Annual Report 2021

For the year ended 31 December 2021

NUCANA

NUCANA

a new era in oncology

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Cover Picture: Victoria Street, Edinburgh, U.K.
Built between 1829 to 1834 as part of a series of improvements to the Old Town, with the aim of improving access around Edinburgh.

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introduction

NuCana was incorporated under the laws of England and Wales on 28 January 1997 under the name Biomed (UK) Limited and commenced operations in 2008. On 28 April 2008, we changed our name to NuCana BioMed Limited. On 29 August 2017, we re-registered as a public limited company and changed our name to NuCana plc. On 2 October 2017, we completed our initial public offering of American Depositary Shares, or ADSs, on the Nasdaq Global Select Market. Our ADSs are traded under the symbol "NCNA". NuCana plc on behalf of itself and its subsidiaries, NuCana, Inc., NuCana Limited (incorporated in Ireland) and NuCana Biomed Trustee Company Limited (which may be referred to as "the Group", "the Company", "we", "us" or "our"), is required to produce a strategic report complying with the requirements of the Companies Act 2006.

overview

We are a clinical-stage biopharmaceutical company focused on significantly improving treatment outcomes for patients with cancer by applying our ProTide™ technology to transform some of the most widely prescribed chemotherapy agents, nucleoside analogs, into more effective and safer medicines. While these conventional agents are central to the treatment of many solid tumours and haematological malignancies, their efficacy can be limited by: rapid breakdown, which can lead to the generation of toxic by-products; poor uptake by cell membrane transporters; inefficient metabolism to the active anti-cancer metabolite; and poor pharmacokinetic, or PK, properties which often require challenging administration schedules. Utilising our proprietary technology, we are developing new medicines called ProTides, designed to overcome all these key limitations, resulting in much higher concentrations of the active anti-cancer metabolites in cancer cells and avoiding the off-target toxicity associated with conventional chemotherapy.

NUC-3373 is a ProTide transformation of the active anti-cancer metabolite of 5-fluorouracil, or 5-FU, which we believe has the potential to replace 5-FU as the standard of care in the treatment of a wide range of cancers. 5-FU is one of the world's most widely prescribed anti-cancer agents and is on the World Health Organization's List of Essential Medicines. NUC-3373 has been evaluated in a Phase 1 clinical study for patients with advanced solid tumours and is currently in a Phase 1b/2 clinical study for patients with advanced colorectal cancer.

NUC-7738 is a ProTide transformation of a novel nucleoside analog, 3'-deoxyadenosine, or 3'-dA, that has shown potent anti-cancer activity in preclinical studies but due to rapid breakdown has not been successfully developed or approved as an anti-cancer agent. We are currently evaluating NUC-7738 in a Phase 1/2 clinical study for patients with advanced solid tumours.

The treatment of cancer can be divided into three major categories: surgery, radiotherapy and therapeutics. Therapeutics include chemotherapy, immunotherapy, cell-based therapies and targeted and hormonal agents. The backbone of treatment for patients with cancer consists of chemotherapeutics, which are expected to achieve revenues of approximately $74.3 billion by 2027. Despite significant progress having been made in the development of new therapeutics, most patients continue to receive chemotherapy either in combination with other treatments or as single agents at some point in their treatment pathway. Thus, we believe that more effective and safer chemotherapeutic agents will have an important role to play in the treatment of patients with cancer for the foreseeable future. We are transforming an important class of chemotherapeutic agents, nucleoside analogs, by applying a well-validated medicinal chemistry approach to overcome their limitations.

Through harnessing the power of phosphoramidate chemistry, we convert nucleoside analogs into activated nucleotide analogs with the addition of a phosphate group, which is protected by specific combinations of aryl, ester and amino acid groupings. By adding and protecting this phosphate group, we design our ProTides to avoid or overcome the limitations associated with breakdown, uptake, activation and administration of nucleoside analogs. In the antiviral field, this phosphoramidate chemistry approach has resulted in two of the most successful drug launches in the history of medicine, Gilead's sofosbuvir, or Sovaldi®, and tenofovir alafenamide fumarate, or TAF, which is a key component of Genvoya®, Descovy® and Odefsey®.

