Bicycle Therapeutics plc

Annual Report and financial statements for the year ended 31 December 2021

Company No: 11036004

Bicycle Therapeutics plc

Annual report and financial statements
for the year ended 31 December 2021

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Bicycle Therapeutics plc
year ended 31 December 2021

General Information

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Bicycle Therapeutics plc
year ended 31 December 2021

Strategic Report

Introduction

Bicycle Therapeutics plc (the "Parent Company") on behalf of itself and its subsidiaries, BicycleTx Limited, BicycleRD Limited and Bicycle Therapeutics Inc. (which together may be referred to as the "Company", "Bicycle", "we", "us" or "our"), is required to produce a strategic report complying with the requirements of the Companies Act 2006 (Strategic Report and Directors' Report) Regulations 2013 (the "Regulations") for the year ended 31 December 2021. Bicycle also filed with the U.S. Securities and Exchange Commission (the "SEC") its Annual Report on Form 10-K for the year ended 31 December 2021 (the "Form 10-K"), which contains additional disclosures regarding some of the matters discussed in this report.

Principal activities

The Company carries out research and development activities developing novel bicyclic peptides both in Cambridge, UK and Lexington, Massachusetts, U.S.A.

Since 28 May 2019 the Parent Company has had American Depositary Shares representing its ordinary shares ("ADSs") traded on The Nasdaq Stock Market ("NASDAQ") in the U.S.

Business 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 stabilise 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, which we believe together support a favourable toxicological profile.

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" cyclisation 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 optimisation 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 BT5528, BT8009 and BT1718, are each a *Bicycle*® Toxin Conjugate, or BTC™. These *Bicycles* are chemically attached to a toxin that when administered is cleaved from the *Bicycle* and kills the tumour cells. We are evaluating BT5528, a second-generation BTC targeting Ephrin type A receptor 2, or EphA2, in a company-sponsored Phase I/II clinical trial and BT8009, a second-generation BTC targeting Nectin-4, in a company-sponsored Phase I/II clinical trial. In addition, BT1718 is being developed to target tumours 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 product candidates BT7480 and BT7455, are each a *Bicycle* tumour-targeted immune cell agonist®, or *Bicycle* TICA™. A *Bicycle* TICA links immune cell receptor binding *Bicycles* to tumour antigen binding

Bicycles. We are evaluating BT7480, a *Bicycle* TICA targeting Nectin-4 and agonising CD137, in a company-sponsored Phase I/II clinical trial, and IND-enabling studies for BT7455, an EphA2/CD137 *Bicycle* TICA, are ongoing. Our discovery pipeline in oncology, includes *Bicycle*-based systemic immune cell agonists and *Bicycle* TICAs.

Beyond our wholly owned oncology portfolio, we are collaborating with biopharmaceutical companies and organisations in additional therapeutic areas in which we believe our proprietary *Bicycle* screening platform can identify therapies to treat diseases with significant unmet medical need. Our partnered programs include collaborations in immuno-oncology, or IO, anti-infective, cardiovascular, ophthalmology, dementia, central nervous system, neuromuscular and respiratory indications.

The following table summarises key information about our programs:

Target / Product	Partner / Sponsor	Indication	Modality	Pre-clinical	IND-enabling	Phase I	Phase II
Internal programs							
BT5528 (EphA2)		Oncology	Bicycle® Toxin Conjugate				
BT8009 (Nectin-4)		Oncology	Bicycle® Toxin Conjugate				
BT7480 (Nectin-4/CD137)		Immuno-oncology	Bicycle TICA™				
BT7455 (EphA2/CD137)		Immuno-oncology	Bicycle TICA™				
Partnered programs							
THR-149 (Kallikrein inhibitor Bicycle)	OXURION	Ophthalmology					
BT1718 (MT1-MMP)	CANCER RESEARCH UK	Oncology	Bicycle® Toxin Conjugate				
BT7401 (multivalent CD137 systemic agonist)	CANCER RESEARCH UK	Immuno-oncology					

We were founded in 2009 based on innovative science conducted by Sir Greg Winter and Professor Christian Heinis. Sir Greg Winter is a pioneer in monoclonal antibodies and, in 2018, was awarded a Nobel Prize in chemistry for the invention of the technology underpinning our proprietary phage display screening platform that we use to identify *Bicycles*. From our founding through 31 December 2021, we have generated substantial intellectual property, including four patent families directed to novel scaffolds, 15 patent families directed to our platform technology, 88 patent families directed to bicyclic peptides and related conjugates, and 15 patent families directed to methods of making or using certain bicyclic peptide conjugates for treating various indications. As of 31 December 2021, our trademark portfolio consisted of 46 trademark registrations across 4 territories (the United Kingdom, European Union, United States and Japan) as well as a number of pending applications for new trademarks. The work we have conducted in developing *Bicycles* and our proprietary screening platform have created substantial know-how that we believe provides us with a competitive advantage.

Our management team includes veteran executives in drug development from leading biopharmaceutical companies including Amgen, AstraZeneca, GlaxoSmithKline, Merck, Novartis, Pfizer and Takeda. Our board of directors and scientific advisory board include industry experts with extensive experience in drug development.

Our Strategy

Our mission is to become a leading biopharmaceutical company by pioneering *Bicycles* as a novel therapeutic modality to treat diseases that are inadequately addressed with existing treatment modalities. Specifically, we seek to execute on the following strategy to maximise the value of our novel technology and pipeline:

- *Progress our most advanced internal candidates, BT5528, BT8009, and BT7480 through clinical development.* We are evaluating BT5528, a second-generation BTC targeting EphA2, in a company-sponsored Phase I/II clinical trial, BT8009, a second-generation BTC targeting Nectin-4, in a company-sponsored Phase I/II clinical trial, and BT7480, a *Bicycle* TICA targeting Nectin-4 and agonising CD137, in a company-sponsored Phase I/II clinical trial. We intend to advance development of these candidates across oncology indications based on target expression.
- *Continue IND-enabling activities for BT7455.* BT7455 is a fully synthetic *Bicycle* TICA that contains a *Bicycle* targeting EphA2 and a *Bicycle* targeting the costimulatory receptor CD137. BT7455 has been shown in preclinical models to rapidly penetrate tumours, demonstrate anti-tumour activity, and induce immune memory specific to the implanted tumour. IND-enabling activities are ongoing.
- *Pursue clinical development of our discovery programs.* We intend to continue our ongoing discovery activities to screen and select promising candidates for oncology indications. For example, early I-O discovery efforts have resulted in the identification of *Bicycle* TICA candidates targeting natural killer, or NK, cells. We are also developing third generation BTCs. We are currently advancing these programs into lead optimisation.
- *Leverage our powerful proprietary screening platform and novel* Bicycle *modality to grow our pipeline.* Our novel and proprietary phage display screening platform allows us to rapidly and efficiently identify potential candidates for development. We can incorporate a wide range of small molecule scaffolds into *Bicycles* to increase diversity and confer differentiated physicochemical and structural properties. We have used our powerful *Bicycle* screening platform to identify our current pipeline of promising BTCs and TICAs, and we intend to use it to develop a broader pipeline of diverse product candidates.
- *Collaborate strategically with leading organisations to access enabling technology and expertise in order to expand the application of our novel* Bicycle *modality to indications beyond oncology.* We are collaborating with leading biopharmaceutical companies and organisations to apply our novel *Bicycle* modality to other disease areas, including, anti-infective, cardiovascular, ophthalmology, dementia, central nervous system, neuromuscular and respiratory indications. We may opportunistically enter into additional collaborations in the future to apply our technology to areas of unmet medical need.
- *Maximise the commercial potential of our product candidates, if approved, by either establishing our own sales and marketing infrastructure or doing so through collaborations with others.* Subject to receiving marketing approval, we intend to pursue the commercialisation of our product candidates either by building internal sales and marketing capabilities or doing so through opportunistic collaborations with others.

Our Collaborations

We have entered into several collaborations, predominantly focused on indications beyond our internal focus in oncology to leverage the broad applicability of *Bicycles*. Our strategic collaborations are based on the ability of *Bicycles* to address a wide variety of targets and we are working with collaborators with deep therapeutic expertise outside of oncology to enable us to more efficiently develop novel medicines for patients.

Ionis

On 31 December 2020, we entered into an evaluation and option agreement, or the Evaluation and Option Agreement, with Ionis Pharmaceuticals, Inc., or Ionis, pursuant to which Ionis had the option, or the Ionis Option, to obtain an exclusive license to our intellectual property for the purpose of continued

research, development, manufacture and commercialisation of products within a particular application of the Company's platform technology. Ionis paid a non-refundable $3.0 million payment that was fully creditable against the upfront payment to be paid upon the execution of a license agreement.

On 9 July 2021, we and Ionis entered into a collaboration and license agreement, or the Ionis Collaboration Agreement, following the exercise on 9 July 2021 by Ionis of the Ionis Option. Pursuant to the Ionis Collaboration Agreement, we granted to Ionis a worldwide exclusive license under our relevant technology to research, develop, manufacture and commercialise products incorporating *Bicycle* peptides directed to the protein coded by the gene TFRC1 (transferrin receptor), or 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, we have 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 optimisation 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 commercialisation activities. We 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 we are responsible for performing, we may use the assistance of a contract research organisation, or CRO. We have 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, or JSC with an equal number of representatives from us 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 us 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, or 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, we are also eligible to receive up to a low double-digit million dollar amount in cumulative sales milestone payments. We are 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.

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.

Concurrently with the execution of the Ionis Collaboration Agreement on 9 July 2021, we entered into a share purchase agreement, or the Ionis Share Purchase Agreement, with Ionis, pursuant to which Ionis purchased 282,485 of our ordinary shares, at a price per share of $38.94, for an aggregate purchase price of approximately $11.0 million. Pursuant to the terms of the Ionis Share Purchase Agreement, Ionis has agreed not to, without our prior written consent and subject to certain conditions and exceptions, among other things, directly or indirectly acquire additional shares of our outstanding equity securities, seek or propose a tender or exchange offer, merger or other business combination involving us, solicit proxies or consents with respect to any matter, or undertake other specified actions related to the potential acquisition of additional equity interests in us, collectively, the Standstill Restrictions. The Standstill Restrictions will expire on the 18-month anniversary of the Ionis Share Purchase Agreement.

The Ionis Share Purchase Agreement also provides that, subject to limited exceptions, Ionis will hold and not sell any of the Ionis Shares until the earlier of (i) the first anniversary of the closing of the sale of the shares under the Ionis Share Purchase Agreement, or the first anniversary of the closing of the sale of the shares under the Ionis Share Purchase Agreement (the "Closing Date"), and (ii) the termination of the Ionis Collaboration Agreement pursuant to its terms (provided, however, that in the event the termination of the Ionis Collaboration Agreement occurs less than six months after the Closing Date, Ionis shall hold and will not sell or otherwise enter into a transaction regarding the Ionis Shares until at least the date that is six months after the Closing Date).

Genentech

On 21 February 2020, we entered into a Discovery Collaboration and License Agreement with Genentech, or 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 I-O targets suitable for Genentech to advance into further development and commercialisation.

Under the terms of the Genentech Collaboration Agreement, we received a $30.0 million upfront, non-refundable payment. The initial discovery and optimisation activities are focused on utilising our phage screening technology to identify product candidates aimed at two I-O targets, or Genentech Collaboration Programs, which may also include additional discovery and optimisation of *Bicycles* as a targeting element for each Genentech Collaboration Program, or each a Targeting Arm. Genentech has the option to nominate up to two additional I-O targets, or each an Expansion Option, which may also include an additional Targeting Arm for each Expansion Option, as additional Genentech Collaboration Programs during a specified period following completion of certain activities under an agreed research plan. If Genentech exercises one or more Expansion Options, Genentech will pay us an expansion fee of $10.0 million per 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 us to perform discovery and optimisation services for certain Targeting Arms, we 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, which entitled us to an additional $1.0 million payment. 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.

In October 2021, Genentech exercised an Expansion Option to add an additional Genentech Collaboration Program and paid to us an expansion fee of $10.0 million during the year ended December 31, 2021. Genentech also elected for us to perform discovery and optimisation services for a Targeting Arm, and we are entitled to receive an additional payment of $1.0 million for additional research services.

We granted to Genentech a non-exclusive research license under our 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, or JRC, with representatives from each of Bicycle 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 we perform the initial discovery and optimisation activities in accordance with an agreed research plan and achieves specified criteria, Genentech will have the option to have us perform initial pre-clinical development and optimisation activities in exchange for an additional specified milestone payment in the mid-single digit millions for each Genentech Collaboration Program, or the LSR Go Option. Upon completion of such initial pre-clinical development and optimisation 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, or the Dev Go Option.

On a Genentech Collaboration Program by Genentech Collaboration Program basis, if Genentech elects to obtain exclusive development and commercialisation rights and pays the applicable LSR Go Option and Dev Go Option fees, Genentech will be required to make milestone payments to us upon the achievement of specified development, regulatory, and initial commercialisation milestones for products arising from each collaboration program, totalling up to $200.0 million. Specifically, we are eligible for additional development milestones totalling up to $65.0 million, as well as regulatory milestones of up to $135.0 million for each collaboration program. In addition, we are 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 commercialised, we 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.

Dementia Discovery Fund

In May 2019, we entered into a collaboration with the Dementia Discovery Fund, or DDF, to use *Bicycle* technology for the discovery and development of novel therapeutics for dementia. DDF is a specialised venture capital fund focused on discovering and developing novel therapies for dementia. In October 2019, the collaboration with DDF was expanded to include Oxford University's Oxford Drug Discovery Institute (ODDI). Under the terms of the agreement, Bicycle and DDF will collaborate to identify *Bicycles* that bind to clinically validated dementia targets. ODDI will then profile these *Bicycles* in a range of target-specific and disease-focused assays to assess their therapeutic potential. If promising lead compounds are identified, DDF, ODDI and Bicycle will establish a jointly-owned new company to advance the compounds through further development towards commercialisation. The jointly-owned company will receive a royalty and milestone-bearing assignment and license of intellectual property from Bicycle for this purpose.

Cancer Research UK

BT1718

In December 2016, we entered into a clinical trial and license agreement with Cancer Research UK and Cancer Research Technology Ltd., a wholly owned subsidiary of Cancer Research UK that Cancer Research

UK's commercial activities operate through, or the Cancer Research UK Agreement. Pursuant to the agreement, as amended in March 2017 and June 2018, Cancer Research UK Centre for Drug Development will sponsor and fund a Phase I/IIa clinical trial of our product candidate, BT1718, in patients with advanced solid tumours.

Cancer Research UK is responsible for designing, preparing, carrying out and sponsoring the clinical trial at its cost. We are responsible for supplying agreed quantities of GMP materials for the study, the supply of which has been completed. In the event that additional quantities are needed, we 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.

We granted to Cancer Research UK a license to our intellectual property in order to design, prepare for, sponsor, and carry out the clinical trial. We retain the right to continue the development of BT1718 during the clinical trial. Upon the completion of the Phase I/IIa clinical study, 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, Cancer Research Technology Limited may elect to receive an assignment and exclusive license to develop and commercialise 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) less certain costs, as defined by 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, 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 terminate the arrangement for safety reasons or if it determines that the objectives of the clinical trial will not be met. We were 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, us 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 we are 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, we 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 us in respect of the results of the clinical trial and we will assign or grant to CRTL an exclusive license to develop and commercialise the product without CRTL being required to make any payment to us.

BT7401

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

We granted to Cancer Research UK a license to our intellectual property in order for Cancer Research UK to design, prepare for, sponsor, and carry out the clinical trial and all necessary preclinical activities to

support the trial. We retain the right to continue the development of BT7401 during the clinical trial. Upon the completion of the Phase I/IIa clinical study, 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 contain BT7401 or all the pharmaceutically active parts of BT7401, we will assign or grant to Cancer Research Technology Limited an exclusive license to develop and commercialise the product on a revenue sharing basis (in which case we 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 in 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 generates its revenue from the sale of tobacco products), or upon written notice by either party prior to the last cycle of treatment has been completed under the clinical trial. If the study is terminated by us prior to the filing of a clinical trial authorisation, or by Cancer Research UK for an insolvency event or a material breach by us prior to the start of a clinical trial, we will reimburse Cancer Research UK for certain costs paid or committed prior to the start of the clinical trial. In such case where we are acquired by an entity that generates its revenue from the sale of tobacco products, Cancer Research UK will not be obliged to grant a license to us in respect of the results of the clinical trial and we will assign or grant to Cancer Research Technology Limited an exclusive license to develop and commercialise the product without Cancer Research Technology Limited being required to make any payment to us.

AstraZeneca

In November 2016, we entered into a research collaboration agreement with AstraZeneca AB, or the AstraZeneca Collaboration Agreement. The collaboration is focused on the research and development of *Bicycle* peptides that bind to an undisclosed number of biological targets for the treatment of respiratory, cardiovascular and metabolic diseases. After discovery and initial optimisation of such *Bicycle* peptides, AstraZeneca will be responsible for all research and development, including lead optimisation and drug candidate selection. AstraZeneca receives development, commercialisation and manufacturing license rights with regard to any selected drug candidate(s).

Under the AstraZeneca Collaboration Agreement, Bicycle performed research activities, under mutually agreed upon research plans. The research plans include two discrete parts, on a research program by research program basis: (i) the Bicycle Research Term, which is focused on the generation of Bicycle peptide libraries using our peptide drug discovery platform, to be screened against selected biological targets, with the goal of identifying compounds that meet agreed criteria set by the parties, and (ii) the AZ Research Term, during which AstraZeneca may continue research activities with the goal of identifying compounds that satisfy the relevant pharmacological and pharmaceutical criteria for clinical testing. Each research program is to continue for an initial period of three years, referred to as the research term, including one year for the Bicycle Research Term and two for the AZ Research Term. AstraZeneca may extend the research term for each research program by twelve months (or fifteen months, if needed to complete certain toxicology studies). The research term for a specific program can be shorter if it is ceased due to a screening failure, a futility determination, or abandonment by AstraZeneca.

Under the terms of the AstraZeneca Collaboration Agreement, we granted to AstraZeneca the right and license (with the right to sublicense) to certain background, foreground and platform intellectual

property, for the duration of the agreement, to the extent reasonably necessary or useful for AstraZeneca to conduct the activities that are assigned to it in the applicable research plan or that are reasonably necessary or useful or the purpose of researching, developing or exploiting resulting compounds and products. We have agreed not to, directly or indirectly, by ourselves or in collaboration with others, screen the Bicycle platform for compounds that bind to a target that is the subject of the AstraZeneca collaboration or otherwise perform any work related to or disclose such a target until the earlier of the tenth anniversary of the date on which such target was selected or the dosing of the first patient in the first Phase III clinical trial for a product that modulates such collaboration target.

AstraZeneca receives development and commercialisation licenses associated with each designated drug candidate, and owes a milestone fee of $8.0 million for the first drug candidate selected from each research program. In addition, AstraZeneca is required to make certain other milestone payments to us upon the achievement of specified development, regulatory and commercial milestones. For each research program, we are eligible to receive, in addition to the milestone fee described above, up to $162.0 million in development, regulatory and commercial milestones on a research program by research program basis, for a total of up to $170.0 million in milestone payments per research program. In addition, to the extent any of the drug candidates covered by the licenses conveyed to AstraZeneca are commercialised, we would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Royalty payments are subject to certain reductions, including in certain countries where AstraZeneca faces generic competition.

Either party may terminate the AstraZeneca Collaboration Agreement if the other party has materially breached or defaulted in the performance of any of its material obligations and such breach or default continues after the specified cure period. In the event of a breach, the AstraZeneca Collaboration Agreement may be terminated in its entirety, or, if the breach is limited to a country or countries, with respect to the country or countries to which the breach applies. Either party may terminate the AstraZeneca Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party that is not dismissed or otherwise disposed of within a specified time period. AstraZeneca may terminate the AstraZeneca Collaboration Agreement, entirely or on a licensed product by licensed product or country by country basis, for convenience.

Under the AstraZeneca Collaboration Agreement, AstraZeneca was granted an option to nominate additional targets on the same contractual terms as the initial targets. In May 2018, AstraZeneca made an irrevocable election to exercise the additional target option, giving AstraZeneca the option to designate additional targets, for $5.0 million that was paid by AstraZeneca to us in January 2019. As of 31 December 2021, two research program are in the AZ Research Term, and the remainder of the AstraZeneca collaboration programs have been terminated.

Oxurion

In August 2013, we entered into a research collaboration and license agreement, or the Oxurion Collaboration Agreement, with Oxurion NV, or Oxurion, which agreement was amended in November 2017. Under the Oxurion Collaboration Agreement, we were responsible for identifying *Bicycle* peptides related to the collaboration target, human plasma kallikrein, for use in various ophthalmic indications. Oxurion is responsible for further development and product commercialisation after the defined research screening is performed by us. THR-149 was selected as a development compound under the Oxurion collaboration agreement. We granted certain worldwide intellectual property rights to Oxurion for the development, manufacture and commercialisation of licensed compounds associated with plasma kallikrein. The Oxurion collaboration agreement provides for certain milestone payments to us upon the achievement of specified research, development, regulatory and commercial milestones. More specifically, for each collaboration compound, we are eligible to receive up to €8.3 million in research and development milestone payments, from which we have received €3.8 million as of 31 December 2021, in connection with the development of THR-149, and up to €16.5 million in regulatory milestone payments (e.g., €5 million for granting of first

regulatory approval in either the United States or the European Union for the first indication). In addition, to the extent any of the collaboration products covered by the licenses granted to Oxurion are commercialised, we would be entitled to receive tiered royalty payments of mid-single digits based on a percentage of net sales. Royalty payments are subject to certain reductions. Also, if Oxurion grants a sublicense to a third party for rights to the program for non-ophthalmic use prior to the filing of an IND, we would be entitled to receive payments in the double digits (no higher than first quartile) based on a percentage of non-royalty sublicensing income. If Oxurion grants a sublicense to a third party for rights to the program for non-opthalmic use after the filing of an IND, we would be entitled to receive payments of mid-single digits to low teen-digits.

Either party may terminate the Oxurion Collaboration Agreement if the other party has breached any of its material obligations and such breach continues after the specified cure period. Either party may terminate the Oxurion Collaboration Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other party. Oxurion may terminate the Oxurion Collaboration Agreement for convenience. We may terminate the Oxurion Collaboration Agreement if Oxurion challenges the validity of any licensed patents or opposes the grant of a licensed patent.

Founder Royalty Arrangements

We have entered into two royalty agreements with our founders, Christian Heinis, John Tite, and Sir Greg Winter, and our initial investors, Atlas Venture Fund VIII LP, Novartis Bioventures LTD. Pursuant to the first royalty agreement, we are obligated to pay an aggregate royalty percentage in the low single digits on net sales arising from products licensed under the Oxurion collaboration agreement. Pursuant to the second royalty agreement, we are obligated to pay an aggregate royalty percentage in the low single digits on net sales arising from products licensed under the AstraZeneca collaboration agreement.

Review of business performance and future developments

Since our inception, we have devoted substantially all of our resources to developing our *Bicycle* platform and our product candidates, BT5528, BT8009, 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 American Depositary Shares, or ADSs, ordinary shares, and convertible preferred shares, proceeds received from upfront payments, research and development payments, and development milestone payments from our collaboration agreements with 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 debt facility with Hercules Capital, Inc., or Hercules. From our inception in 2009 through 31 December 2021, we have received gross proceeds of $557.6 million from the sale of ADSs, ordinary shares and convertible preferred shares, including the proceeds from our initial public offering, follow-on offering and at-the-market, or ATM, offering program; and $124.2 million of cash payments under our collaboration revenue arrangements, including $46.6 million from Ionis, $43.0 million from Genentech, $1.7 million from DDF, $10.3 million from AstraZeneca, $15.0 million from Sanofi, $6.6 million from Oxurion; and borrowings of $30.0 million pursuant to our Loan and Security Agreement, or 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 commercialisation of one or more of our product candidates. Our net losses for the year ended 31 December 2021 were $77.3 million (31 December 2020: $50.4 million) and we had net assets at book value of $346.1 million (31 December 2020: $100.5 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 commercialisation 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 BT5528, BT8009, 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, any future commercialisation efforts and our operations as a public company.

