that we will not have sufficient quantities of such product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not own or operate manufacturing facilities for the production of clinical or commercial supplies of the product candidates that we are developing or evaluating in our development programs. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We rely on third parties, including those located in China, for supply of our product candidates, and our strategy is to outsource all manufacturing of our product candidates and products to third parties. For any activities conducted in China, we are exposed to the increased possibility of supply disruptions and higher costs in the event of changes in the policies of the U.S. or Chinese governments, political unrest or unstable economic conditions including sanctions on China or any of our China-based suppliers. Our manufacturing costs could also increase as a result of future appreciation of the local currency in China or increased labor costs if the demand for skilled laborers increases and/or the availability of skilled labor declines in China.

In order to conduct clinical trials of product candidates, we will need to have them manufactured in potentially large quantities. Our third-party manufacturers 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 and at any other time. For example, ongoing data on the stability of our product candidates may shorten the expiry of our product candidates and lead to clinical trial material supply shortages, and potentially clinical trial delays. Additionally, our manufacturers may experience delays as a result of impacts due to the Russia-Ukraine war. If our third-party manufacturers 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 infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

Our use of new third-party manufacturers increases the risk of delays in production or insufficient supplies of our product candidates as we transfer our manufacturing technology to these manufacturers and as they gain experience manufacturing our product candidates. Even after a third-party manufacturer has gained significant experience in manufacturing our product candidates or even if we believe we have succeeded in optimizing the manufacturing process, there can be no assurance that such manufacturer will produce sufficient quantities of our product candidates in a timely manner or continuously over time, or at all.

We may be delayed if we need to change the manufacturing process used by a third party. Further, if we change an approved manufacturing process, then we may be delayed if the FDA or a comparable foreign authority needs to review the new manufacturing process before it may be used.

We operate an outsourced model for the manufacture of our product candidates, and contract with GMP licensed pharmaceutical contract development and manufacturing organizations. While we have engaged several third-party vendors to provide clinical and non-clinical supplies and fill-finish services, we do not currently have any agreements with third-party manufacturers for long-term commercial supplies. In the future, we may be unable to enter into agreements with third-party manufacturers for commercial supplies of any product candidate that we develop, or may be unable to do so on acceptable terms. Even if we are able to establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails risks, including:

- reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;

- limitations on supply availability resulting from capacity and scheduling constraints of third-parties;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control; and
- the possible termination or non-renewal of the manufacturing agreements by the third-party, at a time that is costly or inconvenient to us.

Third-party manufacturers may not be able to comply with cGMP requirements or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and/or criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates. In addition, some of the product candidates we intend to develop, including BT8009, BT5528, and BT1718 use toxins or other substances that can be produced only in specialized facilities with specific authorizations and permits, and there can be no guarantee that we or our manufacturers can maintain such authorizations and permits. These specialized requirements may also limit the number of potential manufacturers that we can engage to produce our product candidates, and impair any efforts to transition to replacement manufacturers.

Our future product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP requirements that might be capable of manufacturing for us.

If the third parties that we engage to supply any materials or manufacture product for our preclinical tests and clinical trials should cease to continue to do so for any reason, including as a result of the impacts of public health crises on the global workforce and manufacturing operations, we likely would experience delays in advancing these tests and trials while we identify and qualify replacement suppliers or manufacturers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of our product candidates or the substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

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

***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 manufacture our product candidates, and because we collaborate with various organizations and academic institutions on the development of our product candidates, we must, at times, 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, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees 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, such as 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 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.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

### **Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain patent and other intellectual property protection for our products and product candidates, or if the scope of the patent and other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products and product candidates may be adversely affected.***

Our ability to compete effectively will depend, in part, on our ability to maintain the proprietary nature of our technology and manufacturing processes. We rely on research, manufacturing and other know-how, patents, trade secrets, license agreements and contractual provisions to establish our intellectual property rights and protect our products and product candidates. These legal means, however, afford only limited protection and may not adequately protect our rights.

In certain situations and as considered appropriate, we have sought, and we intend to continue to seek to protect our proprietary position by filing patent applications in the United States and, in at least some cases, one or more countries outside the United States relating to current and future products and product candidates that are important to our business. However, we cannot predict whether the patent applications currently being pursued will issue as patents, or whether the claims of any resulting patents will provide us with a competitive advantage or whether we will be able to successfully pursue patent applications in the future relating to our current or future products and product candidates. Moreover, the patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Furthermore, we, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to seek additional patent protection. It is possible that defects of form in the preparation or filing of patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If there are material defects in the form, preparation, prosecution or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents.