In preclinical studies, NUC-3373 overcame the key limitations associated with 5-FU, generating higher intracellular levels of the active anti-cancer metabolite than that of 5-FU while not generating toxic metabolites commonly associated with 5-FU's side effects. NUC-3373 has been evaluated in a Phase 1 clinical study, also known as the NuTide:301 study, in patients with advanced solid tumours. Enrolment in this study has been completed with 59 patients receiving NUC-3373. The maximum tolerated dose and schedule for NUC-3373 monotherapy was established as 2500 mg/m^2 weekly. NUC-3373 generated high levels of the active anti-cancer metabolite inside the patients' cells and demonstrated a favourable pharmacokinetic and safety profile. Evidence of durable anti-cancer activity was observed, with at least 10 patients remaining on treatment for more than four months and three of these patients achieving prolonged stable disease with progression-free survival, or PFS, lasting more than nine months. The results of this study suggest that NUC-3373 has the potential to overcome the limitations associated with 5-FU and may be capable of achieving anti-cancer activity even in patients who have progressed on prior treatment with a fluoropyrimidine. We expect to report final data from the NuTide:301 study in 2022.

NUC-3373 is being evaluated in an ongoing Phase 1b/2 study, known as the NuTide:302 study, in patients with advanced colorectal cancer in which NUC-3373 is being combined with agents typically used with 5-FU, including leucovorin, irinotecan, oxaliplatin and bevacizumab. In October 2019, we presented interim data from this study at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. These interim data supported the previously reported favourable pharmacokinetic profile of NUC-3373. In April 2021, we presented further interim data from this study at the virtual AACR Annual Meeting. These interim data highlighted 38 patients who received NUC-3373 either as monotherapy or in combination with leucovorin. Eleven patient case studies showed NUC-3373's ability to stabilise disease in a heavily pre-treated population of patients with advanced colorectal cancer and achieve prolonged durations of progression-free survival. Several patients achieved periods of progression-free survival that were longer than those achieved on previous regimens and tumour shrinkages have been observed, including in a patient known to be refractory to all prior fluoropyrimidine-containing regimens. NUC-3373 was also shown to have a favourable safety profile with no hand-foot syndrome observed, which is associated with the toxic metabolite, FBAL, and no neutropenia or Grade 3 or 4 mucositis or diarrhoea adverse events, which are associated with the toxic metabolite, FUTP.

The anti-cancer mechanism of action of NUC-3373 has been established in preclinical studies, which we believe further supports the biological advantages of NUC-3373 over 5-FU. We believe NUC-3373 has significant commercial potential as approximately 500,000 patients in North America are estimated to receive intravenous 5-FU each year. Replacing 5-FU with NUC-3373 in the treatment of patients with colorectal cancer offers a substantial commercial opportunity. Colorectal cancer is the third most common cancer type globally, representing 10% of the overall annual global cancer incidence. In the United States alone, more than 150,000 new cases of colorectal cancer are diagnosed each year. It is expected that the global colorectal cancer burden will increase by 60% from approximately 1.9 million cases in 2020 to approximately 3.1 million cases in 2040. As colorectal cancer is often diagnosed late in most patients when it is locally advanced or metastatic, and only 14% of patients with stage 4 disease survive for five years, there is a high unmet need for more effective treatment options.

The NuTide:302 study, which is currently enrolling patients into Part 2 of the study, is investigating NUC-3373 plus leucovorin in combination with either oxaliplatin or irinotecan in patients with advanced colorectal cancer. Once the recommended combination dose has been established, we plan to further assess NUC-3373's efficacy and safety profile with the addition of bevacizumab for the second-line treatment of patients with colorectal cancer. We expect to report additional data from the NuTide:302 study in 2022. Contingent on regulatory guidance and other factors, we also plan to open a randomised Phase 2 clinical study in patients with advanced colorectal cancer in 2022, to be followed by a Phase 3 clinical study in the same indication.

In order to capitalise on the widespread usage of 5-FU and the significant global commercial opportunity for a more effective and safer fluoropyrimidine, we plan to initiate a Phase 1/2 study in 2022 in patients with advanced solid tumours to identify additional indications and combinations, including with immuno-oncology agents such as PD-1 inhibitors, for NUC-3373's further development.

In preclinical studies, NUC-7738 generated significantly higher levels of the key anti-cancer metabolite, 3'deoxyadenosine triphosphate or 3'-dATP, inside cancer cells compared to the parent nucleoside analog, 3'-dA, causing increased cancer cell injury. In October 2019, we announced preclinical data on NUC-7738, detailing multiple potential anti-cancer modes of action.

NUC-7738, is being evaluated in an ongoing Phase 1/2 clinical study, known as the NuTide:701 study, in patients with advanced solid tumours. In September 2021, we presented interim data from the first 29 patients treated in this study at the ESMO Virtual Congress. These interim data indicated a favourable pharmacokinetic and safety profile for NUC-7738. Additionally, three case studies highlighted patients with encouraging tumour reductions who remained on NUC-7738 treatment for extended periods of time. The NuTide:701 study has completed the Phase 1 dose-finding part with the maximum tolerated dose established. Patients are now being enrolled into the Phase 2 part and we expect to report additional interim data from the NuTide:701 study in 2022.