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 utilise third-party contract research organisations, or CROs, to carry out many of 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 commercialisation 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, monetisation transactions or licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favourable 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 commercialisation of one or more of our product candidates. The ongoing COVID-19 pandemic has already resulted in a significant disruption of global financial markets. If the disruption persists

and deepens, whether as a result of the ongoing COVID-19 pandemic or otherwise, we could experience an inability to access additional capital.

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.

Our cash balance as at 31 December 2021 was $438.7 million (31 December 2020: $136.0 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 approval of these financial statements.

Key performance indicators ('KPIs')

We do not consider traditional financial measures to be key performance indicators at this stage of development of our business. However, management closely monitors our cash position and our research and development expenses. In addition, we assess our performance through the clinical advancement of our programs. During the year ended 31 December 2021 we achieved significant advancement of our clinical pipeline: BT8009 and BT5528 demonstrated anti-tumour activity in two tumour types, and we initiated a clinical trial of BT7480 in the fourth quarter of 2021. We also executed a successful partnering strategy including entering into a strategic collaboration agreement with Ionis in July 2021 and the expansion of our collaboration agreement with Genentech. We also raised significant funds including net proceeds of $188.4 million from a public offering of Bicycle's ADSs, net proceeds of $102.6 million from our at-the-market (ATM) offering program, and $15.0 million from our debt facility with Hercules Capital. All of this was in the context of the ongoing COVID-19 pandemic.

Financial risk management

The directors have concluded that the management of price risk and liquidity risk are not material for the assessment of the assets, liabilities, financial position and loss of the Company.

Currency risk

The Company raises funds in U.S. dollars, and pays for goods and services in a variety of currencies but mainly the British pound sterling and U.S. dollar. The Company mitigates this risk by also holding cash in these two currencies. The Company does not use derivatives to manage this risk.

Cash flow

The Company finances its operations primarily with proceeds from the sale of our ADSs, proceeds received from upfront payments, research and development payments, and development milestone payments from our collaboration agreements and borrowings pursuant to our debt facility with Hercules. The Board monitors the level of cash and cash equivalents on a regular basis and cash is placed in deposit accounts to earn a return whilst enabling the cash to be available to meet the Company's day to day needs.

Credit Risk

The Company has receivables and cash from both its operating and financing activities. The Company ensures that invoices are raised when performance conditions are met and that the payment terms with the customer are adhered to. Cash is maintained in accounts of reputable financial institutions with high quality credit ratings.

Interest risk

The Company's outstanding indebtedness with Hercules bears interest at the greater of 8.85%, or 5.60% plus the Wall Street Journal prime rate. As of 31 December 2021, our outstanding indebtedness with Hercules bears interest at 8.85%. If the Wall Street Journal prime rate increases to over 3.25%, the interest on our loan with Hercules will increase. We currently do not engage in any interest rate hedging activity, and we have no intention to do so in the foreseeable future.

Environmental matters

The Company's activities have a minimal environmental impact. The Company complies with all applicable environmental laws and regulations and currently does not consider it has a significant environmental footprint due to the size and nature of its operations. It does not have an internal manufacturing facility.

Following listing of the Parent Company's ADSs on NASDAQ in May 2019, the Company is required under English law to measure and report its greenhouse gas emissions in accordance with the provisions of the Regulations. The sources of emissions relate solely to the electricity and gas purchased by our premises in the UK and U.S., the costs of which are included within these consolidated financial statements. Management has used the most recent evidence or estimates provided by its energy suppliers to generate the disclosure of emissions. These include the purchase of electricity, heat, steam or cooling. Standard emissions factors from Defra's GHG Conversion Factor Repository were applied to estimate emissions. The Company considers that the intensity ratio of tonnes of carbon dioxide per full-time equivalent employee is a suitable metric for its operations. The annual quantity of emissions for the Company for the year ending 31 December 2021 was 383 tonnes (31 December 2020: 531 tonnes) with an intensity ratio of 3.8 tonnes (31 December 2020: 6.7 tonnes) based on the average number of employees in the year of 101 (31 December 2020: 79), as determined based on our electricity and gas consumption provided by our suppliers as converted to emissions by publicly available emission converters. Approximately 55% (31 December 2020: 55%) of these emissions were in the UK. The Company, in preparing these details, considers ways to minimise indirect areas of emissions and where practical enables remote working and also promotes online conferencing facilities to reduce business travel. For all of 2021 significant numbers of employees who are not laboratory based were working substantially from home.

Employee, social, community and human rights matters

The Company places considerable value on the involvement of its employees. Regular meetings are held with employees to discuss the operations and progress of the business and employees are encouraged to become involved in the success of the Company through share option schemes (see note 11 to the financial statements).

We consider a number of measures and objectives in this area, including, among others, employee engagement, development, and training, talent acquisition and retention, employee safety and wellness, diversity and inclusion, and compensation and pay equity. We provide our employees with salaries and bonuses intended to be competitive for our industry and geographic locations, opportunities for equity ownership, development programs that enable continued learning and growth and a robust benefits package to promote well-being across all aspects of their lives, including health care, retirement planning and paid time off. In addition, we have conducted employee surveys to gauge employee engagement and identify areas of future focus for our human capital practices and benefits offerings.

The Company maintains and operates pursuant to a Code of Conduct and Business Ethics. This sets out the Company's approach to ensure that our corporate values are maintained throughout our global business. The Company also has an anti-corruption and anti-bribery policy. The Code of Conduct and

Business Ethics, anti-corruption and anti-bribery policies apply to all employees of the Company and certain designated consultants, who are required to comply with this policy.

The Company endeavours to impact positively on the community in which it operates. The Company does not, at present, have a specific policy on human rights. However, we have several policies that promote the principles of human rights. We will respect the human rights of all our employees, including:

- provision of a safe, clean working environment;
- ensuring employees are free from discrimination and coercion;
- not using child or forced labour; and
- respecting the rights of privacy and protecting access and use of employee personal information.

We also have a policy on equal opportunities and on anti-bullying and harassment.

The Company is fully committed to the elimination of unlawful and unfair discrimination and values the differences that a diverse workforce brings to the organisation. The Company endeavours to not discriminate because of age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race (which includes colour, nationality and ethnic or national origins), religion or belief, sex or sexual orientation.

We believe a diverse workforce is critical to our success and we are fundamentally committed to creating and maintaining a work environment in which employees are treated fairly, with dignity, decency, respect and in accordance with all applicable laws. We understand that varied perspectives lead to the best ideas and outcomes. We believe that by creating a workplace where every individual can feel welcome and valued, we will better able to achieve our corporate objectives. All employees must adhere to a code of business conduct and ethics and our employee handbook, which combined, define standards for appropriate behaviour and are annually trained to help prevent, identify, report, and stop any type of discrimination and harassment.

In 2021, we formed a cross-functional Diversity, Equity, and Inclusion ("DEI") task force. The task force is assessing key DEI metrics and benchmarks and is exploring developing a DEI roadmap.

Employee gender diversity

Our recruitment, hiring, development, training, compensation, and advancement is based on qualifications, performance, skills, and experience. While acknowledging the benefits of diversity, individual appointments are made irrespective of personal characteristics such as race, ethnicity, disability, gender, sexual orientation, religion, or age. A breakdown of employment statistics as of 31 December 2021 and 2020 is as follows:

31 December 2020 (Number of Directors and Employees)

Position	Male	Female	Total
Directors	4	3	7
C-Band	5	0	5
Vice President/Director	12	4	16
Other Employees	19	46	65
Total Directors and Employees	40	53	93

31 December 2021 (Number of Directors and Employees)

Position	Male	Female	Total
Directors	5	2	7
C-Band	5	0	5
Vice President/Director	21	9	30
Other Employees	34	49	83
Total Directors and Employees	65	60	125

Notes: Directors are directors of the Parent Company; C-Band includes the Chief Financial Officer, Chief Scientific Officer, Chief Business Officer, Chief Operating Officer and Chief Medical Officer. In both 2020 and 2021, the Chief Executive Officer was a director of the Parent Company and, accordingly, was included in the directors totals above.

Principal risks and uncertainties

Financial

We are a clinical-stage biopharmaceutical company. We have not commercialised any products or generated any revenues from the sale of products, and absent the realisation of sufficient revenues from product sales, we may never attain profitability in the future. We have a history of significant operating losses (year ended 31 December 2021: $86.9 million; year ended 31 December 2020: $59.8 million) and we do not expect to generate revenue or profitability that is necessary to finance our operations in the short-term. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our ability to become and remain profitable depends on our ability to generate revenue. Generating product revenue will depend on our or our collaborators' ability to obtain marketing approval for, and successfully commercialise, one or more of our product candidates, which cannot be guaranteed. Our failure to become and remain profitable could impair our ability to raise capital, expand our business or continue our operations.

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 will be required to expend significant funds in order to advance the development of the product candidates in our pipeline, as well as any other product candidates we may seek to develop. We cannot be certain that additional funding will be available 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. There is a risk that should we fail to obtain additional funding on the terms or timescales we require, we may be required to delay, limit, reduce or terminate our product development or future commercialisation efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Clinical

Our product candidates will need to undergo preclinical and clinical trials that are time consuming and expensive and can be subject to extensive delays. We may not be able to identify, recruit and enrol a sufficient number of patients, or those with the required or desired characteristics, to complete our clinical trials in a timely manner. Our 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 and/or prevent their marketing approval and/or limit their commercial potential. 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. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in the results of completed clinical trials. Preclinical and clinical data are often susceptible to varying interpretations and analyses and there is no certainty that the results obtained in clinical trials of our existing clinical candidates will be sufficient to enable progression of those candidates through our clinical programmes or the obtaining of regulatory approval or marketing authorisation. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialisation prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects, would be negatively impacted.

Manufacturing

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 and our strategy is to outsource all manufacturing of our product candidates and products to third parties. 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 other times. 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 optimising 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. 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. Our product candidates may be delayed if we need to change the manufacturing process used by a third party, subsequently resulting in further delays from a regulatory authority reviewing the new manufacturing process before it may be used. Reliance on third party manufacturers entails risks, including the 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 agreement by the third party at a time that is costly or inconvenient to us.

Third parties

For certain product candidates, we depend, or will depend, on development and commercialisation 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. We cannot provide assurance that our collaborators will be successful or that they will devote sufficient resources to the development or commercialisation of the products. If our current or future collaboration and commercialisation partners do not perform in the manner we expect or fail to fulfil their responsibilities in a timely manner, 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 commercialisation 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.

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.

Commercialisation

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 commercialised. In addition, we are at a very early stage in our development efforts and our product candidates represent a new category of medicines and may be subject to heightened regulatory scrutiny until they are established as a therapeutic modality. Our clinical trials may not be conducted as planned or completed on schedule, if at all and, even if completed on schedule, there remains no guarantee that the results seen in any clinical trials will be sufficient to progress to the next stage of any clinical approval or ultimately to the obtaining of a marketing approval for any of our programs.

Our estimates of the potential patient population which can be treated may be inaccurate affecting the amount of revenue obtainable for any product. Likewise, the amount of revenue that can be obtained in relation to our programs may be impacted by the nature of pricing reimbursement coverage or schemes available or in place in any specific country and the continuation of such coverage and schemes. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialise our product candidates, even if approved. We currently have no marketing sales or distribution infrastructure with respect to our product candidates and we will have to establish a marketing capability prior to bringing any product candidate to market or outsource this function to a third party. Even if we are successful in obtaining regulatory approval, the commercial success of our product candidates will depend upon the degree of market acceptance by physicians, patients, payors and others in the medical community.

In addition, we face significant competition, and our competitors may develop and market products that are more effective, safer or less expensive than our product candidates, which may negatively impact our commercial opportunities.

Regulation

Our product candidates are highly regulated and the regulatory process is lengthy, time-consuming and expensive. We may experience significant delays in obtaining regulatory approval or be required to make changes to our clinical programmes or product candidates by regulatory authorities. 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. If we are successful in obtaining regulatory approvals in one country, this does not mean that we will be successful in other countries and further clinical programmes may be required to obtain required regulatory approvals in such other countries. In addition, failure to successfully validate, develop and obtain regulatory approvals for companion diagnostics could harm our drug development strategy.

Should we obtain marketing approvals for any current or future product candidates 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. Changes in regulations, statutes or the interpretation of existing regulations could also impact our business in the future. Any failure to comply with regulatory requirements at any stage in the development of our product candidates could result, among other things, in restrictions on the labelling, distribution, marketing or manufacturing of the product, suspension or withdrawal of marketing approvals and fines, restitution or disgorgement of profits or revenues. We are also subject to regulation as a company both in the UK and the U.S. including in relation to anti-bribery 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. In addition, because we have a U.S. subsidiary and substantial

operations in the U.S., we are subject to U.S. laws that regulate non-U.S. investments in U.S. businesses and access by non-U.S. persons to technology developed and produced in the U.S. We are also subject to numerous environmental, health and safety laws and regulations.

Litigation

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 from patients, healthcare providers, pharmaceutical companies and others. We believe our product liability insurance coverage is sufficient in light of our current commercial and clinical programs; however, 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.

In November 2020 the Company entered into a Settlement and License Agreement with Pepscan Systems B.V. ("Pepscan") regarding the Company's use of Pepscan's CLIPS peptide technology. The companies agreed to settle all intellectual property disputes worldwide. Under the terms of the settlement, the Company has been granted a license to use CLIPS peptide technology in the development of its product candidates BT1718 and THR-149. The Company paid €3 million upfront, paid €1 million on the first anniversary of the date of settlement in November 2021, and will make potential additional payments to Pepscan based on achievement of specified clinical, regulatory and commercial milestones

Intellectual Property

Our ability to compete effectively depends, 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. 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. Even if they are unchallenged, our patents and patent applications 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. Third parties may claim that our activities or products infringe upon their intellectual property which will adversely affect our operations and prove costly and time-consuming to defend against and could ultimately prevent or delay us from developing or commercialising our product candidates. Further, our products may infringe the intellectual property rights of others and we may be unable to secure necessary licences to enable us to continue to manufacture or sell our products. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property.

Cybersecurity

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations. We utilise information technology, systems and networks to process, transmit and store electronic information in connection with our business activities. As the use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorised access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks, the confidentiality and the availability and integrity of our data. We have been the target of a cyber-attacks in the past. For example, in 2019 we were targeted in a phishing incident, which included email accounts being accessed by unauthorised third parties. Promptly after discovery, we performed third party investigations and as there was no evidence of access or acquisition of any personal information as a result of the incident, we believe that no further action was required under UK, E.U. (GDPR) or U.S. federal or state law. There was no material impact to our business or financial condition. While we believe we responded appropriately, including implementing remedial measures to stop the cyber-attacks and with the goal of

preventing similar ones in the future, there can be no assurance that we will be successful in these remedial and preventative measures or successfully mitigating the effects of future cyber-attacks. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems.

Any cyber-attack or destruction or loss of data could have material effects on our business and prospects. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to respond appropriately to such breaches and to implement further data protection measures.

Employees

We rely on the ongoing involvement of principal members of our executive team and key employees. The loss of the services of one or more of our executive team and key employees might impede the achievement of our research, development and commercialisation objectives. Furthermore, replacing executive officers or other key employees may be difficult and may take extended 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 commercialise products successfully.

Our focus on the development of our product candidates requires us to optimise cash utilisation and to manage and operate our business in a highly efficient manner. We cannot provide assurance that we will be able to hire or retain adequate staffing levels to develop our product candidates or run our operations or to accomplish all of our objectives.

Russia and Ukraine conflict

The Company's operations have not been directly affected by the conflict between Russia and Ukraine. It does not have any significant suppliers or ongoing clinical trials based in those nations or any of the neighbouring nations.

Brexit

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to a transition period until 31 December 2020 or the Transition Period, during which European Union rules continued to apply. 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 1 May 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 may continue to have, a material impact on the regulatory regime with respect to the development, manufacture, importation, approval and commercialisation of our product candidates in the United Kingdom or the European Union. For example, Great Britain is no longer covered by the centralised procedures for obtaining European Union-wide marketing authorisation from the EMA, and a separate marketing authorisation will be required to market our product candidates in Great Britain. It is currently unclear as to whether the Medicines & Healthcare products Regulatory Agency ("MHRA") is sufficiently prepared to handle the increased volume of marketing authorisation applications that it is likely to receive. Any delay

in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercialising 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.

COVID-19

The Company has implemented work from home policies and followed government guidelines, including social distancing requirements, occupancy limitations and mask mandates arising from the ongoing COVID-19 pandemic. Whilst most of these initial restrictions have since been relaxed, new or renewed restrictions have been imposed from time to time as a result of continually evolving incidence and rates of infection. These could negatively impact productivity and disrupt our business and those of third-party manufacturers, CROs, other services providers, and collaborators with whom we conduct business. The Company continues to closely monitor the ongoing COVID-19 situation and evolves its business continuity plans and response strategy as necessary.

Section 172 Statement

This statement aligns to the section 172 statement requirements contained in section 414CZA of the Companies Act 2006 (the "Companies Act"). This statement focuses on how the directors of the Parent Company have had regard during the year to the matters set out in section 172(1)(a) to (f) of the Companies Act when performing their duties by incorporating information from other areas of the Annual Report to avoid unnecessary duplication. The Board considers that the statement focuses on those risks and opportunities that were of strategic importance to the Parent Company consistent with the size and complexity of the Company.

In the performance of its duty to promote the success of the Parent Company for the benefit of its members as a whole, the Board has regard to a number of matters, including listening to and considering the views of shareholders and holders of ADSs representing the Parent Company's ordinary shares and the Parent Company's other key stakeholders to build trust and ensure it fully understands the potential impacts of the decisions it makes for our stakeholders, the environment and the communities in which the Parent Company operates. Further details are set out below under "Stakeholder Engagement".

The Directors are aware of their duty under s172 of the Companies Act 2006 to act in the way which they consider, in good faith, would be most likely to promote the success of the Company for the benefit of its members as a whole and, in doing so, to have regard (amongst other matters) to:

- the likely consequences of any decision in the long-term;
- the interests of the Company's employees;
- the need to foster the Company's business relationships with suppliers, customers and others;
- the impact of the Company's operations on the community and the environment;
- the desirability of the Company maintaining a reputation for high standards of business conduct; and
- the need to act fairly as between members of the Company.

The governance framework within which the Board operates is set out in the corporate governance guidelines adopted by the Board, a copy of which is available in the Investors & Media section on the Company's website. In addition, the Parent Company maintains and operates pursuant to a Code of Conduct and Business Ethics which sets out the Company's approach to ensuring that our corporate values are maintained throughout our global business.

Strategic Report (continued)

The Board fosters effective stakeholder relationships in order to align with the Parent Company's strategy and is responsible for seeing meaningful engagement with stakeholders. The Board's endeavours to implement various mechanisms to enable management and the Board to understand and consider stakeholder views as part of their oversight and decision making. Throughout the year, the Directors recognised their responsibility to act in good faith to promote the success of the Parent Company for the benefit of investors, while also considering the impact of their decisions on wider stakeholders and other factors relevant to the decision being made. Clear communication and proactive engagement to understand the issues and factors which are most important to stakeholders is fundamental to this. The Board acknowledges that every decision made will not necessarily result in a positive outcome for all stakeholders. By considering our corporate values, together with our strategic priorities, the Board aims to ensure that the decisions made are consistent and intended to promote the Parent Company's long-term success.

Stakeholder Engagement

Our key stakeholders include our workforce, suppliers, lenders, investors and our wider communities. We actively engage with, and listen to, our stakeholders to understand their views, seek opportunities to learn and improve.

We are committed to effective engagement with all of our stakeholders. Our success depends on this engagement. Direct engagement by the Board with its stakeholders, where possible, enables the Directors to deepen their understanding of how the Company's purpose, values and strategy are embedded across the organisation globally. Where direct engagement is not possible, engagement takes place at the operational level, and the Directors are kept fully informed by senior management of all matters on a regular basis for use in the Board's decision-making.

Stakeholder Group	Why we engage	Engagement and influence on decision making	More information
Our Workforce	We believe that our people are our most important and valuable asset. Successful performance can be delivered only through a high level of engagement where our people share the Bicycle vision and values and feel supported by our culture and code of conduct. Maintaining a content and engaged workforce is key to attract and retain top talent.	The Board and senior management are committed to enhancing engagement with employees at all levels to ensure we communicate information on decisions taken, emerging developments, innovations and future growth of the business. The Board recognises the importance of using a variety of communication platforms and activities to maximise employee engagement. While the Board cannot directly consult with employees on all decisions it makes, it apprises itself of their opinions in a variety of ways. An example of	Strategic report – Business overview (page 2) – Our strategy (page 3) – Employee, social, community and human rights matters (page 14) – Employee gender diversity (page 15) Remuneration report – Statement from the Chair of the Compensation Committee (page 28) – Employment conditions (page 41)

Stakeholder Group	Why we engage	Engagement and influence on decision making	More information
		this includes obtaining feedback through regular employee focus groups and opinion surveys which provide the Board with honest feedback that the Board uses to inform and drive business improvements. The Board understands that any decisions it makes may impact employees' performance, engagement and work satisfaction. The Board is mindful that any decisions it makes, as well as the manner in which they are made, will inform the culture of the business. The Board seeks to lead by example in order to ensure that high standards of business conduct are maintained by its employees.	
Our Collaboration Partners	We are focused on building deep, long-term relationships with our collaboration partners which we ultimately believe is the key to the success of these partnerships.	The Company works closely with its key collaborators, including Ionis, Genentech, DDF, Astrazeneca, Oxurion, and Cancer Research UK in accordance with the terms of its agreements with them. The Board receives regular feedback from management on the progress of the collaborations and encourages the management to focus on building long term relationships with our collaboration partners.	Strategic report – Business overview (page 2) – Our strategy (page 3) – Our collaborations (page 4) – Principal risks and uncertainties (page 16)

Stakeholder Group	Why we engage	Engagement and influence on decision making	More information
		The Board is responsible for approving material business transactions and any key strategic changes. Prior to making such decisions the Board considers the potential impact on its collaboration partners.	
Our Suppliers	We recognise the importance of establishing and building strong working relationships with all our suppliers. Working sustainably, respecting human rights, and operating with the highest standards of ethical conduct and professional integrity improve long-term business performance. We are dedicated to these values and require our suppliers to share our commitment.	The Board approves and implements policies based on ethical and legal minimum standards, which it requires the business to adhere to when engaging suppliers. As we continue to progress in our size and stage of development, we intend to continue to implement procedures to ensure that our key suppliers also commit to these standards, including in relation to anti-bribery and corruption, anti-money laundering, human rights and modern slavery and various other matters. The Company engages regularly with its key business partners, including third party manufacturers and suppliers, independent clinical investigators and CROs, to ensure that they all have appropriate standards and policies in place, are financially robust and capable of delivering their services.	Strategic report – Business overview (page 2) – Our strategy (page 3) – Our collaborations (page 4) – Principal risks and uncertainties (page 16) – Manufacturing / Third Parties / Commercialisation (pages 17)

Stakeholder Group	Why we engage	Engagement and influence on decision making	More information
Our Investors	We are a public company with ADSs listed on NASDAQ. Without our investors, we cannot grow or invest for future success. We engage with existing and potential investors to ensure that we provide sufficient, meaningful and relevant information which they can use to make informed investment decisions. We strictly adhere to market regulations and regularly consult our advisors to ensure we are in compliance with such regulations at all times.	Our Board and senior management have regular interaction with investors, to understand their interests and any concerns they may have. This feeds into the Board's strategic discussions and opportunities, ensuring alignment over strategy, operational performance, remuneration policy, capital structure and future expectations of our investors. Examples of investor engagement by the Board and senior management includes Board attendance at the Annual General Meeting (unfortunately this was not possible in 2021 as the Annual General Meeting had to be held as a closed meeting due to the COVID-19 pandemic, although shareholders were encouraged to submit questions for the Board via email), NASDAQ announcements and press releases, Board attendance at conferences, regular reports from the Investor Relations team, direct engagement with investors in relation to remuneration policy, communications such as quarterly trading results, annual reports and notices of general	Strategic report – Business overview (page 2) Remuneration report – Shareholder views (page 40) Bicycle website – Corporate Governance Guidelines

Stakeholder Group	Why we engage	Engagement and influence on decision making	More information
		meetings, and making available detailed information about Bicycle and matters of interest to investors on our website	
Our Wider Communities	Our global operations are an important part of the communities in which they are located. We have environmental responsibilities to the world in which we live, and societal responsibilities to the communities where we live, work and operate.	It is important to the Board that the Group gives back to the communities in which it operates. The Board considers these communities in determining the corporate culture it wishes to promote. We endeavour to have a positive impact on the community in which it operates and aim to provide a safe, clean working environment for employees.	Strategic report – Environmental matters (page 14)

Below are examples of how the Board took into consideration its stakeholders' interests when making principal decisions during the year.