Even if they are unchallenged, our patents and patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected.

Other parties, many of whom have substantially greater resources and have made significant investments in competing technologies, have developed or may develop technologies that may be related or competitive with our approach, and may have filed or may file patent applications and may have been issued or may be issued patents with claims that overlap or conflict with our patent applications, either by claiming the same compositions, formulations or methods or by claiming subject matter that could dominate our patent position. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. As a result, any patents we may obtain in

the future may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our products and product candidates.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that our patents are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

In the future, one or more of our products and product candidates may be in-licensed from third parties. Accordingly, in some cases, the availability and scope of potential patent protection is limited based on prior decisions by our licensors or the inventors, such as decisions on when to file patent applications or whether to file patent applications at all. Our failure to obtain, maintain, enforce or defend such intellectual property rights, for any reason, could allow third parties, in particular, other established and better financed competitors having established development, manufacturing and distribution capabilities, to make competing products or impact our ability to develop, manufacture and market our products and product candidates, even if approved, on a commercially viable basis, if at all, which could have a material adverse effect on our business.

In addition to patent protection, we expect to rely heavily on trade secrets, know-how and other unpatented technology, which are difficult to protect. Although we seek such protection in part by entering into confidentiality agreements with our vendors, employees, consultants and others who may have access to proprietary information, we cannot be certain that these agreements will not be breached, adequate remedies for any breach would be available, or our trade secrets, know-how and other unpatented proprietary technology will not otherwise become known to or be independently developed by our competitors. If we are unsuccessful in protecting our intellectual property rights, sales of our products may suffer and our ability to generate revenue could be severely impacted.

***Issued patents covering our products and product candidates could be found invalid or unenforceable if challenged in court or in administrative proceedings. We may not be able to protect our trade secrets in court.***

If we initiate legal proceedings against a third-party to enforce a patent covering one of our products or product candidates, should such a patent issue, the defendant could counterclaim that the patent covering our product or product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the United States Patent and Trademark Office (USPTO), or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions. An adverse determination in any of the foregoing proceedings could result in the revocation or cancellation of, or amendment to, our patents in such a way that they no longer cover our products or product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we were unaware during prosecution. If a defendant or third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our products and product candidates. Such a loss of patent protection may

materially harm our intellectual property estate, which would impair our ability to establish competitive barriers to entry in the form of intellectual property protections.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach.

In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Competitors and other third parties could purchase our products and product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe, misappropriate or otherwise violate our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. 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, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected or sufficient to provide an advantage over our competitors, our competitive position could be adversely affected, as could our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets.

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

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in the patents and intellectual property that we own or that we may own or license in the future. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own or such assignments may not be self-executing or may be breached. We could be subject to ownership disputes arising, for example, from conflicting obligations of employees, consultants or others who are involved in developing our products or product candidates. Litigation may be necessary to defend against any claims challenging inventorship or ownership. If we fail in defending any such claims, we may have to pay monetary damages and may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property, which could adversely impact our business, results of operations and financial condition.

***Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, 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 applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. The terms of one or more licenses that we enter into the future may not provide us with the ability to maintain or prosecute patents in the portfolio, and must therefore rely on third parties to do so.

***If we do not obtain patent term extension and data exclusivity for our products and product candidates, our business may be materially harmed.***

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. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive 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 patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

In the future, if we obtain an issued patent covering one of our present or future product candidates, depending upon the timing, duration and specifics of any FDA marketing approval of such product candidates, such patent may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. A patent may only be extended once and only based on a single approved product. However, we may not be granted an extension because of, for example, failure to obtain a granted patent before approval of a product candidate, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise our failure to satisfy applicable requirements. A patent licensed to us by a third party may not be available for patent term extension. 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 the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

***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 products and product candidates.***

Changes in either the patent laws or the interpretation of the patent laws in the United States or other jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. When implemented, the Leahy-Smith Act included several significant changes to U.S. patent law that impacted how patent rights could be prosecuted, enforced and defended. In particular, the Leahy-Smith Act also included provisions that switched the United States from a “first-to-invent” system to a “first-to-file” system, allowed third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had made the invention earlier. The USPTO developed new regulations and procedures governing the administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. It remains unclear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, 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.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent rulings from the U.S. Court of Appeals for the Federal Circuit and the U.S. Supreme Court have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a

material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We cannot provide assurance that our efforts to seek patent protection for one or more of our products and product candidates will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact courts' decisions in historical and future cases may have on the ability of life science companies to obtain or enforce patents relating to their products in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent rights and our ability to protect and enforce our intellectual property in the future.