Acelarin is a ProTide transformation of the nucleoside analog gemcitabine. In clinical studies, Acelarin was well tolerated and showed anti-cancer activity in patients who were refractory to, or had progressed on, prior gemcitabine treatment. Disease control, as well as tumour shrinkages, including partial and complete responses, were observed in challenging indications, including ovarian and biliary tract cancers. In March 2022, we announced the discontinuation of the Phase 3 clinical study, also known as the NuTide:121 study, investigating Acelarin in combination with cisplatin versus the standard of care, gemcitabine plus cisplatin, in patients with previously untreated locally advanced or metastatic biliary tract cancer. This decision was made following a pre-planned futility analysis by the study's Independent Data Monitoring Committee. Although a higher objective response rate, as assessed by Blinded Independent Central Review, was observed in the Acelarin plus cisplatin arm, this did not translate into an overall survival benefit. It was concluded that Acelarin plus cisplatin was unlikely to achieve its primary objective of demonstrating at least a 2.2-month improvement in overall survival as compared to gemcitabine plus cisplatin in this difficult-to-treat population. We will review the data from this study to determine future potential development pathways, if any, for Acelarin.

Our proprietary ProTide technology was invented in the Cardiff University laboratory of our late Chief Scientific Officer, Professor Christopher McGuigan, who conceived of and filed the original composition of matter patents for our initial ProTides. The unique feature of his discovery was the specific combination of aryl, ester and amino acid groupings that protect the activated, or phosphorylated, nucleoside analog. This phosphoramidate chemistry approach is the key to the ProTide technology. Every ProTide grouping is distinct, and Professor McGuigan and his team synthesised and tested thousands of compounds in order to identify the optimal ProTide grouping for each underlying nucleoside analog.

We have licensed what we believe to be the foundational patent estate for the application of phosphoramidate chemistry in oncology. We have granted patents in key markets, including the United States, Europe and Japan, protecting the composition of matter of NUC-3373, NUC-7738, Acelarin and other of our product candidates. Professor McGuigan's work preceded and helped lead to the development of several U.S. Food and Drug Administration (FDA)-approved anti-viral drugs containing ProTides, including: sofosbuvir, or Sovaldi®, which is also a key component of Harvoni®, Vosevi® and Epclusa®; and tenofovir alafenamide fumarate, or TAF, which is a key component of Genvoya®, Descovy® and Odefsey®; and remdesivir, or Veklury®.

We are led by Hugh Griffith, our founder and Chief Executive Officer, who brings over 30 years of experience in the biopharmaceutical industry, including at Abbott Laboratories (now AbbVie Inc.) and Parke-Davis Warner Lambert (now Pfizer Inc.). Before founding NuCana, he led the operations of Bioenvision, Inc. from start-up through its acquisition by Genzyme Corporation. While at Bioenvision, he was instrumental in developing and commercialising clofarabine, a nucleoside analog, for the treatment of paediatric acute leukaemia.

our strategy

> *"Our goal is to transform standards of care and improve survival for patients across a wide range of cancer indications."*

Our strategy includes the following key components:

- **Rapidly develop NUC-3373 to replace 5-FU as the standard of care for the treatment of patients with colorectal cancer.**

  We plan to report further interim data from our Phase 1b/2 study, NuTide:302, in patients with advanced, metastatic colorectal cancer in 2022. In this study, NUC-3373 is being assessed for safety and a recommended Phase 2 dose when combined with many of the agents typically combined with 5-FU, including leucovorin, irinotecan, oxaliplatin and bevacizumab. Contingent on regulatory guidance and other factors, we plan to open a randomised Phase 2 clinical study of NUC-3373, NuTide:323, in combination with leucovorin, irinotecan and bevacizumab versus the standard of care FOLFIRI (5-FU, leucovorin, irinotecan and bevacizumab) in patients with second-line colorectal cancer in 2022. Following this, we plan to initiate a Phase 3 clinical study in this patient population.

- **Identify additional indications for development of NUC-3373.**

  In order to capitalise on the widespread usage of 5-FU and the significant global commercial opportunity for a more effective and safer fluoropyrimidine, we plan to initiate a Phase 1/2 study in 2022 in patients with advanced solid tumours to identify additional indications and combinations, including with immuno-oncology agents such as PD-1 inhibitors, for NUC-3373's further development.