Ionis collaboration

In July 2021 we entered into an exclusive worldwide license and collaboration agreement with Ionis. In considering this transaction the Board considered the interests of its stakeholders, and in particular, its investors and employees. The Board believes that entering into the collaboration was in the best interests of these stakeholders. The Board determined that the terms and obligations under the collaboration were fair and that it would enhance our reputation and provide further opportunities for our people.

COVID-19 response

The COVID-19 pandemic has presented unique challenges to all stakeholders. The Board has ensured that all stakeholder groups have been engaged with and supported throughout the pandemic. In light of the uncertain and rapidly evolving situation we have implemented measures intended to help minimise the risk of the virus to our employees and the communities in which we operate whilst continuing progress with our business. To this end we have implemented plans that allow non-laboratory based employees to return to the office, with a focus on employee safety and optimal work environment. All business travel was suspended and has now recommenced in a controlled manner.

Fundraising

In October 2021, the Company issued and sold 3,726,852 ADSs, representing the same number of ordinary shares, at a price to the public of $54.00 per ADS, resulting in gross proceeds of $201.3 million and net proceeds of $188.4 million. During the year the Company continued the at-the-market ("ATM")

offering program that was initiated in 2020, generating gross proceeds of $105.8 million, and drew an additional $15.0 million available under its debt facility with Hercules Capital, Inc. (NYSE: HTGC). In November 2021, the Company achieved certain performance milestones and the interest only period of the debt facility was extended from 1 May 2023 to 1 February 2024 followed by equal monthly payments of principal and interest up to the scheduled maturity date on 1 October 2024.

In considering these fundraisings the Board considered the interests of its stakeholders, and in particular, its investors, collaborators and employees. The Board believes that entering into these arrangements was in the best interests of these stakeholders as it strengthened the balance sheet to further support the Company's operations to advance our clinical and pre-clinical oncology pipeline.

This report was approved by the board of directors on 14 April 2022 and signed on its behalf by:

Kevin Lee
Director
27 April 2022

Bicycle Therapeutics plc
year ended 31 December 2021

Directors' Remuneration Report

Annual Statement from the Chair of the Compensation Committee

Dear Shareholders,

As the Chair of the Compensation Committee (the "Committee"), I am pleased to present, on behalf of the board of directors (the "Board") of Bicycle Therapeutics plc (the "Parent Company" and, together with its subsidiaries, the "Company", "Bicycle", "our", "we" or "us"), the Directors' Remuneration Report for the year ended 31 December 2021 (the "Remuneration Report"), which is the Company's third such report following the Parent Company's initial public offering (the "IPO") and listing on The Nasdaq Stock Market ("NASDAQ") on 23 May 2019.

The Remuneration Report will be subject to an advisory vote at the forthcoming Annual General Meeting to be held on 27 June 2022 (the "AGM"). There are no other matters that the Parent Company requires approval for under Chapter 4A of Part 10 of the Companies Act 2006. The Directors' Remuneration Policy (the "Remuneration Policy") was approved by the shareholders at the Parent Company's first AGM on 29 June 2020. Following the IPO in May 2019, this will be the Parent Company's third AGM as a listed company.

Introduction

Our shareholders approved our Remuneration Policy at our first AGM following our IPO on NASDAQ in 2019. We believe that our approved Remuneration Policy provides an appropriate framework to meet our objectives to establish a broad range of remuneration programs and policies, that both compensate and incentivise directors and senior executives to deliver growth in a long-term and sustainable manner, and that are aligned strategically with our shareholders to appropriately position the Company as a global biopharmaceutical company.

As we move into 2022 and beyond, the Committee's role will be to continue to ensure that directors and senior executives are appropriately compensated and incentivised to deliver growth in a long-term and sustainable manner, and to continue to establishing remuneration programs that are grounded in market practice, effective at driving proper executive behaviours, clearly link pay and performance and are cost-efficient overall to shareholders. Key considerations guiding our Remuneration Policy are described in more detail on page 30 of the Remuneration Report. The Remuneration Policy will be renewed every three years (unless a revised policy is approved by shareholders).

The global marketplace for talent

We are a biopharmaceutical company headquartered in the UK and with operations in both the UK and the U.S. Given that the market for experienced directors and biopharmaceutical executive talent, particularly in the U.S., is very competitive, the Committee references the U.S. market as the leading indicator for executive and director remuneration levels and practices. This will help attract and retain directors and motivate the superior executive talent needed to successfully manage the Company's complex global operations. Being consistent in this market view of the U.S. as the primary benchmark for remuneration practices for our Executive and Non-Executive Directors is key for the Company as it builds its global operations in a manner designed to deliver sustainable long-term growth and shareholder value.

In taking any actions, the Committee is mindful of the general UK compensation framework, including investor bodies' guidance and the UK Corporate Governance Code, and has considered these when determining the remuneration programs and policies where it believes they best serve the long-term interests of shareholders.

Pay for performance

We believe that a significant portion of the remuneration of our Executive Director should be based on achieving objectives designed to create inherent value in the Company, and ultimately on achieving value

creation for our shareholders. In line with this belief, the compensation of our Executive Director includes short term incentives based on corporate and personal goals. Similarly, all directors receive equity incentives designed to reward long-term value creation for our shareholders.

2021 remuneration outcome

As outlined above, a core principle of Bicycle's Remuneration Policy is the link between pay and performance. In the financial year 2021 (being the year ended 31 December 2021), the annual bonus paid to Kevin Lee, our Chief Executive Officer ("CEO"), was determined by the Board following an assessment of the corporate and personal objectives achieved in the year. Kevin Lee received a bonus of 160% of his target bonus, which resulted in a total bonus pay out of 96% of salary earned for the financial year 2021. The bonus was paid in cash in February 2022. This outcome was based on achievements versus goals in the following key areas: Corporate Development, Clinical Development, Financial and Organisational Development. In considering the above outcomes, the Committee assessed whether the outcomes reflected the underlying performance of the Company and concluded that no discretionary adjustments were required.

Some of the key highlights of the 2021 year, all in the context of the ongoing COVID-19 pandemic, included:

- Interim BT5528 phase I clinical trial results and preliminary results from the ongoing BT8009 phase I clinical trial both demonstrated preliminary anti-tumour activity across two tumour types, and reported tolerability profiles that may demonstrate differentiation from antibody-based approaches;
- We initiated a clinical trial of BT7480 in the fourth quarter of 2021;
- Entered into an exclusive license and collaboration agreement with Ionis Pharmaceuticals to develop targeted oligonucleotide therapeutics. The Company received $45 million upfront, which included a license fee, an option fee and an $11 million equity investment; and
- Raised gross proceeds of $201.3 million in upsized underwritten public offering and gross proceeds of $105.8 million from the Company's ATM offering program.

Please see the remainder of the Remuneration Report for additional details on this bonus outcome and the pay for performance linkage.

Conclusion

The Committee believes the proposals put forth in this report will properly motivate our directors and senior executives to deliver sustainable growth and shareholder value over the long term and do so in a responsible and cost-efficient manner.

I hope that you find the information in this report helpful and I look forward to your support at our AGM.

Yours sincerely,

Veronica Jordan
Chair of the Compensation Committee
27 April 2022

Remuneration Policy

This part of the Remuneration Report sets out the Remuneration Policy and has been prepared in accordance with the Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013, the Companies (Miscellaneous Reporting) Regulations 2018, and the Companies (Directors' Remuneration Policy and Directors' Remuneration Report) Regulations 2019.

The Remuneration Policy was approved by shareholders in a binding vote at our first AGM on 29 June 2020 and took effect from the date of approval and will continue to apply for a maximum period of three years (or until a revised policy is approved by shareholders). The Remuneration Policy is unchanged this year, and as such is not subject to a shareholder vote.

The scenario charts have been updated to reflect the intended application of the policy for the 2022 financial year and references to prior financial years have been updated where appropriate to aid understanding. A copy of the shareholder-approved policy (including the scenario charts for the 2020 financial year) is in the Annual Report and Financial Statements for the Year Ended 31 December 2019, which is available on the Company's website.

Key considerations when determining the Remuneration Policy

The Committee designed the Remuneration Policy with a number of specific objectives in mind. The Remuneration Policy should:

- attract, retain and motivate high calibre senior management and focus them on the delivery of the Company's strategic and business objectives;
- encourage a corporate culture that promotes the highest level of integrity, teamwork and ethical standards;
- be competitive against appropriate market benchmarks (being predominantly the U.S. biotech sector) and have a strong link to performance, providing the ability to earn above-market rewards for strong performance;
- be simple and understandable, both internally and externally;
- encourage increased equity ownership to motivate executives in the overall interests of shareholders, the Company, employees and customers; and
- take due account of good governance and promote the long-term success of the Company.

In seeking to achieve the above objectives, the Committee is mindful of the views of a broad range of stakeholders in the business and accordingly takes account of a number of factors when setting remuneration including: market conditions; pay and benefits in relevant comparator organisations; terms and conditions of employment across the Company; the Company's risk appetite; the expectations of institutional shareholders; and any specific feedback received from shareholders and other stakeholders.

Remuneration Policy table

The table in the following pages sets out, for each element of pay, a summary of how remuneration is structured and how it supports the Company's strategy.

Executive Directors

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
Base salary			
To recruit and retain Executive Directors of the highest calibre who are capable of delivering the Company's strategic objectives, reflecting the individual's experience and role within the Company. Base salary is designed to provide an appropriate level of fixed income to avoid any over-reliance on variable pay elements that could encourage excessive risk taking.	Salaries are normally reviewed annually, and changes are generally effective from 1 January each year. The annual salary review for Executive Directors takes a number of factors into consideration, including: • business performance; • salary increases awarded to the overall employee population; • skills and experience of the individual over time; • scope of the individual's responsibilities; • changes in the size and complexity of the Company; • market • competitiveness assessed by periodic benchmarking; and • the underlying rate of inflation. If salary is set in USD but paid to a UK-based Executive Director it will be converted and paid in GBP pursuant to the terms of the applicable service agreement (as amended from time to time).	Whilst there is no prescribed formulaic maximum, any increases will take into account prevailing market and economic conditions and the approach to employee pay throughout the organisation. In assessing base salaries, the Committee takes into account market data, but does not target a specific percentile when setting pay levels, rather considers it as one factor along with several others including Company and individual performance, tenure, past experiences and expected future contributions. Base salary increases are awarded at the discretion of the Committee; however, salary increases will normally be no greater than the general increase awarded to the wider workforce, in percentage of salary terms unless the salary is meaningfully below peers. In addition, a higher increase may be made where an individual had been appointed to a new role at below-market salary while gaining experience. Subsequent demonstration of strong performance may result in a salary increase that is higher than that awarded to the wider workforce.	Not performance related.

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
Benefits			
Reasonable benefits-in-kind are provided to support Executive Directors in carrying out their duties and assist with retention and recruitment.	The Company aims to offer benefits that are in line with market practice. The main benefits currently provided include private health insurance, long-term disability, critical illness and death in service. Under certain circumstances the Company may offer relocation allowances or assistance. Expatriate benefits may be offered where relevant including fees for tax advice associated with completion of international tax returns and, if relevant, any gross-up for tax. Travel, accommodation and any reasonable business-related expenses (including tax thereon) may be reimbursed. Executive Directors may become eligible for other benefits in future where the Committee deems it appropriate. Where additional benefits are introduced for the wider workforce, Executive Directors may participate on broadly similar terms. Executive Directors are eligible to participate in the Company's all-employee share plans on the same terms as other employees in the jurisdiction in which they are engaged.	Not applicable.	Not performance related.

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
Pensions			
The Company aims to provide a contribution towards life in retirement.	Executive Directors are eligible to receive employer contributions to the Company's Group Personal Pension Scheme or a salary supplement in lieu of pension benefits, or a mixture of both.	Up to 12% of salary per annum for Executive Directors, C-level executives and senior managers. The rest of the workforce is up to 10%.	Not performance related.
Annual Performance Bonus			
The annual bonus scheme rewards the achievement of stretching objectives that support the Company's corporate goals and delivery of the business strategy.	Bonuses are determined based on annual corporate and personal performance measures and targets that are agreed between the Executive Directors and the Board (following the Committee's recommendation) at the start of each financial year. Bonuses may be paid in cash or in equity awards, as may be agreed between the Executive Directors and the Committee. Payment of bonuses is conditional on the Executive Directors being in employment (and not having served notice of termination). No deferral period applies to bonuses.	The maximum target bonus opportunity for Executive Directors is 80% of salary, with a maximum bonus opportunity of up to two times the target opportunity. For threshold performance, no more than 50% of target bonus may be payable. For 2022, the target bonus opportunity for Executive Directors will be no more than 65% of salary, with a maximum bonus opportunity of up to 150% of the target opportunity. In addition there is an opportunity based on personal objectives to receive up to an additional 50% of the total bonus outcome (i.e. a maximum total of 146% of salary).	Performance measures are determined by the Committee each year and may vary to ensure that they promote the Company's business strategy and shareholder value. The performance measures may include financial, strategic and/or personal objectives. The Committee may alter the bonus outcome (up or down) if it considers that the pay-out derived from a formula is inconsistent with the Company's overall performance, taking account of any factors it considers relevant. This will help ensure that payments reflect overall Company performance during the period.
2019 Share Option Plan ("SOP")			
The SOP is designed to incentivise the successful execution of business strategy over the longer term and provide long-term retention. Facilitates share ownership to provide	No new options will be granted under the SOP. Awards will typically be granted annually, in the form of options although may also be granted more or less frequently. Options are typically	There is no defined maximum opportunity under the SOP. However, the Committee will generally work within the benchmarking guidelines provided by our compensation consultants. We seek to	Performance conditions may apply to awards. Such conditions may be strategic objectives which may include milestones events, financial, strategic and/or personal objectives.

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
further alignment with shareholders.	subject to vesting over a four-year period, with 25% of the award vesting on the first anniversary of the grant, and the remainder vesting in equal monthly instalments thereafter. The Committee may vary the vesting schedule of options as it considers appropriate. No deferral or holding period applies to options or to the shares acquired on the exercise of options.	establish equity-based remuneration competitive to that offered by a set of comparable companies with whom we may compete for talent.	Share options are granted with an exercise price no less than the fair market value of the shares on the date of grant. Accordingly, share options will only have value to the extent the Company's share price appreciates following the date of grant. Any performance conditions set will be designed to incentivise performance in support of the Company's strategy and business objectives. The Committee has flexibility to vary the mix of measures or introduce new measures for each subsequent award taking into account business priorities at the time of grant. The Committee may amend, relax or waive performance conditions if it considers that they have become unfair or impractical. This will help ensure that vesting reflects overall Company performance during the period. Options vest in full on a change of control.
2020 Equity Incentive Plan ("EIP")			
The EIP is designed to incentivise the successful execution of business strategy over the longer term and provide long-term retention. Facilitates share ownership to provide	Awards may be granted in the form of options, share appreciation rights, restricted shares, restricted share units or such other form as may be permitted under the EIP or by any other equity incentive plan	There is no defined maximum opportunity under the EIP. However, the Committee will generally work within the benchmarking guidelines provided by our compensation consultants. We seek to	Performance conditions may apply to awards. Such conditions may be strategic objectives which may include milestones events, financial, strategic and/or personal objectives.

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
further alignment with shareholders.	operated by the Company from time to time. Awards will typically be granted annually to continuing employees, although may also be granted more or less frequently. Awards are typically subject to vesting over a four-year period, with 25% of the award vesting on the first anniversary of the grant, and the remainder vesting in equal monthly instalments thereafter. The Committee may vary the vesting schedule of awards as it considers appropriate. No deferral or holding period applies to awards or to the shares acquired following the vesting of awards.	establish equity-based remuneration competitive to that offered by a set of comparable companies with whom we may compete for talent.	Any performance conditions set will be designed to incentivise performance in support of the Company's strategy and business objectives. The Committee has flexibility to vary the mix of measures or introduce new measures for each subsequent award taking into account business priorities at the time of grant. The Committee may amend, relax or waive performance conditions if it considers that they have become unfair or impractical. This will help ensure that vesting reflects overall Company performance during the period. Awards vest in full on a change of control.

Chair and Non-Executive Directors

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
Fees and benefits			
To attract Non-Executive Directors who have a broad range of experience and skills to provide independent judgement on issues of strategy, performance, resources and standards of conduct.	Non-Executive Directors receive an annual retainer paid in cash, comprising a base fee plus additional fees for Committee Chairpersonship or membership. Such fees are set based on peer group comparator data. The Chair's fee is reviewed annually by the Committee (without the Chair present). Fee levels for the Non-Executive Directors are	When reviewing fee levels, account is taken of market movements in the fees of Non-Executive Directors, Board Committee responsibilities and ongoing time commitments, as well as the underlying rate of inflation. Actual fee levels are disclosed in the Annual Remuneration Report for the relevant financial year.	Not performance related.

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
	determined by directors upon the recommendation of the Committee. When reviewing fee levels, account is taken of market movements in fee levels, Board committee responsibilities, ongoing time commitments and the general economic environment. In exceptional circumstances, if there is a temporary yet material increase in the time commitments for Non-Executive Directors, the Board may pay additional fees to recognise that additional workload. Non-Executive Directors ordinarily do not participate in any pension, bonus or performance-based share incentive plans. Travel, accommodation and other business-related expenses incurred in carrying out the role as well as fees for tax advice associated with completion of international tax returns will be paid by the Company including, if relevant, any gross-up for tax. Tax equalisation benefits may be provided to Non-Executive Directors who are required to relocate or become tax resident		

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
	in a new jurisdiction. Non-Executive Director fees are generally denominated and paid in USD but may be denominated and/or paid in GBP, USD, or a combination depending on the personal situation of each Non-Executive Director. Any currency conversions are calculated in accordance with the applicable Company procedure from time to time. Non-Executive Director fees in respect of those Non-Executive Directors who are appointed by an investor (or group of investors) in the Parent Company may be paid to those investor(s) on behalf of the relevant Non-Executive Director.		
Equity Awards			
To facilitate share ownership and provide alignment with shareholders.	Non-Executive Directors may receive equity awards under the EIP (or options, share appreciation rights, restricted shares, restricted share units or such other form as may be permitted by any other equity incentive plan operated by the Company from time to time). Non-Executive Directors will receive an initial equity award upon appointment or election. Initial equity awards normally vest	There is no maximum award level for equity awards to Non-Executive Directors. The size of the equity awards is determined by the full Board, upon recommendation of the Compensation Committee. When reviewing award levels, account is taken of market movements in equity awards, Board committee responsibilities, ongoing time commitments and the general economic conditions.	Not performance related. Awards vest in full on a change of control.

Purpose and link to strategy	Operation	Maximum opportunity	Performance metrics
	over a period of three years on a monthly basis from the date of appointment, subject generally to continued service. In addition, Non-Executive Directors who have not announced an intention to either resign from the Board or not to stand for election at the next annual meeting of shareholders will be granted an equity award in January of each year which shall vest in full upon grant. If a new Non-Executive Director joins the Board following the date of grant of this annual grant in any calendar year, such Non-Executive Director will be granted a pro rata portion of the next annual grant, based on the time between his or her appointment and the date of such annual grant.		

Notes to the policy table

Legacy arrangements

For the duration of this Remuneration Policy, the Company will honour any commitments made in respect of current or former directors before the date on which either: (i) the Remuneration Policy becomes effective; or (ii) an individual becomes a director, even when not consistent with the Remuneration Policy set out in this report or prevailing at the time such commitment is fulfilled. For the avoidance of doubt, all outstanding historic awards that were granted in connection with, or prior to, listing on NASDAQ and/or under the SOP remain eligible to vest based on their original or modified terms.

Payments may be made in respect of existing awards under the SOP and the Committee may exercise any discretions available to it in connection with such awards in accordance with the rules of the SOP and relevant award documentation. Options granted under the SOP vest in full on a change of control.

Payments may be made in respect of consultancy services provided by Pierre Legault pursuant to a consulting agreement entered into between Stone Sunny Isles, Inc. and Bicycle Therapeutics Inc. dated

15 March 2019 pursuant to which Stone Sunny Isles, Inc. has agreed to make available Pierre Legault to provide advisory services to us as requested by our Board of Directors or our chief executive officer. In consideration for the provision of the advisory services, we pay Stone Sunny Isles, Inc. a monthly retainer of £10,416, which is billed in U.S. dollars. Pierre Legault is the President, Treasurer and Director of Stone Sunny Isles, Inc.

Retention Bonus

Kevin Lee received a retention bonus to incentivise his continuous service in an aggregate amount of £150k (paid in two tranches, £100k in August 2018 and £50k in October 2019). This bonus was subject to repayment (net of statutory deductions for income tax and employee's National Insurance contributions) if he had given notice to terminate his employment with the Company at any time before 1 August 2020. No such notice was given.

Performance conditions

The choice of annual bonus performance metrics reflects the Committee's belief that any incentive remuneration should be appropriately challenging and tied to the delivery of key strategic objectives intended to ensure that Executive Directors are incentivised to deliver across a range of objectives for which they are accountable. The Committee has retained flexibility on the specific measures which will be used to ensure that any measures are fully aligned with the strategic imperatives prevailing at the time they are set.

The targets for the bonus scheme for the forthcoming year will be set out in general terms, subject to limitations with regards to commercial sensitivity. The full details of the targets will be disclosed when they are in the public domain and are no longer considered commercially sensitive.

Where used, performance conditions applicable to EIP awards (or other equity incentive plans operated by the Company from time to time) will be aligned with the Company's objective of delivering superior levels of long-term value to shareholders. Prior to each award, the Committee has flexibility to select measures that are fully aligned with the strategy prevailing at the time awards are granted.

The Committee will review the calibration of targets applicable to the annual bonus, and the EIP in years where performance measures apply, annually to ensure they remain appropriate and sufficiently challenging, taking into account the Company's strategic objectives and the interests of shareholders.

Recovery and withholding

The Company does not have a policy on recovery and withholding provisions other than on retention bonuses if the individual gives notice of the termination of their employment before a prescribed date (the relevant period for which ended on 1 August 2020).

Differences in remuneration policy between Executive Directors and other employees

The overall approach to reward for employees across the workforce is a key reference point when setting the remuneration of the Executive Directors. When reviewing the salaries of the Executive Directors, the Committee pays close attention to pay and employment conditions across the wider workforce and in normal circumstances the increase for Executive Directors will be no higher than the average increase for the general workforce.

The key difference between the remuneration of Executive Directors and that of our other employees is that, overall, at senior levels, remuneration is increasingly long-term, and 'at risk' with an emphasis on performance-related pay linked to business performance and share-based remuneration. This ensures that remuneration at senior levels will increase or decrease in line with business performance and provides alignment between the interests of Executive Directors and shareholders. In particular, long-term incentives are

provided only to the most senior executives as they are reserved for those considered to have the greatest potential to influence overall levels of performance.

Committee discretion in operation of variable pay schemes

The Committee operates under the powers it has been delegated by the Board. In addition, where relevant, it complies with rules that are either subject to shareholder approval or by approval from the Board. These rules provide the Committee with certain discretions which serve to ensure that the implementation of the Remuneration Policy is fair, both to the individual director and to the shareholders. The Committee also has discretions to set components of remuneration within a range, from time to time. Where appropriate, the extent of such discretions is set out in the relevant rules and/or described in the policy table above. To ensure the efficient administration of the variable incentive plans outlined above, the Committee will apply certain operational discretions.

These include the following:

- selecting the individuals who will receive awards under the plans on an annual basis;
- determining the timing of grants of awards and/or payments;
- determining the quantum of awards and/or payments;
- determining the choice (and adjustment) of any performance measures and targets, vesting schedules, exercise prices (where applicable) and other award terms for each incentive plan;
- determining the extent of vesting, including for leavers;
- making the appropriate adjustments (including to any performance targets) required in certain circumstances, for instance for changes in capital structure;
- determining "good leaver" status and the impact of certain corporate events, if applicable, for incentive plan purposes and determining and applying the appropriate treatment;
- interpreting the plan rules where necessary; and
- undertaking the annual review of weighting of performance measures and setting targets for the annual bonus plan and other incentive schemes, where applicable, from year to year.