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

Filing, prosecuting, maintaining, defending and enforcing patents on products 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 could be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. There can be no assurance that we will obtain or maintain patent rights in or outside the United States under any future license agreements. 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, even in jurisdictions where we pursue patent protection, 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 pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Proceedings to enforce our patent rights, even if obtained, in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. While we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

***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 have U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds and/or methods of use for the treatment of the disease indications for which we are developing our product candidates. If any third-party patents or patent applications are found to cover our product candidates or their methods of use or manufacture, we and our collaborators or sublicensees may not be free to manufacture or market our product

candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all. We may also be required to indemnify our collaborators or sublicensees in such an event.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we were previously party to protracted litigation with Pepscan, which we settled in 2020. We may become party to, or be threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including interference and post-grant proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, use or manufacture of our product candidates. We cannot guarantee that any of our patent searches or analyses including, but not limited to, 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 patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent 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, products or methods 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 is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. 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 pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe 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 or product. 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; alternatively or additionally, it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. 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 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 be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.***

Many of our current and former employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Some of these employees may be subject to proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we have been in the past and may be subject in the future to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be

awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. 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. In addition, our patents may become involved in inventorship, priority, or validity disputes. To counter or defend against such claims can be expensive and time-consuming, and our adversaries may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both.

In an infringement proceeding, a court may decide that a patent is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own or control. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly. Further, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ADSs. 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 conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

***If we fail to comply with our obligations under any future intellectual property licenses with third parties, we could lose license rights that are important to our business.***

In connection with our efforts to build our product candidate pipeline, we may enter into license agreements in the future. We expect that such license agreements will impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the

right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could negatively impact the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

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

Our trademarks or trade names may be challenged, infringed, circumvented or declared invalid, generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. 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 objections. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such objections. In addition, in the USPTO and in comparable Intellectual Property Offices 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 have been and may in the future be filed against our trademarks, and our trademarks may not survive such proceedings. For example, our U.K. trademark application for “TICA” was successfully opposed in the U.K., Japan and the European Union for the majority of goods and services for which we originally applied, and we have abandoned our trademark application for “TICA” in the United States as a result. 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.

#### **Risks Related to Employee Matters and Managing Growth**

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

We are highly dependent on principal members of our executive team and key employees, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time. We do not maintain “key person” insurance policies on the lives of these individuals or the lives of any of our other employees. The loss of the services of one or more of our current key employees might impede the achievement of our research, development and commercialization objectives. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives and personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials may make it more challenging to recruit and retain qualified personnel.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

***Our employees, independent contractors, consultants, collaborators and CROs may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.***

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; (2) manufacturing standards; (3) federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities; and (4) laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, bribery and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee or collaborator misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Further, because of our hybrid work environment, information that is normally protected, including company confidential information, may be less secure. We have adopted a code of conduct and business ethics to which all of our employees must adhere, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

***We have recently expanded our organization significantly and we expect to continue to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We have recently experienced significant growth in the number of our employees and the scope of our operations and expect to continue to expand, particularly in the areas of drug manufacturing, supply chain, clinical development, sales, marketing, as well as to support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to geographic areas beyond those where we have been historically located. For example, we maintain office and laboratory space in Cambridge, U.K. and in Massachusetts, U.S., at which many of our finance, management and administrative personnel work. Due to our limited resources, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

## Risks Related to Ownership of Our Securities

***The market price of our ADSs is highly volatile, and holders of our ADSs may not be able to resell their ADSs at or above the price at which they purchased their ADSs.***

The market price of our ADSs is highly volatile. Since our initial public offering, or IPO, in May 2019, through October 30, 2023, the trading price of our ADSs has ranged from \$6.24 to \$62.08. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, holders of our ADSs may not be able to sell their ADSs at or above the price at which they purchased their ADSs. The market price for our ADSs may be influenced by many factors, including:

- adverse results or delays in preclinical studies or clinical trials;
- reports of adverse events in products similar or perceived to be similar to those we are developing or clinical trials of such products;
- an inability to obtain additional funding;
- failure by us to successfully develop and commercialize our product candidates;
- failure by us to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us to identify additional product candidates for our pipeline;
- failure by us or our licensors and strategic partners to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- changes in the structure of healthcare payment systems;
- an inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- the introduction of new products, services or technologies by our competitors;
- failure by us to meet or exceed financial projections we may provide to the public;
- failure by us to meet or exceed the financial projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;

- significant lawsuits, including patent or shareholder litigation;
- changes in the market valuations of similar companies;
- sales of our ADSs or ordinary shares by us or our shareholders in the future; and
- the trading volume of our ADSs.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, supply chain shortages, increases in inflation rates, higher interest rates and uncertainty about economic stability. For example, the COVID-19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. Similarly, the ongoing war between Russia and Ukraine has created extreme volatility in the global capital markets and is expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely. If the equity and credit markets continue to deteriorate, it may make any necessary debt or equity financings more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs. In addition, higher inflation and macro turmoil and uncertainty could also adversely affect our buyers and sellers, which could reduce demand for our products. These factors may negatively affect the market price of our ADSs, regardless of our actual operating performance.

***The dual class structure of our shares may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.***

As of October 30, 2023, we had 37,715,666 ordinary shares, nominal value £0.01 per share, and 4,705,882 non-voting ordinary shares, nominal value £0.01 per share, outstanding. The dual class structure of our shares may limit your ability to influence corporate matters. Holders of our ordinary shares are entitled to one vote per share, while holders of our non-voting ordinary shares are not entitled to any votes. Nevertheless, non-voting ordinary shares may be re-designated at any time as ordinary shares at the option of the holder by providing written notice to us, subject to certain restrictions as summarized in Exhibit 4.1 of our Current Report on Form 8-K filed with the Securities and Exchange Commission on July 13, 2023.

Consequently, if holders of our non-voting ordinary shares exercise their option to make this re-designation, this will have the effect of increasing the relative voting power of those prior holders of our non-voting ordinary shares, and correspondingly decreasing the voting power of the holders of our ordinary shares, which may limit your ability to influence corporate matters. For example, the ordinary shares currently have 100% of the voting power, but if the holders of non-voting ordinary shares were to re-designate all of their shares as ordinary shares, the prior ordinary shares would have 89% of the voting power, and the former non-voting ordinary shares would represent 11% of the voting power.

***There is no public market for our non-voting ordinary shares.***

There is no public trading market for our non-voting ordinary shares, and we do not expect a market to develop. In addition, we do not intend to list the non-voting ordinary shares on The Nasdaq Global Select Market or any other securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the non-voting ordinary shares will be limited.

***Future sales, or the possibility of future sales, of a substantial number of our securities could adversely affect the price of our ADSs and dilute shareholders.***

Sales of a substantial number of our ADSs in the public market could occur at any time, subject to certain restrictions described below. If our existing shareholders sell, or indicate an intent to sell, substantial amounts of our

securities in the public market, the trading price of the ADSs could decline significantly and could decline below the current trading prices of the ADSs. In addition, ordinary shares subject to outstanding options under our equity incentive plans and the ordinary shares reserved for future issuance under our equity incentive plans will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations.

***Because we do not anticipate paying any cash dividends on our ADSs in the foreseeable future, capital appreciation, if any, will be the sole source of gains for holders of our ADSs, and they may never receive a return on their investment.***

Under current English law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be declared and paid. Therefore, we must have distributable profits before declaring and paying a dividend. In addition, the terms of our indebtedness with Hercules prohibit us from paying dividends. We have not paid dividends in the past on our ordinary shares. We intend to retain earnings, if any, for use in our business and do not anticipate paying any cash dividends in the foreseeable future. As a result, capital appreciation, if any, on our ADSs will be a holder's sole source of gains for the foreseeable future, and holders will suffer a loss on their investment if they are unable to sell their ADSs at or above the original purchase price.

### **Risks Related to Our Incorporation Under the Laws of England and Wales**

#### ***Claims of U.S. civil liabilities may not be enforceable against us.***

We are incorporated under English law. Certain members of our board of directors and senior management are non-residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States.

The United States and the United Kingdom do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in the United Kingdom. In addition, uncertainty exists as to whether U.K. courts would entertain original actions brought in the United Kingdom against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would be treated by the courts of the United Kingdom as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that certain requirements are met. Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the U.S. securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision. If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement.