If an event occurs which results in the annual bonus plan or EIP (where performance conditions apply) performance conditions and/or targets being deemed unfair or impractical (e.g. material acquisition or divestment), the Committee will have the ability to make amend, relax or waive (and/or recommend such alterations to the Board for approval) to the measures and/or targets and alter weightings. Any use of the above discretion would, where relevant, be explained in the Annual Report on Remuneration and may, as appropriate, be the subject of consultation with the Parent Company's major shareholders.

The Committee may make minor amendments to the Remuneration Policy (for regulatory, exchange control, tax or administrative purposes or to take account of a change in legislation) without obtaining shareholder approval for that amendment.

Shareholder views

The Board is committed to dialogue with shareholders and intends to engage directly with them and their representative bodies when considering any significant changes to our remuneration arrangements. The Committee will consider shareholder feedback received following the AGM, as well as any additional feedback and guidance received from time to time. This feedback will be considered by the Committee as it develops the Company's remuneration framework and practices going forward. Assisted by its independent adviser, the Committee also actively monitors developments in the expectations of institutional investors and their representative bodies.

Employment conditions

The Committee is regularly updated throughout the year on pay and conditions applying to Company employees. Where significant changes are proposed to employment conditions elsewhere in the Company these are highlighted for the attention of the Committee at an early stage.

Whilst the Committee does not currently consult directly with employees regarding its policy for directors, the Committee is considering the best method of bringing the employee voice to the boardroom.

Other remuneration policies

Remuneration for new appointments

Where it is necessary to appoint or replace an Executive Director or to promote an existing Executive Director, the Committee's approach when considering the overall remuneration arrangements in the recruitment of a new Executive Director is to take account of the calibre, expertise and responsibilities of the individual, his or her remuneration package in their prior role and market rates. Remuneration will be in line with the Remuneration Policy and the Committee will not pay more than is necessary to facilitate their recruitment.

The remuneration package for a new Executive Director will be set in accordance with the terms of the Company's approved remuneration policy in force at the time of appointment. Further details are provided below:

Salary	The Committee will set a base salary appropriate to the calibre, experience and responsibilities of the new appointee. In arriving at a salary, the Committee may take into account, amongst other things, the market rate for the role and internal relativities. The Committee has the flexibility to set the salary of a new Executive Director at a lower level initially, with a series of planned increases implemented over the following few years to bring the salary to the desired positioning, subject to individual performance. In exceptional circumstances, the Committee has the ability to set the salary of a new Executive Director at a rate higher than the market level to reflect the criticality of the role and the experience and performance of the individual.
Benefits	Benefits will be consistent with the principles of the policy set out on page 32. The Company may award certain additional benefits and other allowances including, but not limited to, those to assist with relocation support, temporary living and transportation expenses, educational costs for children, reimbursement of fees for tax advice associated with completion of international tax returns and tax equalisation to allow flexibility in employing an overseas national.
Pension benefits	A maximum employer pension contribution of 12% of salary (or equivalent cash allowance) may be payable for external appointments. For an internal appointment, his or her existing pension arrangements may continue to operate. Any new Executive Director based outside the UK will be eligible to participate in pension or pension allowance, insurance and other benefit programmes in line with local practice.
Annual bonus	The maximum target bonus opportunity is 80% of base salary and the maximum bonus opportunity for new appointments is 225% of their target bonus.

Other cash or equity-based awards	Executive Directors may receive awards under the EIP (or other equity incentive plan operated by the Company from time to time) on appointment. The Committee will assess and determine the award level, award vehicle, performance conditions and vesting schedule for each individual on a case-by-case basis. In addition, Executive Directors are eligible to participate in the Company's all-employee share plans on the same terms as other employees in the jurisdiction in which they are engaged. In addition, the Committee may offer additional cash and/or equity-based elements in order to "buy-out" remuneration relinquished on leaving a former employer. Any awards made in this regard may have no performance conditions, or different performance conditions, or a different vesting schedule compared to the Company's existing plans, as the Committee considers appropriate.

Depending on the timing and responsibilities of the appointment, it may be necessary to set different annual bonus or SOP performance measures and targets as applicable to other Executive Directors.

The terms of appointment for a Non-Executive Director would be in accordance with the approved remuneration policy for Non-Executive Directors in force at the time of the appointment.

Service contracts and termination policy

Executive Directors have rolling service agreements (entered into with the Parent Company or a subsidiary thereof) which may be terminated in accordance with the terms of these agreements. The period of notice for Executive Directors (to be given by the employer or the Executive Director) will not normally exceed 6 months. Executive Directors' service agreements are available for inspection at the Parent Company's registered office during normal business hours and will also be available to the public if required to be filed by the Parent Company with the SEC. The terms of the current Executive Director's service contract are:

Name	Position	Date of service contract	Notice period
Kevin Lee	Chief Executive Officer	26 September 2019	6 months either party

The Company's policy on remuneration for Executive Directors who leave the Company is set out below. The Committee will exercise its discretion when determining amounts that should be paid to leavers (other than in respect of the relevant leaver's contractual entitlements which will be respected), taking into account the facts and circumstances of each case. Where applicable, the Company may elect to make a payment in lieu of notice ("**PILON**") equivalent in value to basic salary and contractual benefits for any unexpired portion of the notice period (but excluding any annual bonus or holiday entitlement that would have otherwise accrued during the notice period).

Where the Executive Director is terminated by the Company without "Cause" (as defined in the service agreement), by the Executive Director for "Good Reason" (as defined in the service agreement), or on the Executive Director's death, severance pay in addition to any potential PILON and any entitlements in respect of the year to the date of termination in accordance with the applicable terms shall be paid to an Executive Director as set out below, subject to the Executive Director signing a waiver of claims:

Element of pay / benefit	Termination other than within 12 months after a relevant "Change in Control" (as defined in the service agreement)	Termination within 12 months after a relevant "Change in Control" (as defined in the service agreement)
Salary	A lump sum payment equal to 12 months' salary payable.	A lump sum payment equal to 18 months' salary payable.
Contractual benefits	A lump sum payment equal to the	A lump sum payment equal to the

Element of pay / benefit	Termination other than within 12 months after a relevant "Change in Control" (as defined in the service agreement)	Termination within 12 months after a relevant "Change in Control" (as defined in the service agreement)
	cost to the Company of providing contractual benefits for 12 months (or continuation of such benefits).	cost to the Company of providing contractual benefits for 18 months (or continuation of such benefits).
Annual bonus	Not applicable.	A lump sum payment equal to 1.5 times target bonus will be paid.
Share Option Plan (legacy awards)	Options treated in accordance with plan rules. Good leavers may exercise their options to the extent vested at the time of termination within 12 months after termination. The Committee has the discretion to accelerate vesting in whole or in part, to extend the exercise window, and/or to waive any applicable performance conditions in whole or in part.	Options subject to time-based vesting (only) accelerate, vest and become exercisable in full. Options subject to performance conditions treated in accordance with plan rules (as described at left).
Equity Incentive Plan	Awards treated in accordance with plan rules. Unless otherwise determined by the Committee, unvested equity awards lapse on the date of termination of employment.	Awards vest in full on a change of control.

The Company is unequivocally against rewards for failure; the circumstances of any departure, including the individual's performance, would be taken into account in every case. Statutory redundancy payments may be made. Service agreements may be terminated summarily without notice (or on shorter notice periods) and without payment in lieu of notice in certain circumstances, such as gross misconduct or any other material breach of the obligations under their employment contract. The Company may require the individual to work during their notice period or may place them on garden leave during which they would be entitled to full pay and benefits.

Except in the case of gross misconduct or resignation, the Company may at its absolute discretion reimburse for reasonable professional fees relating to the termination of employment and, where an Executive Director has been required to re-locate, to pay reasonable repatriation costs, including possible tax exposure costs and/or settle any other amount the Committee considers reasonable including any statutory entitlements or sums to settle or compromise claims or potential claims in connection with a termination (including, at the discretion of the Committee, reimbursement for legal advice and provision of outplacement services).

Policy on external appointments

The Board believes that it may be beneficial to the Company for executives to hold certain roles outside the Company provided that the Company's business takes priority. Any such appointments are subject to approval by the Board and the director may retain any fees received. Kevin Lee is currently a director of Alchemab Therapeutics Limited and Nodthera Limited in respect of which he received an aggregate of £60k (year ended 31 December 2020: £25k) per annum in fees.

Non-Executive Directors' terms of engagement

Each of the Non-Executive Directors is engaged under a Non-Executive Director appointment letter. Each appointment is normally terminable by either party on no more than three months' written notice (or, in some cases, payment in lieu of notice), but may be terminated immediately in certain circumstances. Under our articles of association, our Board is divided into three classes (Class I, Class II and Class III), with members of each class serving staggered three-year terms. In the event of termination, the Chair and Non-Executive Directors are only entitled to fees accrued to the date of termination together with reimbursement of expenses properly incurred before that date.

The dates of appointment of each of the Non-Executive Directors serving at 31 December 2021 are summarised in the table below. The Parent Company was incorporated on 27 October 2017.

Non-Executive Directors	Date of appointment letter	Date of appointment
Janice Bourque	18 July 2019	18 July 2019
Jose-Carlos Gutierrez-Ramos	17 March 2021	17 March 2021
Veronica Jordan	30 October 2019	30 October 2019
Richard Kender	20 July 2019	18 July 2019
Pierre Legault (Chairman)	15 March 2019	15 March 2019
Gregory Winter	24 May 2019	4 December 2017

At the time of the IPO in May 2019 all Non-Executive Directors then appointed except Pierre Legault entered into new letters of appointment which took effect conditional upon completion of the IPO. Janice Bourque, Richard Kender, Veronica Jordan and Jose-Carlos Gutierrez-Ramos each entered into letters of appointment at the time of their appointment to the Board.

Non-Executive Directors' letters of appointment are available for inspection at the Parent Company's registered office during normal business hours and will be available for inspection at the AGM.

A company affiliated with Pierre Legault, Stone Sunny Isles, Inc., has also entered into a consulting agreement with Bicycle Therapeutics Inc. dated 15 March 2019 under which it will procure the provision of consulting services by Pierre Legault to the Parent Company and is paid a monthly retainer of £10,416, which is billed in U.S. dollars for these services. This consulting agreement is terminable on three months' written notice (or payment in lieu of notice).

Remuneration scenario for Executive Director

The charts below show an estimate of the 2022 remuneration package for the Executive Director under three assumed performance scenarios and these scenarios are based on the remuneration policy set out above.

Minimum (comprising fixed pay only)

Base salary as of 1 January 2022 of $734k and cash in lieu of pension of 12% of base salary net of employer NI costs of the cash in lieu.

Target

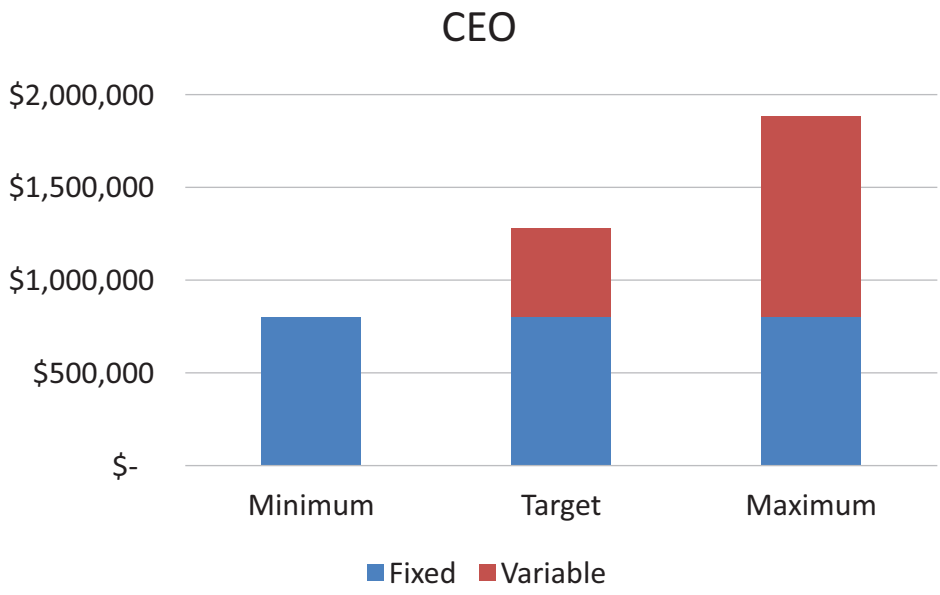
Fixed pay as above.

Assumes target bonus of 65%.

Maximum

Fixed pay as above.

Assumes maximum bonus payout of 146%.



Annual Report on Remuneration

This part of the report has been prepared in accordance with Part 3 of The Large and Medium-sized Companies and Groups (Accounts and Reports) (Amendment) Regulations 2013 and section 420 of the Companies Act 2006. The Annual Report on Remuneration and the Annual Statement by the Chair of the Compensation Committee will be put to a single advisory shareholder vote at the AGM to be held on 27 June 2022. The information in this part of the report has been audited where required under the foregoing regulations and is indicated as audited where applicable.

Compensation Committee

The current members of the Committee, who are all independent and have been members for the whole year, are Veronica Jordan (as Chair of the Committee), Richard Kender and Janice Bourque. Decisions of the Committee are made by majority vote or by unanimous written consent.

The Chair and members of management, the Chief Executive Officer (**"CEO"**), and the Chief Financial Officer (**"CFO"**), are invited to attend meetings where appropriate. Attendees who are not members of the Committee are not involved in any decisions and are not present for any discussions regarding their own remuneration and did not materially assist the Committee.

No conflicts of interest have arisen during the year and none of the members of the Committee has any personal financial interest in the matters discussed, other than as optionholders. The fees of the Non-Executive Directors are approved by the Board on the joint recommendation of the Committee and the CEO/Executive Director.

Meetings attendance

Director	Meetings Attended
Janice Bourque	7 of 8
Richard Kender	8 of 8
Veronica Jordan	8 of 8

Eight meetings of the Committee have taken place during 2021.

Independent advisors

Independent advice on executive remuneration is received from the Executive Compensation practice of Radford. Radford is a member of the Remuneration Consultants Group and is a signatory to its Code of Conduct. Radford advises the Committee on all aspects of senior executive remuneration. Since the IPO, Radford has been appointed by the Committee to assist with the drafting of the Remuneration Policy and has kept the Committee up to date on remuneration trends and corporate governance best practice. Radford does not have any other remuneration-unrelated connection with the Company and is considered to be independent by the Committee. During the year ended 31 December 2021, fees charged by Radford for advice provided to the Committee for 2021 amounted to approximately $130k (year ended 31 December 2020: $9k).

Activity in the year

The Committee's principal function is to develop and implement compensation policies and plans that ensure the attraction and retention of key management personnel, the motivation of management to achieve the Company's corporate goals and strategies, and the alignment of the interests of management with the long-term interests of the Parent Company's shareholders. In determining the remuneration policy, and in constructing the remuneration arrangements for Executive Directors and senior employees, the Board, advised by the Committee, aims to provide remuneration packages that are competitive and designed to attract, retain and motivate Executive Directors and senior employees of the highest calibre.

The Committee is responsible for and considered, where applicable, during the year:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of the CEO and CFO;
- evaluating the performance of the CEO and CFO in light of such corporate goals and objectives and recommending or determining the compensation of the CEO;
- reviewing and recommending or determining the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- preparing the compensation committee report required by the SEC rules to be included in our annual proxy statement, and the directors' remuneration policy and report as required under English law;
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K, if required;
- reviewing and making recommendations to the Board with respect to director compensation; and
- reviewing and discussing with the Board our corporate succession plans for the CEO and other key officers.

The Committee is formally constituted and operates pursuant to a written charter, which is available on the Company's website.

Single total figure of directors' remuneration — year ended 31 December 2021 (audited)

The total remuneration of the individual directors who served during the financial year, from 1 January 2021 to 31 December 2021, together with a comparison with the equivalent figure for the 2020

financial year is shown below. Other than shown, no directors received remuneration in the 2020 financial year. Total remuneration is the sum of emoluments plus Company pension contributions.

		Base salary[1]/ fees $'000	Benefits[2] $'000	Pension[3] $'000	Bonus[4] $'000	Equity-based awards[5] $'000	Total remuneration $'000	Total fixed remuneration $'000	Total variable remuneration $'000
Executive Directors									
Kevin Lee	2021	**677**	**2**	**71**	**654**	—	**1,404**	**750**	**654**
	2020	592	1	62	501	—	1,156	655	501
Non-Executive Directors[6]									
Michael Anstey	2021	—	—	—	—	—	—	—	—
	2020	20	—	—	—	—	20	20	—
Catherine Bingham	2021	**26**	—	—	—	—	**26**	**26**	—
	2020	53	—	—	—	—	53	53	—
Janice Bourque	2021	**63**	**—**	**—**	**—**	**—**	**63**	**63**	**—**
	2020	63	—	—	—	—	63	63	—
Bosun Hau	2021	—	—	—	—	—	—	—	—
	2020	20	—	—	—	—	20	20	—
Jose-Carlos Gutierrez-Ramos	2021	**34**	**—**	**—**	**—**	**—**	**34**	**34**	**—**
	2020	—	—	—	—	—	—	—	—
Veronica Jordan	2021	**58**	**—**	**—**	**—**	**—**	**58**	**58**	**—**
	2020	54	—	—	—	—	54	54	—
Richard Kender	2021	**97**	**—**	**—**	**—**	**—**	**97**	**97**	**—**
	2020	97	—	—	—	—	97	97	—
Pierre Legault[7]	2021	**209**	—	—	—	—	**209**	**209**	—
	2020	198	—	—	—	—	198	198	—
Carolyn Ng	2021	—	—	—	—	—	—	—	—
	2020	20	—	—	—	—	20	20	—
Gregory Winter	2021	**40**	**—**	**—**	**—**	**—**	**40**	**40**	**—**
	2020	40	—	—	—	—	40	40	—
Total	**2021**	**1,204**	**2**	**71**	**654**	—	**1,931**	**1,277**	**654**
	2020	**1,157**	**1**	**62**	**501**	**—**	**1,721**	**1,220**	**501**

(1) As of 1 January 2021, the Executive Director's salary was both set, and paid, in GBP, and the amount reflected is based on a GBP:USD exchange rate of 1.37566 as of 31 December 2021. In 2020, the Executive Director's salary entitlement was expressed in USD and converted to GBP pursuant to a mechanism set out in his service contract.

(2) The Executive Director's benefits included private health insurance, long term disability, critical illness and death in service benefits.

(3) Relates to pension and cash in lieu of pension.

(4) The annual bonus for 2021 was paid in cash in February 2022. The annual bonus for 2020 was paid in cash in February 2021.

(5) There were no performance obligations linked to the equity-based awards. The value of equity-based awards in the table is based on the market value of underlying shares at the date of grant, less the applicable exercise price. For the CEO and Non-Executive Directors this was nil because the exercise price is equal to the market value of the underlying shares at the date of grant. Refer to "Share Option Plan" below. Share price appreciation did not impact the value of awards. No discretion was exercised, and the determination of the levels of awards were not impacted, as a result of share price appreciation.

(6) Catherine Bingham resigned on 28 June 2021 and received no payments in respect of loss of office or otherwise following her termination date. Jose-Carlos Gutierrez-Ramos was appointed on 17 March 2021. Michael Anstey, Bosun Hau and Carolyn Ng all resigned on 30 June 2020 and received no payments in respect of loss of office or otherwise following their termination dates.

(7) Pierre Legault's fees include those payable under a consulting agreement between Stone Sunny Isles, Inc. and Bicycle Therapeutics Inc. dated 15 March 2019, pursuant to which such entity is paid £125k per year for Mr. Legault's advisory services to the Company.

2021 Annual bonus (audited)

In 2021, the CEO's annual bonus was based on corporate and personal objectives. Details of the specific objectives will be disclosed when they are no longer considered commercially sensitive. The overall bonus outcome of percentage of target resulted in a total bonus pay out of $654k or 97% of the CEO's base salary for the year ended 31 December 2021. The Compensation Committee is satisfied that the bonus pay-out for 2021 is appropriate, taking into account the wider stakeholder experience, particularly that of shareholders and employees, based on achievements versus goals in the following key areas: Corporate Development, Clinical Development, Financial and Organisational Development. In 2020, the bonus outcome of percentage of target resulted in a total bonus pay out of $501k or 85% of the CEO's base salary for the year ended 31 December 2020. Specific targets are commercially sensitive. However, full details of the targets and performance against them will be disclosed when they are no longer considered commercially sensitive.

Share Option Plan

Awards granted from 1 January 2021 to 31 December 2021 (audited)

The CEO and Chairman received the following share option awards under the SOP during the year from 1 January 2021 to 31 December 2021, as set forth in the table below:

Executive Director	Form of Award	Date of Grant	Number of Shares Covered	Exercise Price $	Face Value at Date of Grant[1]	Expiry Date	Vest Terms
Kevin Lee	Fair market value options	4 January 2021	250,000	17.95	—	3 January 2031	25% vest after one year, remaining shares vest in 36 equal monthly instalments
Chairman							
Pierre Legault . .	Fair market value options	4 January 2021	38,000	17.95	—	3 January 2031	Vest immediately

(1) The value of equity-based awards in the table is based on the market value of underlying shares at the date of grant, less the applicable exercise price. This was nil because the exercise price is equal to the market value of the underlying shares at the date of grant.

Non-Executive Directors also received the following option awards during the year from 1 January 2021 to 31 December 2021, each vesting based on continued employment only and granted under the SOP:

Non-Executive Director	Form of Award	Date of Grant	Number of Shares Covered	Exercise Price $	Face Value at Date of Grant[1]	Expiry Date	Vest Terms
Catherine Bingham	Fair market value options	4 January 2021	19,000	17.95	—	3 January 2031	Vest immediately
Janice Bourque	Fair market value options	4 January 2021	19,000	17.95	—	3 January 2021	Vest immediately
Jose-Carlos Gutierrez-Ramos	Fair market value options	17 March 2021	32,000	27.90	—	16 March 2031	Vesting in 36 monthly instalments at the end of each calendar month following 17 March 2021
Veronica Jordan	Fair market value options	4 January 2021	19,000	17.95	—	3 January 2031	Vest immediately
Richard Kender	Fair market value options	4 January 2021	19,000	17.95	—	3 January 2031	Vest immediately
Gregory Winter	Fair market value options	4 January 2021	19,000	17.95	—	3 January 2031	Vest immediately

(1) The value of equity-based awards in the table is based on the market value of underlying shares at the date of grant, less the applicable exercise price. This was nil because the exercise price is equal to the market value of the underlying shares at the date of grant.

None of the awards granted are subject to performance based conditions.

No subsequent changes were made to the exercise prices or vesting dates of options.

Statement of directors' shareholding and share interests (audited)

Shareholdings for each director, who has held office during the period 1 January 2021 and 31 December 2021, are set out in the table below as at 31 December 2021 or their date of resignation if they resigned in the year (together with interests held by his or her connected persons):

	Number of Shares	Number of Share Options				
	Beneficially owned shares as at 31 December 2021	Exercised[2]	Vested but unexercised	Unvested with performance conditions	Unvested without performance conditions	Total
Executive Director						
Kevin Lee	225,085	200,000	534,044	—	441,848	1,200,977
Non-Executive Directors						
Catherine Bingham[1]	—	—	35,000	—		35,000
Janice Bourque	—	—	61,666	—	5,334	67,000
Jose-Carlos Gutierrez-Ramos	—	—	8,888	—	23,112	32,000
Veronica Jordan	—	—	59,000	—	8,000	67,000

	Number of Shares	Number of Share Options				
	Beneficially owned shares as at 31 December 2021	Exercised[2]	Vested but unexercised	Unvested with performance conditions	Unvested without performance conditions	Total
Richard Kender	—	—	61,666	—	5,334	67,000
Pierre Legault	—	195,000	175,720	—	34,419	210,139
Gregory Winter	163,927	—	35,000	—	—	198,927

(1) Catherine Bingham resigned on 28 June 2021

(2) In 2021 Kevin Lee and Pierre Legault exercised some options during the year, with weighted average exercise prices of USD 14.00 and USD 8.54, respectively. The aggregate gain received by Dr Lee and Mr. Legault (based on the market value of the shares on the date of exercise) was USD 12,184k.

No shares were unvested.

Share ownership guidelines

Executive Directors are encouraged to build a meaningful shareholding so as to align their interests with those of shareholders but no formal shareholding requirements apply.

Payments to former directors and for loss of office (audited)

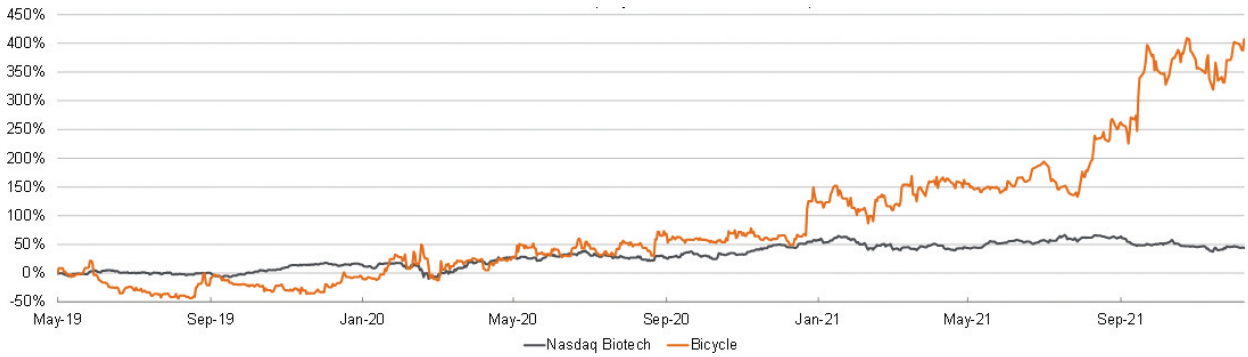
No payments were made to former directors of the Company or in relation to loss of office during the current or prior year. For the avoidance of doubt, Catherine Bingham received no payments in respect of her loss of office or otherwise following her termination date. Her options were fully vested on her termination date.

Performance graph and table

The chart below shows the Parent Company's Total Shareholder Return **("TSR")** performance compared with that of the NASDAQ Biotechnology Index from the date of the Parent Company's listing on NASDAQ to 31 December 2021. The NASDAQ Biotechnology Index has been chosen as an appropriate comparator as it is the index of which the Parent Company is a constituent. TSR is defined as the return on investment obtained from holding a company's shares over a year. It includes dividends paid, the change in the capital value of the shares and any other payments made to or by shareholders within the year.

Stock Price Performance Since IPO

Stock Performance (May 2019-December 2021)



Aligning pay with performance

The total remuneration figure for the CEO is shown in the table below, along with the value of bonuses paid, and SOP vesting, as a percentage of the maximum opportunity As explained in the report in respect of the 2019 financial year, 2019 was the first year reported since listing, it is not possible to provide meaningful comparative data for periods prior to that date.

Chief Executive Officer	**2019**	**2020**	**2021**
Total remuneration ($000)	1,004	1,156	1,404
Actual bonus (% of the maximum)	63%	63%	72%
SOP vesting (% of the maximum)	100%	100%	100%

Percentage change in remuneration of the directors compared to all Company employees

The table below illustrates the increase in salary, benefits and annual bonus for each director and that of the Company's employees as a whole as between the 2019 and 2021 financial years. As explained in the report in respect of the 2019 financial year, 2019 was the first year reported since listing on NASDAQ. There was no change in remuneration of the CEO in that year and it was therefore not possible to provide meaningful comparative data for prior years.

	Percentage change 2019-2020			Percentage change 2020-2021		
	Base salary / fees	Benefits	Bonus	Base salary / fees	Benefits	Bonus
Executive Directors						
Kevin Lee	15%	50%	16%	14%	100%	31%
Non-Executive Directors						
Michael Anstey	(17)%	—	—	—	—	—
Catherine Bingham	71%	—	—	(51)%	—	—
Janice Bourque	117%	—	—	—	—	—
Jose-Carlos Gutierrez-Ramos	—	—	—	—	—	—
Bosun Hau	(17)%	—	—	—	—	—
Veronica Jordan	500%	—	—	7%	—	—
Richard Kender	120%	—	—	—	—	—
Pierre Legault	40%	—	—	6%	—	—
Carolyn Ng	(17)%	—	—	—	—	—
Gregory Winter	67%	—	—	—	—	—
Average pay of employees as a whole	27%	7%	25%	10%	80%	35%

Non-Executive Directors did not receive fees for the period prior to the IPO on NASDAQ in May 2019. Catherine Bingham resigned on 28 June 2021. Jose-Carlos Gutierrez-Ramos was appointed on 17 March 2021. Michael Anstey, Bosun Hau and Carolyn Ng resigned on 30 June 2020. Veronica Jordan, Richard Kender and Janice Bourque were all appointed during the course of 2019 with 2020 being their first full year in office.

Relative importance of spend on pay

The table below illustrates the Company's expenditure on employee pay in comparison to total expenditure on research and development. These costs are included in the disclosures in notes 6 and 9 in the notes to the financial statements.

	2020	2021	% change
Total expenditure on research and development ($'000)[1]	34,116	47,778	40%
Total employee pay expenditure ($'000)[2]	24,833	44,491	79%

(1) The Committee considers the Company's research and development expenditure relative to salary expenditure for all employees, to be the most appropriate metric for assessing overall spend on pay due to the nature and stage of the Company's business.

(2) Total pay expenditure includes wages and salaries, social security costs, pension contributions, bonus, equity compensation plans and termination benefits.

Statement of implementation of remuneration policy in 2022

Annual base salary

The annual base salary of the CEO is shown in the table below:

	Base salary 2021 $'000	Base salary 2022 $'000
Executive Directors		
Kevin Lee	677	734

Prior to 2021, Kevin Lee's salary entitlement has been expressed in USD and converted to GBP pursuant to a mechanism set out in his service contract. To simplify administration, as of 1 January 2021, Kevin Lee's salary has been both set, and paid, in GBP. Accordingly, Kevin Lee's annual base salary was GBP 494,602, effective on and from 1 January 2021 and will be GBP 544,100 on and from 1 January 2022. For consistency and ease of comparison, we will continue to provide disclosures in USD (converted by reference to the GBP: USD exchange rate on 31 December 2021 of 1.3497 (31 December 2020: 1.36589)).

Benefits and pension

In 2022, Executive Directors are eligible for the same benefits (such as health insurance) as provided to all senior employees in the jurisdiction in which they reside. In the UK, where the CEO is based, this means that employer pension contributions are 12% of base salary for Executive Directors and employees with job title of 'director' and above and 10% (increased from 8% in 2021) for all other employees (or, in each case, cash equivalent at the election of the relevant employee).

Bonus

The CEO will be entitled to a target bonus of 65% base salary in 2022 (which is an increase from 60% in 2021), with final payout of up to 135% of base salary in the event of 'stretch' performance being achieved. The bonus will be paid cash or in an equity award, as may be agreed between the Executive Director and the Committee, and subject to the achievement of a number of corporate and personal objectives determined by the Committee. Details of the specific objectives will be disclosed when they are no longer considered commercially sensitive.

Specific targets are commercially sensitive and therefore are not disclosed in advance. However, full details of the targets and performance against them will be disclosed when they are no longer considered commercially sensitive.

Equity Incentive Plan

The Company granted the following equity incentive awards to directors and the Chairman in 2022 up to the date of this directors' remuneration report under the Equity Incentive Plan. These grants are a mix of RSUs and market value options, rather than being 100% market value options as was the case in prior years. This change was made following a review and benchmarking against our peers by our independent compensation advisor.

Director	Form of Award	Date of Grant	Number of Shares Covered	Exercise Price $[(1)]	Face Value at Date of Grant[(2)] $	Expiry Date	Vest Terms
Kevin Lee	Fair market value options	3 January 2022	100,000	60.87	—	2 January 2032	25% vest after one year, remaining shares vest in 36 equal monthly instalments
Pierre Legault	Fair market value options	3 January 2022	20,000	60.87	—	2 January 2032	Vest immediately
Janice Bourque	Fair market value options	3 January 2022	10,000	60.87	—	2 January 2032	Vest immediately
Jose-Carlos Gutierrez-Ramos	Fair market value options	3 January 2022	10,000	60.87	—	2 January 2032	Vest immediately
Veronica Jordan	Fair market value options	3 January 2022	10,000	60.87	—	2 January 2032	Vest immediately
Richard Kender	Fair market value options	3 January 2022	10,000	60.87	—	2 January 2032	Vest immediately
Gregory Winter	Fair market value options	3 January 2022	10,000	60.87	—	2 January 2032	Vest immediately
Kevin Lee	Restricted Share Units	3 January 2022	50,000	—	60.87	—	25% vest after one year, remaining shares vest in 12 equal quarterly instalments
Pierre Legault	Restricted Share Units	3 January 2022	10,000	—	60.87	—	Vest immediately
Janice Bourque	Restricted Share Units	3 January 2022	5,000	—	60.87	—	Vest immediately
Jose-Carlos Gutierrez-Ramos	Restricted Share Units	3 January 2022	5,000	—	60.87	—	Vest immediately
Veronica Jordan	Restricted Share Units	3 January 2022	5,000	—	60.87	—	Vest immediately
Richard Kender	Restricted Share Units	3 January 2022	5,000	—	60.87	—	Vest immediately
Gregory Winter	Restricted Share Units	3 January 2022	5,000	—	60.87	—	Vest immediately

(1) Exercise price is equal to the market value of the underlying shares at the date of grant.

(2) The value of equity-based awards in the table is based on the market value of underlying shares at the date of grant, less the applicable exercise price. This was nil for fair market value options because the exercise price is equal to the market value of the underlying shares at the date of grant.

No other grants are currently proposed for 2022.

Non-Executive Directors' fees

Non-Executive Directors will receive the following annual fees for 2022, which will be paid in cash, as follows. These have been increased from the 2021 fees following review and benchmarking against our peers:

	Fees (effective from 1 January 2022) 000s
Base fee:	
Board Chair	£ 5
Board member	$45
Additional fees:	
Audit Committee Chair	$20
Audit Committee member	$ 9
Compensation Committee Chair	$14
Compensation Committee member	$ 7
Nomination Committee Chair	$10
Nomination Committee member	$ 5
Strategic Committee member	$30
Scientific Committee Chair	$10
Scientific Committee member	$ 5

Non-Executive Director fees may be paid in GBP, USD, or a combination depending on the personal situation of each Non-Executive Director.

Non-Executive Directors will not be eligible to participate in any performance-based incentive plans.

Each Non-Executive Director will also be entitled to reimbursement of reasonable expenses and reimbursement of fees for tax advice associated with completion of international tax returns and, if relevant, any gross-up for tax due to their role as a Bicycle Therapeutics plc Non-Executive Director.

Shareholder voting on remuneration matters at AGM

The table below sets out the previous votes cast at our AGM in June 2021 in respect of the Annual Remuneration Report.

	Votes for		Votes against		Votes withheld
	%	Number	%	Number	Number
Annual Remuneration Report	97.17	19,098,902	2.83	556,551	1,969,184

Withheld votes are not counted when calculating voting outcomes. The Directors' Remuneration Policy is renewed at least every three years.

On behalf of the Board

Veronica Jordan
Chair of the Compensation Committee
27 April 2022

Bicycle Therapeutics plc
year ended 31 December 2021

Directors' Report

The directors present their report and the audited financial statements of Bicycle Therapeutics plc (the "Parent Company") for the year ended 31 December 2021 and, the audited consolidated financial statements of Bicycle Therapeutics plc and its subsidiaries, BicycleTx Limited, BicycleRD Limited and Bicycle Therapeutics Inc. (the "Company") for the year ended 31 December 2021.

Bicycle Therapeutics plc is a public company limited by shares and incorporated and domiciled in England and Wales. BicycleTx Limited and BicycleRD Limited are registered in England and Wales. Bicycle Therapeutics Inc. is registered in the U.S.

This is the third year that UK statutory audited consolidated financial statements have been presented.

Where stated certain information is not shown in the directors report because it is shown in the Strategic Report instead under section 414C(11) of the Companies Act 2006 (the "Companies Act").

Change of name

On 22 May 2019, the Parent Company re-registered as a public company and changed its name from Bicycle Therapeutics Limited to Bicycle Therapeutics plc.

Results and dividends

The results of the Company for the year are set out on page 68. During the year ended 31 December 2021, no dividend was declared or paid (31 December 2020: $Nil). The directors do not recommend the payment of any further dividend.

Directors

The directors of the Parent Company who held office during the year and up to the date of signing the financial statements, unless otherwise stated, were as follows:

Catherine Bingham (resigned 28 June 2021)
Janice Bourque
Jose-Carlos Gutierrez-Ramos (appointed 17 March 2021)
Veronica Jordan
Richard Kender
Kevin Lee
Pierre Legault
Gregory Winter

Capital structure

Details of the issued share capital, together with details of shares issued during the year, are set out in note 18 to the financial statements. Following the Parent Company's initial public offering there is one class of ordinary shares which carries no right to fixed income. Each ordinary share carries the right to one vote at a general meeting of the Parent Company.

There are no specific restrictions on the size of a holding or on the transfer of shares, which are both governed by the general provisions of the Parent Company's articles of association and prevailing legislation. The directors are not aware of any agreements between holders of the Parent Company's shares that may result in restrictions on the transfer of securities or on voting rights.

No person has any special rights of control over the Parent Company's share capital and all issued shares are fully paid. Subject to the Companies Act and any relevant authority of the Parent Company in general meeting, the Parent Company has authority to issue new shares.

Political donations

No political donations were made, and no political expenditure was incurred, by the Company during the current and prior year. No contributions were made to any non-UK political party by the Company during the current and prior year.

Research and development activities

The directors are satisfied that research activities of the Company are progressing satisfactorily. Total research and development expenditure during the year was $47.8 million (year ended 31 December 2020: $34.1 million). The Directors have identified that the expenditure on research and development disclosed within Note 6 'Operating Loss' to the financial statements in the prior year was overstated by $14.8 million and has been corrected within these financial statements. The correction has no impact on profit or cash flows for the year or on opening reserves in the current year.

Going concern

The Company is involved in research and development activities and until it is able to convert this activity into a significant product revenue stream, it will be reliant upon obtaining additional funding in connection with continuing operations. More detailed analysis of the risks faced by the Company is given in the Strategic Report.

At 31 December 2021, the Company had cash of $438.7 million and the directors estimate the Company's existing cash at the date of approval of these financial statements is sufficient to continue to fund the Company's operating expense for at least 12 months from the date of that approval and that is therefore appropriate to prepare these financial statements on a going concern basis.

Employee involvement

The Company is committed to the continued development of employee involvement by an effective communications and consultative framework. Please refer to the "Employee, social, community and human rights matters" section included in our Strategic Report, beginning on page 14 of this document.

Greenhouse gas emissions, energy consumption and energy efficiency action

Please refer to the "Environmental matters" section included in our Strategic Report, beginning on page 14 of this document.

Financial risk management

Please refer to the "Financial risk management" section included in our Strategic Report, beginning on page 13 of this document.

Qualifying third party indemnity provisions

The Parent Company has made qualifying third-party indemnity provisions for the benefit of its directors and certain executives that were in force during the year and at the date of this report.

Disclosure of information to the auditors

So far as each person who was a director at the date of approving this report is aware, there is no relevant audit information, being information needed by the auditors in connection with preparing its reports, of which the auditors are unaware. Having made enquiries of fellow directors and the company's

auditors, each director has taken all the steps that he/she is obliged to take as a director in order to make himself/herself aware of any relevant audit information and to establish that the auditors are aware of that information.

Branches outside of the UK

The Parent Company has no overseas branches.

Future developments

Information on likely future developments in the business of the Company has been included in the Strategic Report on page 11.

Post balance sheet events

The directors are not aware of any events that have occurred subsequent to the year-end that may materially impact the results of the financial statements.

Statement of directors' responsibilities in respect of the financial statements

The directors are responsible for preparing the Annual Report and the financial statements in accordance with applicable law and regulation.

Company law requires the directors to prepare financial statements for each financial year. Under that law the directors have prepared the Parent Company's and the Company's financial statements in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards, comprising FRS 102 "The Financial Reporting Standard applicable in the UK and Republic of Ireland", and applicable law).

Under company law, directors must not approve the financial statements unless they are satisfied that they give a true and fair view of the state of affairs of the Parent Company and the Company and of the profit or loss of the Company for that period. In preparing the financial statements, the directors are required to:

- select suitable accounting policies and then apply them consistently;
- state whether applicable United Kingdom Accounting Standards, comprising FRS 102 have been followed, subject to any material departures disclosed and explained in the financial statements;
- make judgements and accounting estimates that are reasonable and prudent; and
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the Parent Company and the Company will continue in business.

The directors are responsible for safeguarding the assets of the Parent Company and the Company and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The directors are also responsible for keeping adequate accounting records that are sufficient to show and explain the Parent Company's and the Company's transactions and disclose with reasonable accuracy at any time the financial position of the Parent Company and the Company and enable them to ensure that the financial statements and the Directors' Remuneration Report comply with the Companies Act 2006.

Directors' confirmations

In the case of each director in office at the date the directors' report is approved:

- so far as the director is aware, there is no relevant audit information of which the Parent Company's and the Company's auditors are unaware; and
- they have taken all the steps that they ought to have taken as a director in order to make themselves aware of any relevant audit information and to establish that the Parent Company's and the Company's auditors are aware of that information.

Independent auditors

The auditors, PricewaterhouseCoopers LLP, have indicated their willingness to continue in office and a resolution concerning their re-appointment will be proposed at the forthcoming Annual General Meeting to be held on 27 June 2022.

The financial statements on pages 68 to 103 were approved by the board of directors on 14 April 2022.

This report was approved by the board of directors on 14 April 2022 and signed on behalf of the board of directors by:

Kevin Lee
Director
27 April 2022

Independent auditors' report to the members of Bicycle Therapeutics plc

Report on the audit of the financial statements

Opinion

In our opinion, Bicycle Therapeutics plc's group financial statements and parent company financial statements (the "financial statements"):

- give a true and fair view of the state of the group's and of the parent company's affairs as at 31 December 2021 and of the group's loss and the group's cash flows for the year then ended;
- have been properly prepared in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards, comprising FRS 102 "The Financial Reporting Standard applicable in the UK and Republic of Ireland", and applicable law); and
- have been prepared in accordance with the requirements of the Companies Act 2006.

We have audited the financial statements, included within the Annual report and financial statements (the "Annual Report"), which comprise: the consolidated and parent company balance sheets as at 31 December 2021; the consolidated statement of comprehensive income, the consolidated statement of changes in equity, the Parent Company statement of changes in equity and the consolidated statement of cash flows for the year then ended; and the notes to the financial statements, which include a description of the significant accounting policies.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) ("ISAs (UK)") and applicable law. Our responsibilities under ISAs (UK) are further described in the Auditors' responsibilities for the audit of the financial statements section of our report. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Independence

We remained independent of the group in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, which includes the FRC's Ethical Standard, as applicable to listed entities, and we have fulfilled our other ethical responsibilities in accordance with these requirements.

Our audit approach

Overview

Audit scope

- Full scope audit for four entities.
- 100% coverage of group's revenue and total assets and liabilities.

Key audit matters

- Revenue recognition (group)
- Recoverability of investments in subsidiaries and amounts owed by group undertakings (parent)

Materiality

- Overall group materiality: US$4,400,000 (2020: US$2,980,000) based on 5% of loss before tax.
- Overall parent company materiality: US$5,400,000 (2020: US$2,100,000) based on 1% of total assets, (restricted to 95% of overall group materiality for the purposes of our group audit).
- Performance materiality: US$3,300,000 (2020: US$2,235,000) (group) and US$4,050,000 (2020: US$1,575,000) (parent company).

The scope of our audit

As part of designing our audit, we determined materiality and assessed the risks of material misstatement in the financial statements.

Key audit matters

Key audit matters are those matters that, in the auditors' professional judgement, were of most significance in the audit of the financial statements of the current period and include the most significant assessed risks of material misstatement (whether or not due to fraud) identified by the auditors, including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. These matters, and any comments we make on the results of our procedures thereon, were addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

This is not a complete list of all risks identified by our audit.

Recoverability of investments in subsidiaries and amounts owed by group undertakings is a new key audit matter this year. COVID-19, which was a key audit matter last year, is no longer included because of the limited impact of the pandemic on the Group. Otherwise, the key audit matters below are consistent with last year.

Key audit matter	How our audit addressed the key audit matter
Revenue recognition (group) Refer to Note 3, Note 4 and Note 5 of the financial statements for management's disclosure of accounting policies, significant judgements and further explanation in the notes to the financial statements. The Group entered into a Collaboration and Licence Agreement with Ionis Pharmaceuticals Inc. ("Ionis") in the year. The Group granted to Ionis a worldwide exclusive licence under its relevant technology to research, develop, manufacture and commercialise products incorporating Bicycle peptides directed to the protein coded by the gene TFRC1 (transferrin receptor), or 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 made a non-refundable upfront payment of $31 million and will be required to make a low-single-digit million dollar payment upon acceptance of an investigational new drug application. Ionis will also 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. The Group concluded that the low-single-digit million dollar payments upon acceptance of an Investigational New Drug filing is a customer option, as Ionis has the contractual right to	We have performed the following procedures to address the key audit matter: • We have gained an understanding of the control environment surrounding the revenue cycle; • We have read the underlying collaboration and licence agreement and checked the consistency of the research scope in the executed agreement and management's accounting analysis; • We have assessed management's accounting memorandum including management's determination that the licence and research services are not distinct, the estimated standalone fair values of performance obligations, and the manner in which revenue should be recognised (over time or at a point in time) and concluded that the accounting treatment and methodology adopted is in line with FRS 102, other guidance available and industry practice; • We tested the arithmetic accuracy of the model developed to determine an option as a material right, to determine the probability of Ionis exercising an option, to determine transaction price and allocate it to the separately identifiable components, and considered the reasonableness of key assumptions, such as, in the case of

Key audit matter	How our audit addressed the key audit matter
choose to make the payment in exchange for the continued exclusive right to research, develop, manufacture and commercialise the product candidate, and the Group is not presently obligated to provide, and does not have a right to the consideration, for the additional goods or services prior to Ionis's exercise of the option. In assessing whether the options under the Agreement represent material rights, the Group considered the additional consideration the Group would be entitled to upon the option exercise and the standalone selling price of the underlying goods and services. For the material rights identified as performance obligations above, the Group concluded that each of the options to obtain credits provided Ionis with a discount that it otherwise would not have received without entering the Ionis Collaboration Agreement. The amount allocated to the material rights is recorded as deferred revenue and the Group commences revenue recognition upon exercise of or upon expiry of the respective option. The total transaction price was initially determined to be $38 million, consisting of the $31 million non-refundable upfront fee, the $3 million 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 licences and research and discovery performance obligation was based on the nature of the licences 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 realised 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. During the year, the Group recognised revenue of $4.2 million and $34.1 million of deferred revenue in connection with this agreement.	material rights, the probability that Ionis would exercise the option; • We tested the accounting model being applied to determine the extent of progress where revenue for performance obligations is recognised over time, including checking the arithmetic accuracy, time incurred to date and expected time yet to be incurred; • We have performed testing over manual journal postings which are considered to be at a heightened risk of fraud using our data analysis tool.

Key audit matter	How our audit addressed the key audit matter
Recoverability of investments in subsidiaries and amounts owed by group undertakings (parent) Refer to Note 14 for investment in subsidiaries and note 15 for amounts owed by the group undertakings. The Parent Company has investments in and intercompany receivables from both BicycleTx Limited and BicycleRD Limited (wholly owned subsidiary companies), both of which are currently loss making. The carrying value of the investment in subsidiary companies in the Parent Company's balance sheet at 31 December 2021 is $32,319k and that of amounts receivable from subsidiary companies is $130,434k. Under FRS102, the intrinsic value of the subsidiary company can be determined on an expected value basis, rather than considering specific scenarios of default. The measurement and recoverability of these balances has been assessed by management and they have concluded that there is no impairment since the market capitalisation of the Parent company implies a valuation of the subsidiary companies significantly greater than the carrying value of these balances since the intellectual property and collaboration contracts of the group are within the subsidiary companies.	We have performed following procedures to address the key audit matter: • We have gained an understanding of the control environment over investments in subsidiaries and intercompany transactions and balances; • We have obtained management's analysis of recoverability of intercompany receivables and investments, tested its mathematical accuracy; • We confirmed that the market capitalisation of the Parent Company exceeded the carrying value of these balances which was the primary evidence supporting management's conclusions; • We concluded that the accounting treatment and methodology adopted is in line with FRS 102, other guidance available and industry practice.