As a result, U.S. investors may not be able to enforce against us or our senior management, board of directors or certain experts named herein who are residents of the United Kingdom or countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

#### ***If we are a controlled foreign corporation, there could be adverse U.S. federal income tax consequences to certain U.S. holders.***

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for U.S. federal income tax purposes generally is required to report annually and include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income," "global intangible low-taxed income," and investment of earnings in U.S. property, even if the CFC has made no

distributions to its shareholders. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. An individual that is a Ten Percent Shareholder with respect to a CFC generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a U.S. corporate that is a Ten Percent Shareholder with respect to a CFC. Failure to comply with these reporting and tax paying obligations may subject a Ten Percent Shareholder to significant monetary penalties and may prevent the statute of limitations from starting with respect to such shareholder's U.S. federal income tax return for the year for which reporting was due. A non-U.S. corporation generally will be classified as a CFC for U.S. federal income tax purposes if Ten Percent Shareholders own (directly, indirectly or constructively through the application of attribution rules) more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own (directly, indirectly or constructively through the application of attribution rules) 10% or more of the total combined voting power of all classes of stock entitled to vote or 10% or more of the total value of all classes of stock of such corporation.

Each Ten Percent Shareholder should also be aware that because our group includes a U.S. subsidiary, certain of our non-U.S. subsidiaries will be treated as CFCs (regardless of whether or not we are treated as a CFC). We cannot provide any assurances that we will assist shareholders in determining whether we are or any of our non-U.S. subsidiaries is treated as a CFC or whether any shareholder is treated as a Ten Percent Shareholder with respect to any such CFC or furnish to any shareholders information that may be necessary to comply with reporting and tax paying obligations. The Internal Revenue Service has provided limited guidance on situations in which investors may rely on publicly available information to comply with their reporting and tax paying obligations with respect to foreign-controlled CFCs.

The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. United States persons should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC.

***If we are a passive foreign investment company, there could be adverse U.S. federal income tax consequences to U.S. holders.***

Under the Code, we will be a passive foreign investment company, or PFIC, for any taxable year in which (1) 75% or more of our gross income consists of passive income or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income, including cash. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as holding and receiving directly its proportionate share of assets and income of such corporation. If we are a PFIC for any taxable year during which a United States person holds our shares, such U.S. shareholder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred and additional reporting requirements.

Based on our analysis of our income, assets, activities and market capitalization, we believe that we were not a PFIC in the 2022 taxable year. However, no assurances can be provided that we will not be a PFIC for the current or any future taxable year or that we have not been a PFIC in any prior taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies that in some circumstances are unclear and subject to varying interpretation. As a result, there can be no assurance regarding if we will be PFIC or will not be a PFIC in the future. In addition, the total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our ordinary shares or ADSs from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which will depend on the transactions we enter into and our corporate structure.

***We may be unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments or benefit from favorable U.K. tax legislation.***

As an entity incorporated and tax resident in the United Kingdom, we are subject to U.K. corporate taxation. Due to the nature of our business, we have generated losses since inception and therefore have not paid any U.K. corporation tax. Subject to numerous utilization criteria and restrictions (including the Corporate Income Loss Restriction and the Corporate Capital Loss Restriction that, broadly, restrict the amount of carried forward losses that can be utilized to 50% of group profits or gains arising above £5.0 million per tax year, we expect losses to be eligible for carry forward and utilization against future operating profits. In addition, if we were to have a major change in the nature of the conduct or the conduct of our trade, loss carryforwards may be restricted or extinguished.

As a group that carries out extensive research and development activities, we seek to benefit from one of two U.K. research and development tax relief programs, the Small and Medium-sized Enterprises R&D Tax Relief program, or SME Program, and for certain specific categories of expenditure the Research and Development Expenditure Credit program, or RDEC Program. The SME Program may be particularly beneficial to us, as under such program the trading losses that arise from our qualifying R&D activities can be surrendered for a cash rebate of up to 33.35% of qualifying expenditure incurred prior to April 1, 2023, and up to 18.6% of qualifying expenditure incurred thereafter (unless we qualify as “R&D intensive” for an accounting period (broadly, a loss making SME whose qualifying R&D expenditure for an accounting period represents 40% or more of its total expenditure for that accounting period), in which case the cash rebate that may be claimed will be 26.97% of qualifying expenditure). Further, amendments to the U.K. R&D tax credit regime have recently been proposed that may (unless limited exceptions apply) introduce restrictions on the tax relief that can be claimed for expenditure incurred on sub-contracted R&D activities or externally provided workers, where such sub-contracted activities are not carried out in the U.K. or such workers are not subject to U.K. payroll taxes. These amendments are expected to take effect from April 1, 2024. In addition, the U.K. Government is currently considering a proposal to merge the SME Program and the RDEC Program into a single scheme with effect from April 2024; if such proposal is implemented, it may be the case that we are no longer able to make claims in respect of sub-contracted R&D activities, and that different (and potentially lower) caps are imposed on the amount of tax relief that we can claim. These and other potential future changes to the U.K. research and development tax relief programs may be made which mean we may no longer qualify or have a material impact on the extent to which we can make claims.

We may benefit in the future from the United Kingdom’s “patent box” regime, which allows certain profits attributable to revenues from patented products (and other qualifying income) to be taxed at an effective rate of 10% by giving an additional tax deduction. We are the exclusive licensee or owner of several patent applications which, if issued, would cover our product candidates, and accordingly, future upfront fees, milestone fees, product revenues and royalties could be eligible for this tax deduction. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term rate of corporation tax lower than the statutory rate to apply to us. If, however, there are unexpected adverse changes to the U.K. research and development tax relief programs or the “patent box” regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments then our business, results of operations and financial condition may be adversely affected. This may impact our ongoing requirement for investment and the timeframes within which additional investment is required.

***Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.***

The tax treatment of the company is, and our ADSs and ordinary shares are, subject to changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, as well as tax policy initiatives and reforms related to the Organization for Economic Co-Operation and Development’s, or OECD, Base Erosion and Profit Shifting, or BEPS, Project (including “BEPS 2.0”), the European Commission’s state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid, or the stamp duty or stamp duty reserve tax treatment of our ADSs or ordinary shares.

In the United States on August 16, 2022, President Biden signed into law the IRA, which includes a minimum tax equal to 15% of the adjusted financial statement income of certain corporations, as well as a 1% excise tax on share buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act of 2017 eliminates the option to deduct research and development expenditures and requires taxpayers to amortize them over five years pursuant to IRC Section 174, 15 years for expenditures attributable to research and development conducted outside the United States. Although Congress is considering legislation that would defer the amortization requirement to later years, we have no assurance that the provision will be repealed or otherwise modified. If the requirement is not modified or deferred, it may materially reduce our cash flows. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

***Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an unforeseen manner, resulting in unanticipated costs, taxes or non-realization of expected benefits.***

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, while we believe that we operate in compliance with applicable transfer pricing laws and intend to continue to do so, our transfer pricing procedures are not binding on applicable tax authorities. HMRC, the Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a “permanent establishment” under international tax treaties and, such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

***Provisions in the U.K. City Code on Takeovers and Mergers that may have anti-takeover effects do not apply to us.***

The U.K. City Code on Takeovers and Mergers, or the Takeover Code, applies to an offer for, among other things, a public company whose registered office is in the United Kingdom if the company is considered by the Panel on Takeovers and Mergers, or the Takeover Panel, to have its place of central management and control in the United Kingdom (or the Channel Islands or the Isle of Man). This is known as the “residency test.” The test for central management and control under the Takeover Code is different from that used by the U.K. tax authorities. Under the Takeover Code, the Takeover Panel will determine whether we have our place of central management and control in the United Kingdom by looking at various factors, primarily where the directors are resident.

In September 2019, the Takeover Panel Executive confirmed that, based on our current circumstances, we are not subject to the Takeover Code. As a result, our shareholders are not entitled to the benefit of certain takeover offer protections provided under the Takeover Code. We believe that this position is unlikely to change at any time in the near future but, in accordance with good practice, we will review the situation on a regular basis and consult with the Takeover Panel if there is any change in our circumstances which may have a bearing on whether the Takeover Panel would determine our place of central management and control to be in the United Kingdom.