How we tailored the audit scope

We tailored the scope of our audit to ensure that we performed enough work to be able to give an opinion on the financial statements as a whole, taking into account the structure of the group and the parent company, the accounting processes and controls, and the industry in which they operate.

The Group comprises four entities, Bicycle Therapeutics plc (the parent company), BicycleTX Limited, BicycleRD Limited and Bicycle Therapeutics Inc. (the subsidiary companies). Full scope audits were performed over the financial information of these four entities and our work was fully substantive in nature. This approach provided 100% coverage of the Group's revenue and total assets and liabilities.

Materiality

The scope of our audit was influenced by our application of materiality. We set certain quantitative thresholds for materiality. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures on the individual financial statement line items and disclosures and in evaluating the effect of misstatements, both individually and in aggregate on the financial statements as a whole.

Based on our professional judgement, we determined materiality for the financial statements as a whole as follows:

	Financial statements – group	Financial statements – parent company
Overall materiality	US$4,400,000 (2020: US$2,980,000).	US$5,400,000 (2020: US$2,100,000).
How we determined it	5% of loss before tax	1% of total assets, (restricted to 95% of overall group materiality for the purposes of our group audit)
Rationale for benchmark applied	Based on the benchmarks used in the annual report and financial statements, loss before tax is one of the financial metrics used by the shareholders in assessing the performance of the Group and is a generally accepted auditing benchmark.	We believe that total assets is the most appropriate benchmark as the Parent Company is a holding company.

For each component in the scope of our group audit, we allocated a materiality that is less than our overall group materiality. The range of materiality allocated across components was $0.1 million and $4.2 million. Certain components were audited to a local statutory audit materiality that was also less than our overall group materiality.

We use performance materiality to reduce to an appropriately low level the probability that the aggregate of uncorrected and undetected misstatements exceeds overall materiality. Specifically, we use performance materiality in determining the scope of our audit and the nature and extent of our testing of account balances, classes of transactions and disclosures, for example in determining sample sizes. Our performance materiality was 75% (2020: 75%) of overall materiality, amounting to US$3,300,000 (2020: US$2,235,000) for the group financial statements and US$4,050,000 (2020: US$1,575,000) for the parent company financial statements.

In determining the performance materiality, we considered a number of factors — the history of misstatements, risk assessment and aggregation risk and the effectiveness of controls — and concluded that an amount at the upper end of our normal range was appropriate.

We agreed with those charged with governance that we would report to them misstatements identified during our audit above $220,000 (group audit) (2020: $130,000) and $270,000 (parent company audit) (2020: $105,000) as well as misstatements below those amounts that, in our view, warranted reporting for qualitative reasons.

Conclusions relating to going concern

Our evaluation of the directors' assessment of the group's and the parent company's ability to continue to adopt the going concern basis of accounting included:

- Discussion with management on progress of research programs in the year as well as future developments;
- Obtaining management's cash flow forecasts for the period to 31 December 2024, testing the mathematical accuracy of the calculations and assessing the completeness and accuracy of the data used; and
- Evaluation of management's assessment of key assumptions contained within the cash flow forecasts.

Based on the work we have performed, we have not identified any material uncertainties relating to events or conditions that, individually or collectively, may cast significant doubt on the group's and the parent company's ability to continue as a going concern for a period of at least twelve months from when the financial statements are authorised for issue.

In auditing the financial statements, we have concluded that the directors' use of the going concern basis of accounting in the preparation of the financial statements is appropriate.

However, because not all future events or conditions can be predicted, this conclusion is not a guarantee as to the group's and the parent company's ability to continue as a going concern.

Our responsibilities and the responsibilities of the directors with respect to going concern are described in the relevant sections of this report.

Reporting on other information

The other information comprises all of the information in the Annual Report other than the financial statements and our auditors' report thereon. The directors are responsible for the other information. Our opinion on the financial statements does not cover the other information and, accordingly, we do not express an audit opinion or, except to the extent otherwise explicitly stated in this report, any form of assurance thereon.

In connection with our audit of the financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements or our knowledge obtained in the audit, or otherwise appears to be materially misstated. If we identify an apparent material inconsistency or material misstatement, we are required to perform procedures to conclude whether there is a material misstatement of the financial statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report based on these responsibilities.

With respect to the Strategic report and Directors' report, we also considered whether the disclosures required by the UK Companies Act 2006 have been included.

Based on our work undertaken in the course of the audit, the Companies Act 2006 requires us also to report certain opinions and matters as described below.

Strategic report and Directors' report

In our opinion, based on the work undertaken in the course of the audit, the information given in the Strategic report and Directors' report for the year ended 31 December 2021 is consistent with the financial statements and has been prepared in accordance with applicable legal requirements.

In light of the knowledge and understanding of the group and parent company and their environment obtained in the course of the audit, we did not identify any material misstatements in the Strategic report and Directors' report.

Directors' Remuneration

In our opinion, the part of the Directors' Remuneration Report to be audited has been properly prepared in accordance with the Companies Act 2006.

Responsibilities for the financial statements and the audit

Responsibilities of the directors for the financial statements

As explained more fully in the Statement of directors' responsibilities in respect of the financial statements, the directors are responsible for the preparation of the financial statements in accordance with the applicable framework and for being satisfied that they give a true and fair view. The directors are also responsible for such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the directors are responsible for assessing the group's and the parent company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the directors either intend to liquidate the group or the parent company or to cease operations, or have no realistic alternative but to do so.

Auditors' responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditors' report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

Irregularities, including fraud, are instances of non-compliance with laws and regulations. We design procedures in line with our responsibilities, outlined above, to detect material misstatements in respect of irregularities, including fraud. The extent to which our procedures are capable of detecting irregularities, including fraud, is detailed below.

Based on our understanding of the group and industry, we identified that the principal risks of non-compliance with laws and regulations related to clinical trial regulations, patent protection and regulatory compliance, employment laws including health and safety at work regulations, and we considered the extent to which non-compliance might have a material effect on the financial statements. We also considered those laws and regulations that have a direct impact on the financial statements such as corporate taxation and the Companies Act 2006. We evaluated management's incentives and opportunities for fraudulent manipulation of the financial statements (including the risk of override of controls), and determined that the principal risks were related to misappropriation of funds, posting of inappropriate accounting entries to manipulate financial results and management bias in significant accounting estimates. Audit procedures performed by the engagement team included:

- enquiries of management and the entity's General Counsel around actual and potential litigation and claims including known or suspected instances of non-compliance with laws and regulations and fraud;
- inspecting minutes of meetings of the Board of Directors and its Committees;
- evaluation of control environment designed by management to detect and prevent irregularities;
- verifying financial statements disclosures and agreeing to supporting documentation to assess that disclosures are in compliance with applicable laws and regulations;
- identifying and testing journal entries, in particular any journal entries posted with unusual account combinations;
- challenging the assumptions made by management in their significant accounting estimates, in particular in relation to revenue recognition and project accruals; and
- designing audit procedures to incorporate unpredictability around nature, timing and extent of our testing.

There are inherent limitations in the audit procedures described above. We are less likely to become aware of instances of non-compliance with laws and regulations that are not closely related to events and transactions reflected in the financial statements. Also, the risk of not detecting a material misstatement due to fraud is higher than the risk of not detecting one resulting from error, as fraud may involve deliberate concealment by, for example, forgery or intentional misrepresentations, or through collusion.

Our audit testing might include testing complete populations of certain transactions and balances, possibly using data auditing techniques. However, it typically involves selecting a limited number of items for testing, rather than testing complete populations. We will often seek to target particular items for testing based on their size or risk characteristics. In other cases, we will use audit sampling to enable us to draw a conclusion about the population from which the sample is selected.

A further description of our responsibilities for the audit of the financial statements is located on the FRC's website at: www.frc.org.uk/auditorsresponsibilities. This description forms part of our auditors' report.

Use of this report

This report, including the opinions, has been prepared for and only for the parent company's members as a body in accordance with Chapter 3 of Part 16 of the Companies Act 2006 and for no other purpose. We do not, in giving these opinions, accept or assume responsibility for any other purpose or to any other person to whom this report is shown or into whose hands it may come save where expressly agreed by our prior consent in writing.

Other required reporting

Companies Act 2006 exception reporting

Under the Companies Act 2006 we are required to report to you if, in our opinion:

- we have not obtained all the information and explanations we require for our audit; or
- adequate accounting records have not been kept by the parent company, or returns adequate for our audit have not been received from branches not visited by us; or
- certain disclosures of directors' remuneration specified by law are not made; or
- the parent company financial statements and the part of the Directors' Remuneration Report to be audited are not in agreement with the accounting records and returns.

We have no exceptions to report arising from this responsibility.

David Farmer (Senior Statutory Auditor)
for and on behalf of PricewaterhouseCoopers LLP
Chartered Accountants and Statutory Auditors
Cambridge
27 April 2022

Bicycle Therapeutics plc
Registered in England No: 11036004

Consolidated statement of comprehensive income for the year ended 31 December 2021

	Note	Year ended 31 December 2021 $'000	Year ended 31 December 2020 $'000
Revenue	5	**11,144**	**10,390**
Administrative expenses – exceptional item	6	**—**	**(4,696)**
Administrative expenses – other	6	**(101,039)**	**(66,070)**
Operating income	6	**2,988**	**570**
Operating loss	6	**(86,907)**	**(59,806)**
Interest receivable and similar income	7	**120**	**683**
Interest payable and similar expenses	7	**(3,017)**	**(487)**
Net interest (expense)/income		**(2,897)**	**196**
Loss before taxation		**(89,804)**	**(59,610)**
Tax on loss	8	**12,474**	**9,255**
Loss for the financial year		**(77,330)**	**(50,355)**
Other comprehensive income/(expenses)			
Foreign exchange translation differences		**1,948**	**(4,132)**
Total comprehensive expense for the year		**(75,382)**	**(54,487)**
Basic and diluted loss per ordinary share	23	**$ (3.09)**	**$ (2.63)**
Weighted average ordinary shares		**25,061,734**	**19,145,938**

The notes of pages 73 to 103 are an integral part of the consolidated financial statements.

Bicycle Therapeutics plc
Registered in England No: 11036004

Consolidated and Parent Company balance sheets as at 31 December 2021

	Note	Consolidated		Parent Company	
		As at 31 December 2021 $'000	As at 31 December 2020 $'000	As at 31 December 2021 $'000	As at 31 December 2020 $'000
Fixed assets					
Intangible assets	12	**64**	85	—	—
Tangible assets	13	**3,123**	2,317	—	—
Investments in subsidiaries	14	—	—	**32,319**	17,048
		3,187	2,402	**32,319**	17,048
Current assets					
Debtors	15	**23,746**	21,341	**130,463**	84,192
Cash at bank and in hand		**438,680**	135,990	**381,774**	109,745
		462,426	157,331	**512,237**	193,937
Creditors: amounts falling due within one year	16	**(39,927)**	(23,287)	—	—
Net current assets		**422,499**	134,044	**512,237**	193,937
Total assets less current liabilities		**425,686**	136,446	**544,556**	210,985
Creditors: amounts falling after more than one year	17	**(79,572)**	(35,954)	**(29,873)**	(14,505)
Net assets		**346,114**	100,492	**514,683**	196,480
Capital and reserves					
Called up share capital	18	**384**	266	**384**	266
Share premium account	18	**414,071**	105,014	**414,071**	105,014
Other reserve	18	**(3,442)**	—	**(3,442)**	—
Exchange reserve	18	**(3,188)**	(5,136)	**(10)**	(10)
General reserve	18	**31,857**	16,586	**31,857**	16,586
(Accumulated losses)/retained earnings	18	**(93,568)**	(16,238)	**71,823**	74,624
Total shareholders' funds		**346,114**	100,492	**514,683**	196,480

The Parent Company's loss for the financial year ended 31 December 2021 is $2,801k (year ended 31 December 2020: income of $126k).

The Consolidated and Parent Company financial statements on pages 68 to 103 were approved by the board of directors on 14 April 2022 and signed on behalf of the board of directors by:

Kevin Lee
Director
27 April 2022

The notes of pages 73 to 103 are an integral part of the financial statements.

Bicycle Therapeutics plc
Registered in England No: 11036004

Consolidated statement of changes in equity for the year ended 31 December 2021

	Called up share capital $'000	Share premium account $'000	Exchage reserve $'000	General reserve $'000	(Accumulated losses)/ retained earnings $'000	Total shareholders' funds $'000
Balance as at 1 January 2020	**227**	**56,652**	**(1,004)**	**7,596**	**34,117**	**97,588**
Loss for the year	—	—	—	—	(50,355)	(50,355)
Shares issued	39	48,362	—	—	—	48,401
Share options granted	—	—	—	8,990	—	8,990
Total transactions with owners, recognised directly in equity	**39**	**48,362**	—	**8,990**	—	**57,391**
Currency translation adjustment	—	—	(4,132)	—	—	(4,132)
Balance as at 31 December 2020	**266**	**105,014**	**(5,136)**	**16,586**	**(16,238)**	**100,492**
Loss for the year	—	—	—	—	(77,330)	(77,330)
Shares issued ADS's (net of costs of issue)	104	290,888	—	—	—	290,992
Shares issued pursuant to the Ionis share purchase agreement (note 5)	4	10,996	—	—	—	11,000
Premium to fair value of shares issued with respect to the Ionis Share Purchase Agreement (note 5)	—	—	—	—	(3,442)	(3,442)
Shares issued from the exercise of options	10	7,173	—	—	—	7,183
Share options granted	—	—	—	15,271	—	15,271
Total transactions with owners, recognised directly in equity	**118**	**309,057**	—	**15,271**	**(3,442)**	**321,004**
Currency translation adjustment	—	—	1,948	—	—	1,948
Balance as at 31 December 2021	**384**	**414,071**	**(3,188)**	**31,857**	**(97,010)**	**346,114**

The notes of pages 73 to 103 are an integral part of the consolidated financial statements.

Bicycle Therapeutics plc
Registered in England No: 11036004

Parent Company statement of changes in equity for the year ended 31 December 2021

	Called up Share Capital $'000	Share premium account $'000	Exchange reserve $'000	General reserve $'000	Retained earnings $'000	Total shareholders' funds $'000
Balance as at 1 January 2020	**227**	**56,652**	**(10)**	**7,596**	**74,498**	**138,963**
Profit for the year	—	—	—	—	126	126
Shares issued	39	48,362	—	—	—	48,401
Share options granted	—	—	—	8,990	—	8,990
Total transactions with owners, recognised directly in equity	**39**	**48,362**	**—**	**8,990**	—	**57,391**
Currency translation adjustment	—	—	—	—	—	—
Balance as at 31 December 2020	**266**	**105,014**	**(10)**	**16,586**	**74,624**	**196,480**
Loss for the year	—	—	—	—	(2,801)	(2,801)
Shares issued ADS's (net of costs of issue)	104	290,887	—	—	—	290,991
Shares issued pursuant to the Ionis share purchase agreement (note 5)	4	10,996	—	—	—	11,000
Premium to fair value of shares issued with respect to the Ionis Share Purchase Agreement (note 5)	—	—	—	—	(3,442)	(3,442)
Shares issued from the exercise of options	10	7,174	—	—	—	7,184
Share options granted	—	—	—	15,271	—	15,271
Total transactions with owners, recognised directly in equity	**118**	**309,057**	—	**15,271**	**(3,442)**	**321,004**
Currency translation adjustment	—	—	—	—	—	—
Balance as at 31 December 2021	**384**	**414,071**	**(10)**	**31,857**	**68,381**	**514,683**

The notes of pages 73 to 103 are an integral part of the financial statements.

Bicycle Therapeutics plc
Registered in England No: 11036004

Consolidated statement of cash flows for the year ended 31 December 2021

	Note	Year ended 31 December 2021 $'000	Year ended 31 December 2020 $'000
Cash flow from operating activities	19	**(24,657)**	(24,728)
Taxation received		**9,135**	6,777
Net cash used in operating activities		**(15,522)**	(17,951)
Cash flow from investing activities			
Purchase of tangible assets		**(2,030)**	(1,200)
Interest received		**120**	756
Net cash used in investing activities		**(1,910)**	(444)
Cash flow from financing activities			
Interest paid		**(2,515)**	(408)
Proceeds from issuance of ADS's (net of costs of issue)		**290,992**	48,129
Proceeds from issuance of ordinary shares pursuant to the Ionis share purchase agreement		**11,000**	—
Proceeds from the exercise of share options		**7,183**	272
Proceeds from issuance of debt (net of costs of issue)		**15,000**	14,427
Net cash generated from financing activities		**321,660**	62,420
Net increase in cash and cash equivalents		**304,228**	44,025
Exchange loss on cash and cash equivalents		**(1,538)**	(152)
Cash and cash equivalents at the beginning of the year		**135,990**	92,117
Cash and cash equivalents at the end of the year		**438,680**	135,990

The notes of pages 73 to 103 are an integral part of the consolidated financial statements.

1 General information

Bicycle Therapeutics plc (the "Parent Company") and, together with its subsidiaries (the "Company"), is a clinical-stage biopharmaceutical company developing a novel and differentiated 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 Parent Company is a public company limited by shares and incorporated in England and Wales and quoted on the NASDAQ capital market under the ticker BCYC.

Its registered number is: 11036004.

Its registered office is: Building 900, Babraham Research Campus, Cambridgeshire, CB22 3AT.

2 Statement of compliance

The consolidated financial statements of the Company and the financial statements of the Parent Company have been prepared in compliance with UK Accounting Standards, including Financial Reporting Standard 102, 'The Financial Reporting Standard applicable in the United Kingdom and the Republic of Ireland' and the Companies Act 2006 (the "Companies Act").

3 Summary of significant accounting policies

Basis of preparation

These financial statements are prepared on a going concern basis, under the historical cost convention, as modified by the recognition of certain financial assets and liabilities measured at fair value. Currently there are no financial assets and liabilities measured at fair value.

The accompanying consolidated financial statements of the Company 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 financial statements have been prepared under the historical cost accounting rules and in accordance with the Companies Act.

Accounting policies have been applied consistently other than when new policies have been adopted.

The Company has taken advantage of the exemption in section 408 of the Companies Act from presenting its individual profit and loss account.

The preparation of financial statements requires the use of certain critical accounting estimates. It also requires management to exercise its judgement in the process of applying the Parent Company and the Company accounting policies. The areas involving a higher degree of judgement or complexity, or areas where assumptions and estimates are significant to the financial statements, are disclosed in note 4.

Exemptions for qualifying entities under FRS 102

FRS 102 allows a qualifying entity certain disclosure exemptions, subject to conditions, from preparing a Parent Company statement of cash flows, on the basis that it is a qualifying entity and the Parent Company's cash flows are included in the consolidated statement of cashflows. In addition, the Parent Company is exempted from disclosing share based payment arrangements required under FRS 102 paragraphs 26.18(b), 26.19 to 26.21 and 26.23 concerning its own equity instruments as the Parent Company financial statements are presented with the consolidated financial statements and the relevant disclosures are included therein.

3 Summary of significant accounting policies (continued)

Parent Company has also taken the exemption available from disclosing the company key management compensation as required by FRS102 paragraph 33.7.

Going concern

The Company is involved in research and development activities and until it is able to convert this activity into a significant product revenue stream, it will be reliant upon obtaining additional funding in connection with continuing operations. More detailed analysis of the risks faced by the Company is given in the Strategic Report.

At 31 December 2021, the Company had cash of $438.7 million and the directors estimate the Company's existing cash at the date of approval of these financial statements is sufficient to continue to fund the Company's operating expense for at least 12 months from the date of that approval and that is therefore appropriate to prepare these financial statements on a going concern basis.

Revenue

Revenue represents the fair value of amounts received or receivable in respect of collaborative research agreements, license fees or milestone payments (excluding value added tax). These are recognised as revenue when the specific conditions stipulated in the agreements have been satisfied and the significant risks and rewards of ownership have been transferred to the customer.

Licensing agreements may consist of multiple elements and provide for various forms of consideration terms, such as upfront development, regulatory and sales milestones, sales-based royalties and similar payments. To account for arrangements with multiple elements, separately identifiable components within the contract and the arrangement transaction price are identified. Development and regulatory approval milestones are included within the allocated transaction price only when it becomes probable that economic benefits will flow to the entity and the amount of revenue can be measured with reliability.

The fair value of the arrangement transaction price is allocated to the different separately identifiable components based on the relative stand-alone selling price of those services provided. The allocated transaction price is recognised over the respective performance period of each separately identifiable component. Amounts received in advance of the revenue recognition criteria being met are initially reported as deferred revenue.

The Company provides research and development services to its customers which often culminate in the provision of a license to developed intellectual property. Where services are provided in the development or identification of a licensed molecule, the services are not considered to be a separately identifiable component to the customer/licensor. Any upfront income received under such arrangements is considered to be consideration for the development services and it is recognised over the development term. When the services performed are an indeterminate number of acts over a specified period of time, revenue is recognised on a straight-line basis. When performance of services can be estimated reliably, the Company recognises revenue associated with the transaction by reference to the stage of completion of the transaction at the end of the reporting period. Where arrangements involve upfront consideration allowing customers the option to select licenses and/or research and development services in relation to additional targets that represent a material right, such consideration is deferred until the option is exercised (in which case the revenue is recognised as the related services are performed) or expires (in which case the revenue is recognised immediately, as the Company has no further obligations under the arrangement).

Customer options for future deliverables are accounted for as separate arrangements when they occur.

Where the Company grants a license to its intellectual property and there are no further conditions stipulated in the agreement related to separately identifiable components and the significant risks and rewards

3 Summary of significant accounting policies (continued)

of ownership have been transferred to the customer the license revenues are recognised when receipt of subsequent milestones is probable. This is typically when the milestone event is achieved or satisfied.

Exceptional items

The Company classifies certain one-off charges or credits that have a material impact on the company's financial results as 'exceptional items'. They are items that are material either because of their size or their nature and are non-recurring. They are disclosed separately to provide further understanding of the financial performance of the Company.

Impairment of debtors

The Company makes an estimate of the recoverable value of trade and other debtors. When assessing impairment of trade and other debtors, management considers factors including the current credit rating of the debtor, the ageing profile of debtors and historical experience.

Impairment of non-financial assets

At each balance sheet date non-financial assets not carried at fair value are assessed to determine whether there is an indication that the asset may be impaired. If there is such an indication the recoverable amount of the asset is compared to the carrying amount of the asset. If the recoverable amount of the asset is estimated to be lower than the carrying amount, the carrying amount is reduced to its recoverable amount. An impairment loss is recognised in the profit and loss account.

Tangible assets and depreciation

Tangible fixed assets are stated at cost less accumulated depreciation and accumulated impairment losses. The cost of tangible fixed assets is their purchase cost, together with any incidental costs of acquisition. The assets' residual values and useful lives are reviewed, and adjusted, if appropriate, at the end of each reporting period. The effect of any change is accounted for prospectively.

Land is not depreciated. Depreciation on other assets is calculated using the straight-line method to their residual values over their estimated useful lives, as follows:

Laboratory equipment	3 to 5 years
Office equipment	3 years
Computer equipment	3 years
Leasehold improvements	over the remaining period of the lease

Intangible assets and amortisation

Intangible assets comprise intellectual property licenses and are stated at capitalised cost less accumulated amortisation and accumulated impairment losses.

Amortisation is calculated, using the straight-line method, to allocate the depreciable amount of the assets to their residual values over their estimated useful lives, assessed by the directors on a case-by-case basis, as follows:

- Intellectual property licences 5 to 15 years

The assets are reviewed for impairment if there is an indication that the carrying amount may be impaired. Provision is made against the carrying value of such assets when an impairment in value is deemed to have occurred.

3 Summary of significant accounting policies (continued)

Costs associated with maintaining intellectual property are recognised as an expense as incurred. Amortisation is included in other operating expenses in the profit and loss account.

Cash and cash equivalents

Cash and cash equivalents includes cash in hand, deposits held at call with banks, other short-term highly liquid investments with original maturities of three months or less and bank overdrafts. Bank overdrafts, when applicable, are shown within borrowings in current liabilities.

Leases

Leases that do not transfer all the risks and rewards of ownership are classified as operating leases. Payments under operating leases are charged to the profit and loss account on a straight-line basis over the period of the lease. Incentives received to enter into an operating lease are credited to the profit and loss account, to reduce the lease expense, on a straight line basis over the period of the lease.