***The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.***

We are incorporated under English law. The rights of holders of ordinary shares and, therefore, certain of the rights of holders of ADSs, are governed by English law, including the provisions of the U.K. Companies Act 2006, or the Companies Act, and by our Articles of Association. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations. The principal differences include the following:

- under English law and our articles of association, each shareholder present at a meeting has only one vote unless demand is made for a vote on a poll, in which case each holder gets one vote per share owned. Under U.S. law, each shareholder typically is entitled to one vote per share at all meetings;
- under English law, the number of shares determines the number of votes a holder may cast only on a poll. However, that the voting rights of ADSs are also governed by the provisions of a deposit agreement with our depository bank;
- under English law, subject to certain exceptions and disapplications, each shareholder generally has preemptive rights to subscribe on a proportionate basis to any issuance of ordinary shares or rights to subscribe for, or to convert securities into, ordinary shares for cash. Under U.S. law, shareholders generally do not have preemptive rights unless specifically granted in the certificate of incorporation or otherwise;
- under English law and our articles of association, certain matters require the approval of 75% of the shareholders who vote (in person or by proxy) on the relevant resolution (or on a poll of shareholders representing 75% of the ordinary shares voting (in person or by proxy)), including amendments to the articles of association. This may make it more difficult for us to complete corporate transactions deemed advisable by our board of directors. Under U.S. law, generally only majority shareholder approval is required to amend the certificate of incorporation or to approve other significant transactions;
- in the United Kingdom, takeovers may be structured as takeover offers or as schemes of arrangement. Under English law, if we were to be subject to the Takeover Code, a bidder seeking to acquire us by means of a takeover offer would need to make an offer for all of our outstanding ordinary shares/ADSs. If acceptances are not received for 90% or more of the ordinary shares/ADSs under the offer, under English law, the bidder cannot complete a “squeeze out” to obtain 100% control of us. Accordingly, acceptances of 90% of our outstanding ordinary shares/ADSs will likely be a condition in any takeover offer to acquire us, not 50% as is more common in tender offers for corporations organized under Delaware law. By contrast, a scheme of arrangement, the successful completion of which would result in a bidder obtaining 100% control of us, requires the approval of a majority of shareholders voting at the meeting and representing 75% of the ordinary shares voting, as well as the sanction of the U.K. court;
- under English law and our articles of association, shareholders and other persons whom we know or have reasonable cause to believe are, or have been, interested in our shares may be required to disclose information regarding their interests in our shares upon our request, and the failure to provide the required information could result in the loss or restriction of rights attaching to the shares, including prohibitions on certain transfers of the shares, withholding of dividends and loss of voting rights. Comparable provisions generally do not exist under U.S. law; and
- the quorum requirement for a shareholders’ meeting is a minimum of two shareholders entitled to vote at the meeting and present in person or by proxy or, in the case of a shareholder that is a corporation, represented by a duly authorized officer. Under U.S. law, a majority of the shares eligible to vote must generally be present (in person or by proxy) at a shareholders’ meeting in order to constitute a quorum. The minimum number of shares required for a quorum can be reduced pursuant to a provision in a company’s certificate of incorporation or bylaws, but typically not below one-third of the shares entitled to vote at the meeting.

## General Risks

***Effective as of December 31, 2023, we will be a large accelerated filer, which may increase our costs and demands on management.***

As a result of the market value of our ordinary shares and ADSs held by non-affiliates as of June 30, 2023, we will be a large accelerated filer as of December 31, 2023 and we will no longer qualify as a “smaller reporting company” as defined in the Exchange Act. However, we are not required to reflect the change in our smaller reporting company status and comply with the associated increased disclosure obligations, until our first quarterly report in our next fiscal year (i.e., the quarterly report for the three-month period ending March 31, 2024).

As a large accelerated filer, we will be subject to certain disclosure and compliance requirements that apply to other public companies. These requirements include, but are not limited to:

- the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act of 2002;
- compliance 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; and
- the requirement that we provide full and more detailed disclosures regarding executive compensation.

Compliance with the additional requirements of being a large accelerated filer may increase our legal and financial compliance costs and may cause management and other personnel to divert attention from operational and other business matters to devote increased time to public company reporting requirements. In addition, if we are not able to comply with the changing requirements in a timely manner, the market price of our ADSs could decline, and we could be subject to sanctioning or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

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

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. Our management is required to assess the effectiveness of our controls over financial reporting annually. Pursuant to Section 404, we are also required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm at such time when we are no longer a smaller reporting company. Any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ADSs.

***Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.***

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, 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. 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 or insufficient disclosures due to error or fraud may occur and not be detected.

***We could be subject to securities class action litigation.***

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

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

The trading market for our ADSs depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. Although we have obtained research coverage from certain analysts, there can be no assurance that analysts will continue to cover us or provide favorable coverage. If one or more analysts downgrade our ADSs or change their opinion of our ADSs, our ADS price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our ADS price or trading volume to decline.

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

Not Applicable.

**Item 3. Defaults Upon Senior Securities.**

Not Applicable.

**Item 4. Mine Safety Disclosures.**

Not Applicable.

**Item 5. Other Information.**

Not Applicable.

**Item 6. Exhibits.**

<u>Exhibit Number</u>	<u>Description</u>
3.1	<a href="#">Articles of Association (incorporated by reference to Exhibit 3.2 to Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).</a>
10.1*+	<a href="#">Amendment No.1 to Service Agreement, dated July 24, 2023, by and between BicycleTx Limited and Kevin Lee.</a>
31.1*	<a href="#">Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>
31.2*	<a href="#">Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</a>
32.1#	<a href="#">Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</a>
101.INS	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File – the cover page XBRL tags are embedded within the Inline XBRL document (included in Exhibit 101)

---

\* Filed herewith.

+ Indicates a management contract or compensatory plan.

# The certification attached as Exhibit 32.1 accompanying this Quarterly Report on Form 10-Q is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Quarterly Report on Form 10-Q, irrespective of any general incorporation language contained in such filing.



**AMENDMENT NO. 1 TO SERVICE AGREEMENT**

This Amendment No. 1 (“**Amendment No. 1**”) to Service Agreement, dated 26 September 2019, between BicycleTX Limited (the “**Company**”) and Dr Kevin Lee (“**you**”) (the “**Service Agreement**”), is entered into by the Company and you (collectively the “**Parties**”), to amend certain terms of the Service Agreement, as agreed by the Parties.

**Amendments to Clause 11 of the Service Agreement:**

1. Clause 11.8(a)(i) will be deleted and replaced with:

the Company shall: pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the sum of (A) 2 times your annual salary as of the Termination Date (or your annual salary in effect immediately prior to the Change in Control, if higher) plus (B) 1.5 times your target annual performance bonus amount under the Annual Bonus Plan for the then-current year (the “Change in Control Payment”), which payment shall not be reduced by either the value of any salary paid to you during your notice period or by the value of any payment made to you in lieu of notice pursuant to paragraph 11.2; and

2. Clause 11.8(a)(ii) will be deleted and replaced with:

the Company shall: pay you (or your authorised representative or estate if the termination is due to your death) an amount equal to the cost to the Company of providing you with the contractual benefits under paragraph 5 for twenty-four (24) months or, at the Company’s option, continue to provide you with such benefits for twenty-four (24) months; and

The Parties agree that they have voluntarily entered into this Amendment No. 1.

AGREED on 24\_\_ July 2023.

Executed and delivered as a Deed  
by **BICYCLETX LIMITED** acting by  
Mirza Zafar Qadir as a director:

/s/Mirza Zafar Qadir\_\_\_\_\_  
Signature

on the:24\_day of July 2023

in the presence of:

/s/ Amanda Dalton\_\_\_\_\_  
Witness Signature

Witness Name: Amanda Dalton  
Witness Address:

Executed and delivered as a Deed by  
**KEVIN LEE:**

/s/ Kevin Lee\_\_\_\_\_  
Signature

on the: 20 day of July 2023

in the presence of:

/s/ Amanda Dalton\_\_\_\_\_  
Witness Signature

Witness Name: Amanda Dalton  
Witness Address:

**Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Kevin Lee, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Bicycle Therapeutics plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2023

By: /s/ Kevin Lee

Kevin Lee, Ph.D., MBA  
Chief Executive Officer  
(Principal Executive Officer)

---

**Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Alethia Young, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Bicycle Therapeutics plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2023

By: /s/ Alethia Young  
Alethia Young  
Chief Financial Officer  
(Principal Financial Officer)

---

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

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Kevin Lee, Chief Executive Officer of Bicycle Therapeutics plc (the "Company"), and Alethia Young, Chief Financial Officer of the Company, each hereby certifies that, to the best of their knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2023, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and
2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: November 2, 2023

By: /s/ Kevin Lee

\_\_\_\_\_  
**Kevin Lee, Ph.D., MBA**  
**Chief Executive Officer**

By: /s/ Alethia Young

\_\_\_\_\_  
**Alethia Young**  
**Chief Financial Officer**

*This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Bicycle Therapeutics plc under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.*

---