Leases of assets that transfer substantially all the risks and rewards incidental to ownership are classified as finance leases. The Company has no finance leases. The Company's lease terms include the period covered by extension options or exclude the period covered by termination options when it is reasonably certain that the Company will exercise that option.

Debtors

Short term debtors are measured at transaction price, less any impairment.

Creditors

Short term creditors are measured at the transaction price. Other financial liabilities, including loans, are measured initially at fair value, net of transaction costs, and are measured subsequently at amortised cost using the effective interest method.

Investments in subsidiaries — Parent Company

Investments in subsidiaries are held at cost less accumulated impairment losses.

Provisions and contingencies

Provisions

Provisions are recognised when the Company has a present legal or constructive obligation as a result of past events; it is probable that an outflow of resources will be required to settle the obligation; and the amount of the obligation can be estimated reliably.

Where there are a number of similar obligations, the likelihood that an outflow will be required in settlement is determined by considering the class of obligations as a whole.

Provisions are measured at the present value of the expenditures expected to be required to settle the obligation using a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the obligation. The increase in the provision due to passage of time is recognised as a finance cost.

3 Summary of significant accounting policies (continued)

Contingencies

Contingent liabilities are not recognised, except those acquired in a business combination. Contingent liabilities arise as a result of past events when i) it is not probable that there will be an outflow of resources or that the amount cannot be reliably measured at the reporting date or ii) when the existence will be confirmed by the occurrence or non-occurrence of uncertain future events not wholly within the Company's control. Contingent liabilities are disclosed in the financial statements unless the probability of an outflow of resource is remote. Contingent assets are not recognised. Contingent assets are disclosed in the financial statements when an inflow of economic benefits is probable.

Grant income

Government grants are not recognised until there is reasonable assurance that the Company will comply with the conditions of the grants and also that the grants will be received. Government grants are recognised in profit or loss on a systematic basis over the periods in which the Company recognises as expenses the related costs for which the grants are intended to compensate. Grant income is recognised gross in the income statement as operating income.

Interest income

Interest income is recognised using the effective interest rate method.

Employee benefits

The Company provides a range of benefits to employees, including annual bonus arrangements, paid holiday arrangements and defined contribution pension plans.

Short term benefits

Short term benefits, including holiday pay and other non-monetary benefits are recognised as an expense in the period in which the service is received.

Pension costs

The Company operates a defined contribution plan for its UK employees and a defined-contribution savings plan under Section 401(k) for its US employees. Under these plans the company pays fixed contributions into a separate entity. Once the contributions have been paid the company has no further payment obligations. The contributions are recognised as an expense when they are due. Differences between contributions payable and contributions actually paid in the period are shown as either accruals or prepayments at the year end. The assets of the plan are held separately from the Company in independently administered funds.

Share-based payments

The Company provides share-based payment arrangements to certain employees.

Equity-settled arrangements are measured at fair value (excluding the effect on non-market based vesting conditions) at the date of the grant. The fair value is expensed on a graded basis over the vesting period. The amount recognised as an expense is adjusted to reflect the actual number of shares or options that will vest. An attrition rate based on the Company's average historic attrition over the past period corresponding to the length of the vesting period is used.

3 Summary of significant accounting policies (continued)

Where equity-settled arrangements are modified, and are of benefit to the employee, the incremental fair value is recognised over the period from the date of modification to date of vesting. Where a modification is not beneficial to the employee there is no change to the charge for share-based payment. Settlements and cancellations are treated as an acceleration of vesting and the unvested amount is recognised immediately in the income statement.

The fair value of each share option award is based on the fair value of the Parent Companys shares, less any applicable purchase price. The fair value of each share option is estimated using the Black-Scholes option-pricing model which requires inputs based on certain subjective assumptions, including the fair value of shares, the expected share price volatility, the expected term of the award, the risk-free interest rate and expected dividends. Expected volatility is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information was available. The historical volatility is calculated based on a period of time commensurate with the assumption used for the expected term.

Provision is made for National Insurance contributions on outstanding share options that are expected to be exercised using the latest enacted National Insurance rates applied to the difference between the market value of the underlying shares at the balance sheet date and the option exercise price. The Company has no cash-settled arrangements. The Parent Company has no employees and thus there is no charge in the income statement for share-based payments. The charge for share-based payments has been recognised as an increase in cost of investment in subsidiaries.

Annual bonus plan

The Company operates an annual bonus plan for employees. An expense is recognised in the profit and loss account when the Company has a legal or constructive obligation to make payments under the plan as a result of past events and a reliable estimate of the obligation can be made.

Taxation

Taxation expense for the year comprises current and deferred tax recognised in the reporting year. Tax is recognised in the statement of comprehensive income, except to the extent that it relates to items recognised in other comprehensive income or directly in equity. In this case tax is also recognised in other comprehensive income or directly in equity respectively.

Current tax

Current tax is the amount of income tax payable in respect of the taxable profit for the year or prior years. Tax is calculated on the basis of tax rates and laws that have been enacted or substantively enacted by the year end. Management periodically evaluates positions taken in tax returns with respect to situations in which applicable tax regulation is subject to interpretation. It establishes provisions where appropriate on the basis of amounts expected to be paid to the tax authorities.

Income tax credit

The Company benefits from the UK research and development tax credit regime under both the small and medium sized enterprise ("SME") scheme and by claiming a Research and Development Expenditure Credit ("RDEC") in respect of grant funded projects. Under the SME regime, a portion of the Company's losses are surrendered for a cash rebate of up to 33.3% of eligible expenditures. Such credits are calculated based on the amount and nature of the research and development expenditure incurred and are accounted for within the tax provision in the year in which the expenditures were incurred.

3 Summary of significant accounting policies (continued)

Deferred Tax

Full provision is made for deferred tax assets and liabilities arising from timing differences between the recognition of gains and losses in the accounts and their recognition for tax purposes.

Deferred tax is measured using tax rates and laws that have been enacted or substantively enacted by the period end and that are expected to apply to the reversal of the timing difference.

Deferred tax is recognised on all timing differences at the reporting date. Unrelieved tax losses and other deferred tax assets are only recognised when it is probable that they will be recovered against the reversal of deferred tax liabilities or other future taxable profits.

Research and development

Expenditure on research and development is written off against the profits in the year which it is incurred.

Related party transactions

The Company discloses transactions with related parties which are not wholly owned within the same group. Where appropriate, transactions of a similar nature are aggregated unless, in the opinion of the directors, separate disclosure is necessary to understand the effect of the transactions on the financial statements.

Foreign currencies

Transactions in foreign currencies are recorded using the rate of exchange ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are translated using the rate of exchange ruling at the balance sheet date and the gains or losses on translation are included in the statement of comprehensive income. 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. Adjustments that arise from exchange rate changes on transactions denominated in a currency other than the local currency are included as income or expense as incurred.

Basis of consolidation

Subsidiaries are entities controlled by the Parent Company. Control exists when the Parent Company has the power to govern the financial and operating policies of an entity to obtain benefits from its activities. In assessing control, the Parent Company takes into consideration potential voting rights. The acquisition date is the date on which control is transferred to the acquirer. The financial statements of subsidiaries are included in the financial statements from the date control is achieved to the date control ceases. All intra-group transactions, balances, income and expenses are eliminated on consolidation.

Functional and presentational currency

Functional currency

The Parent Company's functional currency is the U.S. dollar.

The Parent Company's subsidiaries in the UK, BicycleTx Limited and BicycleRD Limited, use British pound sterling as their functional currencies and their results have been translated into U.S. dollars for inclusion in these consolidated financial statements. The functional currency of the Parent Company's subsidiary in the U.S., Bicycle Therapeutics Inc., is the U.S. dollar.

3 Summary of significant accounting policies (continued)

Presentational currency

The presentational currency is U.S. dollars, rounded to the nearest $000, for all years presented in these financial statements.

The Company translates the assets and liabilities of BicycleTx Limited and BicycleRD Limited into U.S. dollars at the exchange rate in effect on the balance sheet date. Revenue and expenses are translated at the average exchange rate in effect during the period. Unrealised translation gains and losses are recorded as a cumulative translation adjustment, which is included in the statement of changes in equity.

Share Capital

Ordinary shares are classified as equity. Incremental costs directly attributable to the issue of new ordinary shares or options are shown in equity as a deduction from the proceeds.

Warrants issued by the Company are recognised and classified as equity when upon exercise, the Parent Company would issue a fixed amount of its own equity instruments (ordinary shares) in exchange for a fixed amount of cash or another financial asset. Consideration received, net of incremental costs directly attributable to the issue of such new warrants, is shown in equity. Such warrants are not remeasured at fair value in subsequent reporting periods.

Finance costs

Finance costs are charged to the statement of comprehensive income over the term of the debt using the effective interest method so that the amount charged is at a constant rate on the carrying amount. Issue costs are initially recognised as a reduction in the proceeds of the associated capital instrument.

Financial Instruments

The Company has chosen to adopt Sections 11 and 12 of FRS102 in respect of financial instruments.

Financial assets:

Basic financial assets, including trade and other receivables, cash and bank balances, loans to the Parent Company's subsidiaries and investments in commercial paper, are initially recognised at transaction price, unless the arrangement constitutes a financing transaction, where the transaction is measured at the present value of the future receipts discounted at a market rate of interest.

Such assets are subsequently carried at amortised cost using the effective interest method.

At the end of each reporting year financial assets measured at amortised cost are assessed for objective evidence of impairment. If an asset is impaired the impairment loss is the difference between the carrying amount and the present value of the estimated cash flows discounted at the asset's original effective interest rate. The impairment loss is recognised in profit or loss.

If there is a decrease in the impairment loss arising from an event occurring after the impairment was recognised the impairment is reversed. The reversal is such that the current carrying amount does not exceed what the carrying amount would have been had the impairment not previously been recognised. The impairment reversal is recognised in profit or loss.

Financial assets are derecognised when (a) the contractual rights to the cash flows from the asset expire or are settled, or (b) substantially all the risks and rewards of the ownership of the asset are transferred to

3 Summary of significant accounting policies (continued)

another party or (c) control of the asset has been transferred to another party who has the practical ability to unilaterally sell the asset to an unrelated third party without imposing additional restrictions

Financial liabilities:

Basic financial liabilities, including trade and other payables, bank loans and preference shares that are classified as debt net of issue costs, are initially recognised at transaction price, unless the arrangement constitutes a financing transaction, where the debt instrument is measured at the present value of the future receipts discounted at a market rate of interest.

Debt instruments are subsequently carried at amortised cost, using the effective interest rate method.

Trade payables are obligations to pay for goods or services that have been acquired in the ordinary course of business from suppliers. Accounts payable are classified as current liabilities if payment is due within one year or less. If not, they are presented as non-current liabilities. Trade payables are recognised initially at transaction price and subsequently measured at amortised cost using the effective interest method.

Financial liabilities are derecognised when the liability is extinguished, that is when the contractual obligation is discharged, cancelled or expires.

4 Critical accounting judgements and estimation uncertainty

Estimates and judgements are continually evaluated and are based on historical experience and other factors, including expectations of future events that are believed to be reasonable under the circumstances.

Revenue in respect of the Discovery Collaboration and License Agreement with Genentech and the Evaluation and Option, Collaboration and Share Purchase Agreements with Ionis are recognised according to the revenue accounting policy. Because of the size and scope Note 5 includes more details of the key assumptions and estimates. Management has identified the separate components of the agreements and has allocated the arrangement considerations to the identified components of the agreements based on the relative estimated fair value.

Genentech expansion option

In October 2021, Genentech exercised an expansion option to add an additional Genentech Collaboration Program and paid to the Company an expansion fee of $10.0 million. Genentech also elected for Bicycle to perform discovery and optimisation services for a targeting arm, and the Company received an additional payment of $1.0 million for additional research services. Management concluded that the exercise of the expansion option and targeting arm option is a continuation of an existing contract as the customer decided to purchase additional goods and services contemplated in the original contract. The arrangement consideration was allocated to the separate components on the same basis as the initial allocation of the Genentech Collaboration Agreement (note 5).

Ionis collaboration and license

In July 2021 the Company entered into a Collaboration and Licence agreement with Ionis following Ionis's exercise of its option under the Evaluation and Option Agreement dated 31 December 2020. Management determined that the option exercise by Ionis constituted a continuation of the existing arrangement. Therefore, the $3.0 million in deferred revenue under the Evaluation and Option Agreement at 31 December 2020 was included in the transaction price of the collaboration and license agreement.

Concurrently with the execution of the Ionis Collaboration Agreement in July, 2021, the Company entered into the Ionis Share Purchase Agreement with Ionis, pursuant to which Ionis purchased the Ionis

4 Critical accounting judgements and estimation uncertainty (continued)

Shares at a price per share of $38.94, for an aggregate purchase price of approximately $11.0 million. 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. Management 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.

The Company has concluded that the exclusive license to research, develop, manufacture and commercialise products under the Collaboration and Licence agreement 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, and as such are a single component. In assessing whether options to purchase additional goods and services under the Ionis Collaboration Agreement represent material rights, management 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. Management 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 (note 5) and therefore are separate components. The transaction price was allocated to the separate identifiable components based on the relative estimated standalone selling prices of each separate component. The transaction price was allocated to the performance obligations based on the relative estimates by management of standalone selling prices of each separate component.

Ionis amendment

In December 2021, the Company and Ionis entered into an amendment to the Ionis Collaboration Agreement. Ionis paid the Company $1.6 million and the Company agreed to perform additional research Services. Management concluded that the 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 standalone selling price. The Company concluded that the option does not contain a material right and the Company will recognise the $0.8 million as revenue as the underlying services are performed using a proportional performance model over the period of service using input based measurements.

Parent company investments

The Parent Company has investments in and intercompany receivables due from both BicycleTx Limited and BicycleRD Limited both of which are currently loss making. The Directors have assessed the recoverability of these balances and has concluded that there is no impairment. The Company's value is based on its intellectual property which is held within BicycleTx Limited and BicycleRD Limited.

The Directors do not consider there to be any other critical accounting estimates or assumptions that have a significant risk of causing a material adjustment to the carrying amounts of assets or liabilities within the next financial year.

5 Revenue

All the Company's revenue was generated from research collaborations. The Company's revenues are attributed to the operations of the Company in the United Kingdom. The following is a summary of the Company's customers by their geography:

5 Revenue (continued)

	2021 $'000	2020 $'000
Europe	851	5,087
North America	9,902	4,892
United Kingdom	391	411
	11,144	10,390

No further segmental information is given. A segment is a distinguishable component of the Company that is engaged in either providing related products or services which is subject to risks and rewards that are different from those of other segments. The CEO reviews the Company's internal reporting in order to assess performance and allocate resources. Management has determined that there is one operating segment based on these reports.

Ionis Evaluation and Option Agreement

Due to the scope of this collaboration and size of the upfront fee further details of the accounting judgements are provided below.

On 31 December 2020 the Company entered into an Evaluation and Option Agreement with Ionis. Under the terms of this agreement, the Company agreed to transfer 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 agreed to pay a non-refundable $3.0 million option fee within five business days after the Effective Date.

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 commercialisation 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 agreement were immaterial in the context of the contract. The Company accounted for the $3.0 million payment as deferred revenue as of 31 December 2020. On 9 July 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 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 9 July 2021, the Company and Ionis entered into a collaboration and license agreement Pursuant to this agreement, the Company granted to Ionis a worldwide exclusive license under the Company's relevant technology to research, develop, manufacture and commercialise 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

5 Revenue (continued)

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 optimisation 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 commercialisation 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 organisation. The Company has retained certain rights, including the right to use TfR1 Bicycles for all non-oligonucleotide therapeutic purposes.

Under this 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 contract research organisation. 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 agreement. Ionis paid the Company $1.6 million and the Company agreed to perform additional research services utilising its proprietary phage screening technology to identify and optimise new product candidates that target the TfR1 receptor. The Company will perform the additional research services for an initial six-month period in exchange for consideration of $0.8 million. Ionis has an option for the Company to perform additional research services for an additional six months if specified criteria are mutually agreed to and achieved, in exchange for the remaining consideration of $0.8 million. If the option is not exercised, the Company will refund $0.8 million to Ionis.

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 9 July 2021, the Company entered into the Ionis Share Purchase Agreement with Ionis, pursuant to which Ionis purchased shares of the Company at a price per share of $38.94, with an aggregate purchase price of approximately $11.0 million.

5 Revenue (continued)

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. The Company concluded that the premium paid by Ionis under this 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.

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 commercialise 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 customise and optimise 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 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 contract research organisation 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 identifiable components based on the relative estimated standalone selling prices of each identifiable component. 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 realised 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.

The Company has concluded that the exclusive license to research, develop, manufacture and commercialise products under the Collaboration and Licence agreement 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. In assessing whether the options under the Ionis Collaboration Agreement represent material rights, management 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 as performance obligations 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.

Based on the relative standalone selling price, the allocation of the transaction price as of 31 December 2021 to the separate identifiable components is as follows (in thousands):

	Allocation of Transaction Price $'000
Separately identifiable components:	
Combined licenses and research and discovery performance obligation	34,100
Four material rights associated with credits for IND Acceptance fees	3,900
	38,000

5 Revenue (continued)

The Company is recognising 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. 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 amendment to the agreement 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 will recognise the $0.8 million 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. As of 31 December 2021, the Company had not commenced services related to the amendment and had recorded deferred revenue of $1.6 million.

Revenue recognised in the financial statements is subject to ongoing estimates. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognised, are subject to estimates by management and may change over the course of the research and development and licensing agreement. Changes in the estimated total level of effort expected to be performed would accelerate or decrease the rate or revenue recognised related to combined licenses and research and discovery component that is recognised over time, which is currently expected to be recognised over a period of approximately two years. Specifically, a change in the overall expected effort for the combined licenses and research and discovery components of 5% would result in a change in revenue of approximately $146k.

Discovery Collaboration and License Agreement with Genentech

Due to the scope of this collaboration and size of the upfront fee further details of the accounting judgements are provided below.

The total transaction price under the collaboration 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 utilises 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 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

5 Revenue (continued)

expected to be realised 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 allocation of the transaction price as of 31 December 2021 to the separate performance obligations is as follows (in thousands):

	Allocation of Transaction Price $'000
Separately identifiable components:	
Genentech Collaboration Program Number 1	4,019
Genentech Collaboration Program Number 2	8,037
Specified Targeting Arm Material Right Arm for Genentech Collaboration Program Number 1	352
Two material rights associated with the LSR Go Option for Collaboration Programs Number 1 and Number 2	12,400
Material rights associated with limited substitution rights	1,187
Two material rights for Expansion Options	7,005
	33,000

The Company will recognise revenue related to amounts allocated to the Genentech Collaboration Program Number 1 and Genentech Collaboration Program Number 2 separately identifiable components 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 time and external 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 Program Number 1 and Genentech Collaboration Program Number 2 components will be performed over a period of approximately two years, and the material rights will be exercised or expire within approximately four years from the start of the collaboration in February 2020.

In October 2021, Genentech exercised an expansion option to add an additional Genentech Collaboration Program (Genentech Collaboration Program Number 3) and paid to the Company an expansion fee of $10.0 million during the year ended 31 December 2021. Genentech also elected for Bicycle to perform discovery and optimisation services for a Targeting Arm, and the Company is entitled to receive an additional payment of $1.0 million for additional research services. The Company accounted for this as a continuation of an existing contract as the customer decided to purchase additional goods and services contemplated in the original contract, as such, the additional arrangement consideration of $11.0 million received upon the option exercises together with the amount originally allocated to the Expansion Option material right of $3.5 million is allocated to the underlying goods and services associated with the Expansion Option. The arrangement consideration was allocated to the separate performance obligations on the same basis as the initial allocation of the Genentech Collaboration Agreement. The Company will recognise $6.4 million allocated to Genentech Collaboration Program Number 3 and Targeting Arm services as the underlying services are performed using a proportional performance model over the period of service of approximately 2 years using input-based measurements of total full-time equivalent efforts and external costs incurred to date as a percentage of total full-time equivalent time and external expected, which best reflects the progress towards satisfaction of the performance obligation. The amount

5 Revenue (continued)

allocated to the material right associated with an LSR Go Option for Collaboration Program Number 3 of $7.4 million, and limited substitution material rights of $0.7 million, are recorded as deferred revenue and the Company will commence revenue recognition upon exercise of or upon expiry of the respective option. 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.

Revenue recognised in the financial statements is subject to ongoing estimates. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognised, are subject to estimates by management and may change over the course of the research and development and licensing agreement. Changes in the estimated total level of effort expected to be performed would accelerate or decrease the rate or revenue recognised related to the Genentech Collaboration Program Number 1 and Genentech Collaboration Program Number 2 components that are recognised over time, which is currently expected to be recognised over a period of approximately two years. Specifically, a change in the overall expected effort for the Genentech Collaboration Program Number 1 and Genentech Collaboration Program Number 2 components of 5% would result in a change in revenue of approximately $56k.

6 Operating loss

The Company's consolidated operating loss is stated after charging/(crediting):

	2021 $'000	2020 $'000
Expenditure on research and development*	47,778	34,116
Depreciation of tangible assets	1,398	1,276
Amortisation of intangible assets	21	20
Operating lease charges	1,095	921
Loss (gain) on foreign exchange	2,162	(3,195)
Wages and salaries (note 9)	19,441	13,346
Social security costs (note 9)	8,789	1,826
Other pension costs (note 9)	990	671
Share-based payments (note 11)	15,271	8,990
Grant income	(2,988)	(570)
Exceptional item on dispute settlement	—	4,696
Auditors' remuneration		
Audit of these financial statements	62	56
Audit of the Parent Company's subsidiaries	60	55
Audit-related assurance services for U.S. SEC financial statements	1,231	957

In addition, auditors' remuneration of $149k relating to share issuance costs were charged to the share premium account in the year ending 31 December 2021 (31 December 2020: $100k).

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* The Directors have identified that the expenditure on research and development in the prior year was overstated by $14,758k and has been corrected within these financial statements. The correction has no impact on profit or cash flows for the year or on opening reserves in the current year.

An exceptional item arose when the Company entered into a Settlement and License Agreement with Pepscan Systems B.V. ("Pepscan") regarding BicycleRD Limited's use of Pepscan's CLIPS peptide technology.

6 Operating loss (continued)

The companies agreed to settle all intellectual property disputes worldwide. Under the terms of the settlement, the Company has been granted a license to use CLIPS peptide technology in the development of its product candidates BT1718 and THR-149. The Company paid €3 million upfront, and paid a further €1 million on the first anniversary of the date of settlement on 21 November 2021, and will make potential additional payments to Pepscan based on achievement of specified clinical, regulatory and commercial milestones.

Expenditure on research and development includes staff costs as follows:

	2021 $'000	2020 $'000
Wages and salaries	12,592	8,501
Social security costs	2,105	1,186
Other pension costs	725	507

7 Net interest (expense)/income

a) Interest receivable and similar income

The Company's interest receivable and other income consisted of the following:

	2021 $'000	2020 $'000
Bank interest	120	683

b) Interest payable and similar expenses

The Company's interest payable and similar expenses consisted of the following:

	2021 $'000	2020 $'000
Interest payable on loan and other borrowings	2,909	422
Finance charge	108	65
Interest payable and similar expenses	3,017	487

8 Tax on Loss

The Company's tax on loss consisted of the following:

	2021 $'000	2020 $'000
Current tax:		
UK corporation tax on losses for the year	(10,906)	(8,551)
Foreign corporation tax on profits for the year	—	(37)
Adjustment in respect of prior years	101	10
Total current tax	(10,805)	(8,578)
Deferred tax:		
Origination and reversal of timing differences	(1,669)	(677)
Deferred tax recognised in the year	(1,669)	(677)
Tax credit on loss	(12,474)	(9,255)

8 Tax on Loss (continued)

The tax assessed for the year is higher (31 December 2020: higher) than the standard rate of corporation tax in the UK (19%) (31 December 2020: 19%). The tax reconciliation for the year is given below:

	2021 $'000	2020 $'000
Loss before taxation	(89,804)	(59,610)
Loss reconciled to the current tax rate of 19% (December 2020: 19%)	(17,063)	(11,326)
Effects of:		
(Income)/expenses not deductible for tax purposes	(57)	47
Surrender of tax losses for research and development tax credit refund	3,381	2,655
Fixed asset and other timing differences not recognised	(115)	(28)
Deferred tax not recognised on share-based payment and payroll taxes	(721)	1,270
Deferred tax not recognised on tax losses	10,726	5,168
Research & Development enhanced allowance	(8,066)	(6,332)
Difference in overseas tax rates	(47)	12
Research and development expenditure credits	(613)	(731)
Adjustment in respect of prior periods	101	10
Total tax credit on loss	(12,474)	(9,255)

No corporation tax liability arises on the results for the year due to the loss incurred. A tax credit of $10,906k (31 December 2020: $8,551k) has arisen as a result of tax losses being surrendered in respect of research and development expenditure.

Deferred taxation

In the Spring Budget 2021, the UK Government announced that from 1 April 2023 the corporation tax rate will increase to 25% and as it is now considered enacted its effects are included in these financial statements. In the Spring Budget 2020, the UK Government announced that from 1 April 2020 the corporation tax rate would remain at 19% (rather than reducing to 17%, as previously enacted). This new law was substantively enacted on 17 March 2020. Deferred taxes at the balance sheet date have been measured using these enacted tax rates and reflected in these financial statements.

The Company had potential and actual deferred tax assets at the prevailing rate of 25% (31 December 2020: 19%) as follows:

	Amount unrecognised 31 December 2021 $'000	Amount unrecognised 31 December 2020 $'000
Tax effect of timing differences because of:		
Fixed asset and other timing differences	(238)	(67)
Share-based payment	6,228	2,084
Tax losses carried forward	31,011	13,128
Deferred Tax Asset	37,001	15,145

Deferred tax assets are not recognised where there is insufficient evidence that they are recoverable. Deferred tax is calculated using tax rates that apply based on rates enacted or substantively enacted by the reporting date.

8 Tax on Loss (continued)

The Company regularly assesses its ability to realise its deferred tax assets. Assessing the realisation of deferred tax assets requires significant judgment. After consideration of the evidence, including the Company's history of cumulative net losses in the UK, and has concluded that it is more likely than not that the Company will not realise the benefits of its UK deferred tax assets and accordingly the Company has not recognised UK deferred tax assets. 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 realise the benefits of its U.S. deferred tax assets and has recognised net U.S. deferred tax assets.

The Company has recognised deferred tax assets/(liabilities) within its U.S. subsidiary as follows:

	Amount recognised 31 December 2021 $'000	Amount recognised 31 December 2020 $'000
Tax effect of timing differences because of:		
Share-based payment	1,054	553
Research credit carry forwards	1,862	1,233
Other	312	(227)
Deferred Tax Asset	3,228	1,559

Of the above $1,060k is non-current (31 December 2020: $146k). The Parent Company had no recognised or unrecognised deferred tax assets.

Deferred tax recognised in the year is as follows:

	2021 $'000	2020 $'000
Deferred tax asset brought forward	1,559	882
Share-based payment	501	213
Research credit carry forwards	629	799
Other	539	(335)
Deferred tax asset carried forward	3,228	1,559

9 Staff costs

The average monthly number of persons (including executive directors) employed by the Company during the year was:

	2021 Number	2020 Number
By activity		
Research and development	78	61
Administration	23	18
	101	79

9 Staff costs (continued)

Their aggregate remuneration comprised:

	2021 $000	2020 $000
Wages and salaries	19,441	13,346
Social security costs	8,789	1,826
Other pension costs	990	671
Share-based payment compensation	15,271	8,990
	44,491	24,833

The Parent Company had no employees other than directors.

10 Directors' emoluments

The aggregate emoluments of the directors of the Company are set out below:

	2021 $'000	2020 $'000
Aggregate emoluments	14,108	1,720
Company pension contributions to money purchase schemes	6	1
	14,114	1,721

One director had retirement benefits accruing to them under a money purchase scheme. One director received cash in lieu of contributions to the money purchase scheme. One director is associated with Stone Sunny Isles, Inc., which provided consultancy services to the Company totalling $173k for the year ended 31 December 2021 (2020: $162k) and is included in the amounts above.

Two directors exercised share options during the year (2020: Nil) at weighted average exercise prices of USD 14.00 and USD 8.54. The gain on exercised share options included within aggregate emoluments (based on the market value of the shares on the date of exercise) is $12,184k.

Emoluments paid to the highest paid director are set out below:

	2021 $'000	2020 $'000
Aggregate emoluments	8,581	1,155
Pension contributions to money purchase schemes	—	1
	8,581	1,156

A gain on exercise of share options of $8,471k is included within aggregate emoluments of the highest paid director (based on the market value of the shares on the date of exercise).

Further details of the directors' remuneration and directors' share options are contained in the Directors' Remuneration Report.

11 Share-based payments

Employees of the Parent Company's subsidiaries have been granted options to purchase ordinary shares in the Parent Company. Options granted typically vest over a four-year service year with 25% of the

11 Share-based payments (continued)

award vesting on the first anniversary of the commencement date and the balance thereafter in 36 equal monthly instalments. Certain awards granted to non-employee directors are fully vested on the date of grant.

Certain historic equity awards were issued for which 20% of the award vests upon the first anniversary of the vesting start date, 60% vests thereafter in 36 equal monthly instalments, and 20% vest upon the earlier of the fourth anniversary of the vesting start date, or the achievement of a specified revenue threshold from the Company's collaboration arrangements.

Options granted generally expire 10 years from the date of grant.

A reconciliation of the Company's share option movements over the years ended to 31 December 2021 and 31 December 2020 is shown below:

	Number (000)	2020 Weighted average exercise price	Weighted Average Remaining Contractual (in years)	Aggregate Intrinsic value $'000
Outstanding at 1 January 2020	2,634	$ 9.57	9.04	6,101
Granted	1,371	$12.00	—	—
Forfeited	(189)	$11.10	—	—
Exercised	(79)	$ 3.42	—	—
Outstanding at 31 December 2020	3,737	$10.51	8.54	27,553

	Number (000)	2021 Weighted average exercise price	Weighted Average Remaining Contractual (in years)	Aggregate Intrinsic value $'000
Outstanding at 1 January 2021	3,737	$10.51	8.54	27,553
Granted	1,677	$23.07	—	—
Forfeited	(107)	$18.67	—	—
Exercised	(704)	$10.21	—	—
Outstanding at 31 December 2021	4,603	$14.97	8.13	207,009

The expense recognised for share-based payments in respect of employee services received during the year ended 31 December 2021 is $15,271k (2020: $8,990k).

The assumptions used in the Black-Scholes option pricing model to determine the value of share options granted to employees and directors during the years ended 31 December 2021 and 31 December 2020 were as follows:

	2021	2020
Risk-free interest rate	0.6%	1.3%
Expected volatility	79.8%	74.8%
Expected dividend yield	—	—
Expected term (in years)	5.98	5.98

12 Intangible assets

Intangible assets of the Company consist of the following:

	Intellectual Property License $'000
Cost	
At 1 January 2021	326
Foreign exchange	(4)
At 31 December 2021	322
Accumulated amortisation	
At 1 January 2021	241
Charge made in the year	21
Foreign exchange	(4)
At 31 December 2021	258
Net book value	
As at 31 December 2021	64
As at 31 December 2020	85

The Parent Company had no intangible assets.

13 Tangible assets

Tangible assets of the Company, consist of the following:

	Office equipment $'000	Laboratory equipment $'000	Computer equipment $'000	Leasehold Improvement $'000	Total $'000
Cost					
At 1 January 2021	196	5,582	188	383	6,349
Additions	35	1,789	—	436	2,260
Disposals	(3)	(549)	(45)	—	(597)
Foreign exchange	(2)	(75)	—	(10)	(87)
At 31 December 2021	226	6,747	143	809	7,925
Accumulated depreciation					
At 1 January 2021	89	3,575	175	193	4,032
Charge for the year	53	1,198	10	138	1,399
Disposals	(3)	(531)	(45)	—	(579)
Foreign exchange	(1)	(46)	—	(3)	(50)
At 31 December 2021	138	4,196	140	328	4,802
Net book value					
At 31 December 2021	88	2,551	3	481	3,123
At 31 December 2020	107	2,007	13	190	2,317

The Parent Company had no tangible assets.

14 Investments in subsidiaries

Investments of the Parent Company consisted of the following:

	Investment in subsidiary undertaking $'000
Cost	
At 1 January 2020	8,058
Capital contribution arising from equity settled share-based payments	8,990
At 31 December 2020	17,048
Net book value	
At 31 December 2020	17,048
Cost	
At 1 January 2020	17,048
Capital contribution arising from equity settled share-based payments	15,271
At 31 December 2021	32,319
Net book value	
At 31 December 2021	32,319
At 31 December 2020	17,048

The Parent Company has three wholly owned subsidiaries: BicycleTx Limited and BicycleRD Limited which are based in Cambridge, UK and Bicycle Therapeutics Inc, which is based in Boston, Massachusetts, U.S. All these subsidiaries perform research and development activities.

Subsidiary undertakings

Name	Class of shares	Country of incorporation	Holding	Principal activity
BicycleTx Limited	Ordinary	England and Wales	100%	Development of novel bicyclic peptides
BicycleRD Limited	Ordinary	England and Wales	100%	Development of novel bicyclic peptides
Bicycle Therapeutics Inc	N/A	United States	100%	Development of novel bicyclic peptides

The registered office address of BicycleTx Limited and BicycleRD Limited is Building 900, Babraham Research Campus, Cambridge, CB22 3AT. The registered office address of Bicycle Therapeutics Inc. is 4 Hartwell Place, Lexington, MA, 02421-3122, U.S.

15 Debtors

	Consolidated		Parent Company	
	31 December 2021 $'000	31 December 2020 $'000	31 December 2021 $'000	31 December 2020 $'000
Amounts falling due within one year				
Trade debtors	1,000	5,456	—	—
Amounts owed by group undertakings	—	—	130,434	84,092
Deferred corporation tax	3,228	1,559	—	—
Research and development tax credit	10,910	9,177	—	—

15 Debtors (continued)

	Consolidated		Parent Company	
	31 December 2021 $'000	31 December 2020 $'000	31 December 2021 $'000	31 December 2020 $'000
Other debtors	1,311	713	29	—
Prepayments and accrued income	7,297	4,436	—	100
	23,746	21,341	130,463	84,192

Amounts owed by group undertakings are interest free with no fixed terms of repayment.

16 Creditors: amounts falling due within one year

	Consolidated		Parent Company	
	31 December 2021 $'000	31 December 2020 $'000	31 December 2021 $'000	31 December 2020 $'000
Amounts falling due within one year				
Trade creditors	2,721	1,327	—	—
Taxation and social security	5,758	584	—	—
Accruals and deferred income	31,448	21,376	—	—
	39,927	23,287	—	—

17 Creditors: amounts falling due after more than one year

	Consolidated		Parent Company	
	31 December 2021 $'000	31 December 2020 $'000	31 December 2021 $'000	31 December 2020 $'000
Amounts falling due after more than one year				
Loans and other borrowings	29,873	14,505	29,873	14,505
Accruals and deferred income	49,699	21,449	—	—
	79,572	35,954	29,873	14,505

On 30 September 2020 the Company entered into a loan and security agreement with Hercules Capital, Inc. ("Hercules"), which provided for aggregate maximum loan of up to $40.0 million, consisting of (i) a term loan of $15.0 million, which was drawn down immediately in 2020, (ii) subject to customary conditions, an additional term loan of up to $15.0 million available from 30 September 2020 to 15 March 2021, and (iii) subject to the Company achieving certain performance milestones and satisfying customary conditions and available until 15 March 2022, an additional term loan of $10.0 million. On 10 March 2021 the Company drew down the additional term loan of $15.0 million that had been available from 30 September 2020 to 15 March 2021.

The loan bears interest at an annual rate equal to the greater of (i) 8.85% or (ii) 5.60% plus the Wall Street Journal prime rate. Payments are interest only until the first principal payment which was due on 1 November 2022. In November 2021, the Company achieved certain performance milestones and the interest only period was extended from 1 May 2023 to 1 February 2024 followed by equal monthly payments of principal and interest up to the scheduled maturity date on 1 October 2024.

17 Creditors: amounts falling due after more than one year (continued)

The Parent Company may prepay all or any portion greater than $5.0 million of the outstanding borrowings, subject to a prepayment premium equal to (i) 2.0% of the principal amount outstanding if the prepayment occurs within the first year (ii) 1.5% of the principal amount outstanding if the prepayment occurs during the second year and (iii) 1.0% of the principal amount outstanding if the prepayment occurs thereafter but prior to the maturity date. The agreement also provides for an end of term charge payable upon maturity or the repayment of obligations under the agreement, equal to 5.0% of the principal amount repaid.

The loan is collateralised by substantially all of the Company's assets, other than its intellectual property.

The Parent Company incurred fees and transaction costs totalling $573k associated with the initial term loan, which are recorded as a reduction to the carrying value of the long-term debt in the consolidated balance sheets. The fees and transaction costs are amortised to interest expense up to the scheduled maturity date using the effective interest method. The effective interest rate was 11.2% at 31 December 2021 (2020: 12.2%). The Parent Company assessed all terms and features of the Loan Agreement determined that the loan is a basic financial instrument as defined in FRS102, paragraph 11. Interest expense for the year ended 31 December 2021 was $2,909k (2020: $422k).

Loans and other borrowings consisted of the following:

	Consolidated		Parent Company	
	31 December 2021 $'000	31 December 2020 $'000	31 December 2021 $'000	31 December 2020 $'000
Loan principal	30,000	15,000	30,000	15,000
End of term charge	376	58	376	58
Unamortised debt issuance costs	(503)	(553)	(503)	(553)
	29,873	14,505	29,873	14,505

Future repayments of principal, including the end of term charge, are as follows:

	31 December 2021 $'000	31 December 2020 $'000
Within one year	—	—
Between one and five years	31,500	15,750
Total	31,500	15,750

18 Called up share capital and reserves

The Parent Company's called up share capital and reserves consisted of the following:

	31 December 2021 $'000	31 December 2020 $'000
Issued, allotted, called up and fully paid		
29,579,364 (31 December 2020: 21,094,557) ordinary shares of £0.01 each	384	266
	384	266

18 Called up share capital and reserves (continued)

No dividends have been proposed or paid as at the date of approval of these financial statements.

On 9 July 2021, the Company entered into a share purchase agreement with Ionis Pharmaceuticals, Inc. pursuant to which Ionis purchased 282,485 of the Company's ordinary shares at a price per share of $38.94, for an aggregate purchase price of approximately $11.0 million. On 15 October 2021, the Company issued and sold 3,726,852 ADSs, representing the same number of ordinary shares, at a price to the public of $54.00 per ADS, resulting in gross proceeds of $201.3 million before deducting underwriting discounts, commissions and offering expenses, for net proceeds for $188.4 million.

On 5 June 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, American Depositary Shares ("ADSs"), each ADS representing one ordinary share. During the year ended 31 December 2021, the Company issued and sold 3,771,684 ADSs, representing the same number of ordinary shares for gross proceeds of $105.8 million, resulting in net proceeds of $102.6 million after deducting sales commissions and offering expenses of $3.2 million. During the year ended 31 December 2020, the Company issued and sold 2,928,813 ADSs, representing the same number of ordinary shares for gross proceeds of $50.0 million, resulting in net proceeds of $48.1 million after deducting sales commissions and offering expenses of $1.9 million.

During the year ended 31 December 2021 the Company issued 703,786 ADSs (2020: 79,158) following the exercise of share options (note 11).

Nature and purpose of reserves

Share premium

The share premium account represents the premium arising on the issue of shares net of issue costs.

Exchange reserve

The exchange reserve comprises all foreign currency differences arising from the translation of the financial statements.

General reserve

The general reserve represents the value of share-based payments granted to employees of the Company.

(Accumulated losses)/retained earnings

Retained earnings represents cumulative profits and losses net of dividends and other adjustments including the premium to fair value of shares issued with respect to the Ionis Share Purchase Agreement which is part of the consideration for the goods and services to be provided under the Ionis Collaboration Agreement (Note 5).

19 Notes to the consolidated cash flow statement

	2021 $'000	2020 $'000
Loss for the financial year	(77,330)	(50,355)
Tax on loss	(12,474)	(9,255)
Interest receivable and similar income	(120)	(683)
Interest payable and similar charges	3,017	487
Operating loss	(86,907)	(59,806)
Amortisation of intangible assets	21	20
Depreciation of tangible fixed assets	1,398	1,276
Equity settled share-based payment	15,271	8,990
Loss on disposal of tangible fixed assets	18	—
Working capital movements:		
Decrease/(increase) in debtors	602	(4,481)
Increase in creditors	42,550	31,839
Net exchange differences	2,390	(2,566)
Cash flow from operating activities	(24,657)	(24,728)

Following the change in functional currency of the Parent Company in 2019 the intercompany balances with the UK subsidiaries were designated as denominated in U.S. dollars which are not intended to be repaid as such foreign exchange difference on these loans are reflected as non-cash net exchange differences.

20 Pensions

The Company operated a defined contribution pension scheme for its UK executive directors and employees.

The Company has established a defined-contribution savings plan under Section 401(k) for its US employees.

The amount recognised as an expense for the defined contribution schemes of the Company for the year was $990k (31 December 2020: $671k) and the amount outstanding at the 31 December 2021 was $Nil (31 December 2020: $Nil). The Parent Company has no employees other than the directors and does not operate a pension plan.

21 Financial instruments

The carrying amounts of the Company's financial instruments are as follows:

	31 December 2021 $'000	31 December 2020 $'000
Financial assets measured at amortised cost		
Debtors		
Trade debtors	1,000	5,456
Cash and cash equivalents	438,680	135,990
Financial liabilities measured at amortised cost		

21 Financial instruments (continued)

	31 December 2021 $'000	31 December 2020 $'000
Creditors		
Trade creditors	2,721	1,327
Accruals	12,175	10,636
Loans and other borrowings	29,873	14,505
	44,769	26,468

The income, expenses, net gains and net losses attributable the Company's consolidated financial instruments are summarised as follows:

	2021 $'000	2020 $'000
Income and (expense)		
Financial assets measured at amortised cost	120	683
Financial liabilities measured at amortised cost	(3,017)	(487)
	(2,897)	196

There were no net gains or net losses for financial assets measured at amortised cost for the years ended 31 December 2021 and 31 December 2020. The total interest income and interest expense for financial assets and financial liabilities that are not measured at fair value through profit or loss was $120k (31 December 2020: $683k) and $3,017k (31 December 2020: $487k), respectively.

Cash and cash equivalents, trade and other creditors and trade and other debtors with remaining life of less than one year, the notional amount is deemed to reflect fair value.

The carrying amounts of the Parent Company's financial instruments are as follows:

	31 December 2021 $'000	31 December 2020 $'000
Financial assets measured at amortised cost		
Debtors		
Other debtors	—	—
Amounts owed by group undertakings	130,434	84,092
	130,434	84,092
Cash and cash equivalents	381,774	109,745
Financial liabilities measured at amortised cost		
Creditors		
Loans and other borrowings	29,873	14,505
	29,873	14,505

The income, expenses, net gains and net losses attributable the Parent Company's financial instruments are summarised as follows:

21 Financial instruments (continued)

	2021 $'000	2020 $'000
Income and (expense)		
Financial assets measured at amortised cost	119	491
Financial liabilities measured at amortised cost	(2,909)	(422)
	(2,790)	69

The total interest income and interest expense for financial assets and financial liabilities that are not measured at fair value through profit or loss was $119k (31 December 2020: $491k) and $2,909k (31 December 2020: $422k), respectively.

The Company and Parent Company had no financial instruments subject to interest rate benchmark reform (31 December 2020: $nil).

22 Financial commitments and contingencies

Cash and cash equivalents, trade and other creditors and trade and other debtors with remaining life of less than one year, the notional amount is deemed to reflect fair value.

At 31 December 2021, the Company had annual commitments under non-cancellable operating leases as follows:

	Land and buildings 31 December 2021 $'000	Land and buildings 31 December 2020 $'000
Within one year	3,310	921
Between one and five years	13,716	483
Total	17,026	1,404

There were contracted capital commitments of $2,467k at 31 December 2021 (31 December 2020: $66k). These commitments are largely in respect of leasehold improvements to the new premises.

See note 17 for the Company's commitments related to the long-term debt.

The Company has entered into various agreements with contract research organisations and contract manufacturing organisations. These payments are not included in the commitments table above since the contracts are generally cancellable 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. Under such agreements, the Company is contractually obligated to make certain minimum payments to the vendors, with the payments in the event of a termination with less than 90 days' notice based on the timing of the termination and the exact terms of the agreement.

Operating Leases

The existing lease for Building 900, Babraham Research Campus, Cambridge, CB22 3AT ended on 11 December 2021 and the Company entered into a new lease for a period of 5 years from 12 December 2021. On 7 December 2021 the Company entered into a lease for new premises to which it intends to relocate to in mid-2022. The lease has a contractual period of 10 years, but may be cancelled by the Company after 5 years.

During 2021, the amount charged to the consolidated statement of comprehensive income in respect of operating leases was $1,095k (2020: $921k).

22 Financial commitments and contingencies (continued)

The Parent Company had no annual commitments under non-cancellable operating leases.

Cancer Research UK Agreement

The agreement with Cancer Research UK Agreement to sponsor and fund the Phase Ia and Phase IIa clinical trial of BT1718, 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 generates its revenue from the sale of tobacco products). Cancer Research UK may terminate the arrangement for safety reasons or if it determines that the objectives of the clinical trial will not be met, in which case, if the study is terminated by Cancer Research UK prior to the completion of the Phase I dose escalation part of the study for such reasons, or if Cancer Research UK refuses release of any additional quantities of good manufacturing practice ("GMP") materials, or if the parties cannot agree upon a plan to supply the additional quantities of GMP materials, the Company will be obligated to refund 50% of the costs and expenses incurred or committed by Cancer Research UK to perform the clinical trial. If the study is terminated by Cancer Research UK for an insolvency event, a material breach by the Company, or if the Company is acquired by an entity that generates its revenue from the sale of tobacco products, 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 where the Company is acquired by an entity that generates its revenue from the sale of tobacco products 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 Cancer Research Technology Limited an exclusive license to develop and commercialise the product without Cancer Research Technology Limited being required to make any payment. As at 31 December 2021 Cancer Research UK had incurred costs of approximately $3.3 million (31 December 2020: $2.6 million). Management does not consider it probable or likely that these costs will be required to be reimbursed to Cancer Research UK.

Legal proceedings

In November 2020, the Company entered into a settlement and license agreement with Pepscan Systems B.V. regarding Bicycle's use of Pepscan's CLIPS peptide technology. The companies agreed to settle all intellectual property disputes worldwide. Under the terms of the settlement, the Company has been granted a license to use CLIPS peptide technology in the development of its product candidates BT1718 and THR-149. The Company paid €3 million in November 2020, paid €1 million on the first anniversary of the date of settlement in November 2021 and will make potential additional payments to Pepscan based on achievement of specified clinical, regulatory and commercial milestones.

23 Basic and diluted loss per ordinary share

Basic and diluted loss per ordinary share is determined by dividing net loss by the weighted average number of ordinary shares outstanding during the period.

The Parent Company's potentially dilutive securities, which include share options to subscribe for ordinary shares 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 used to calculate both basic and diluted net loss per share attributable to ordinary shareholders 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 attributable to ordinary shareholders for the periods indicated because including them would have had an anti-dilutive effect:

23 Basic and diluted loss per ordinary share (continued)

	Number 31 December 2021	Number 31 December 2020
Options to purchase ordinary shares	4,603,486	3,736,663
	4,603,486	3,736,663

24 Related party disclosures

The Company has taken advantage of the exemptions contained within FRS 102 paragraph 33.1A not to disclose transactions with wholly owned group undertakings.

Pierre Legault, a director of the Parent Company, is associated with Stone Sunny Isles, Inc., which provided consultancy services to the Company totalling $173k for the year ended 31 December 2021 (2020: $162k). The amount outstanding at the year-end was $Nil (2020: $Nil).

Key management personnel include the CEO and a number of senior managers across the Company who together have authority and responsibility for planning, directing and controlling the activities of the Company.

The total compensation paid to key management personnel for services provided to the Company was $5,369k (2020: $4,109k). In addition, key management personnel received an aggregate gain on the exercise of share options (based on the market value of the shares on the date of exercise) of £5,573k (2020: $Nil).

25 Post balance sheet events

The directors are not aware of any events that have occurred subsequent to the year-end that may materially impact the results of the financial statements.