- **Rapidly develop NUC-7738 as a treatment for patients with solid tumours.**

  We have recently completed enrolment in the Phase 1 part of the ongoing Phase 1/2 study, NuTide:701, of NUC-7738 in patients with advanced solid tumours and have initiated the Phase 2 part of this study. We plan to report further data from the NuTide:701 study in 2022.

- **Leverage our proprietary ProTide technology platform to develop additional product candidates.**

  We are pursuing the transformation of both well-established and widely used nucleoside analogs as well as novel nucleoside analogs, which we believe have the potential to address additional areas of unmet medical need in oncology.

- **Continue to protect and strengthen our intellectual property position.**

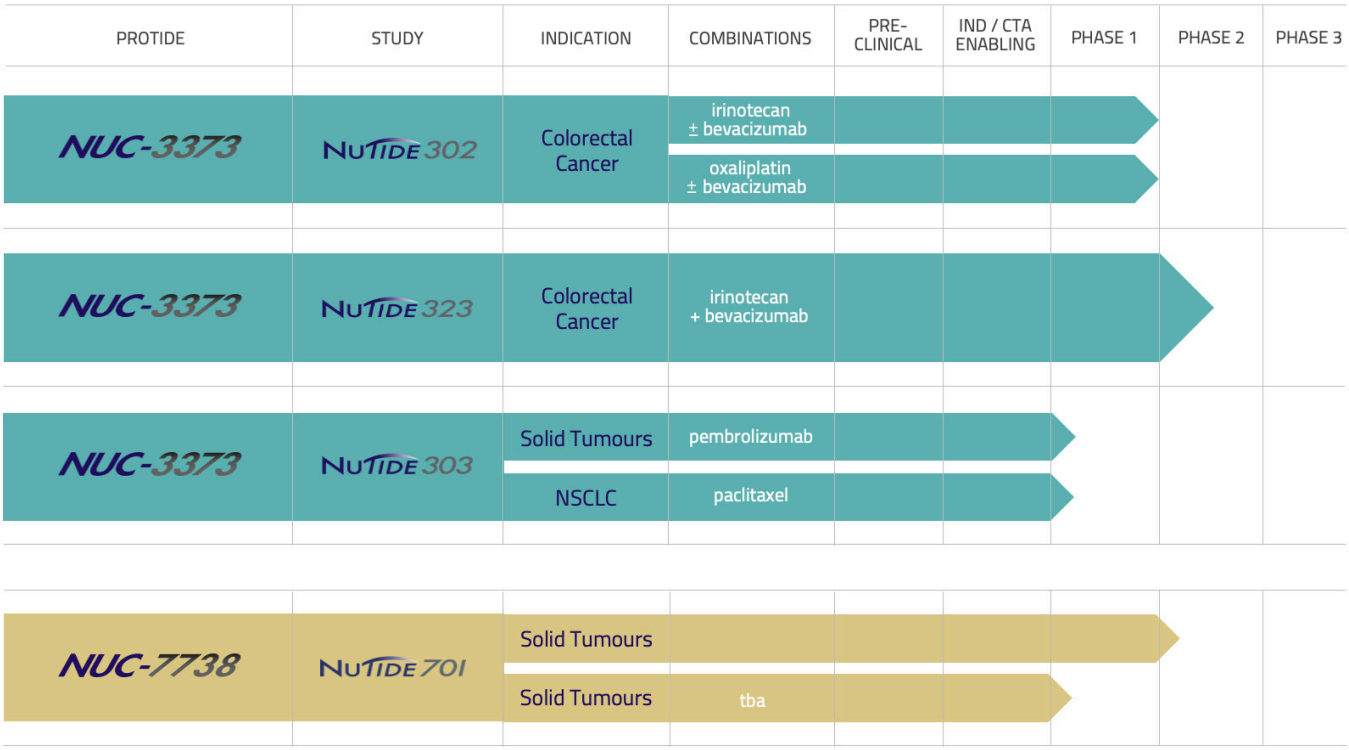
  We own or have exclusive rights to the core technologies underlying our ProTide technology platform. We have been granted patents in key markets, including the United States, Europe and Japan, protecting the composition of matter of NUC-3373, NUC-7738, Acelarin and other of our product candidates. We intend to further expand and enhance our intellectual property position. Our patent portfolio has grown substantially in the past year and we are actively evaluating new intellectual property opportunities as they arise, with the intention of further expanding our intellectual property position.

- **Build a focused commercial organisation.**

  We have worldwide rights to all product candidates that we are developing. We believe that many of the cancers we are initially targeting with our ProTides can be addressed commercially by a focused sales and marketing team. We plan to commercialise any product candidates for which we receive regulatory marketing approval using a specialised sales force in the United States and Europe.

our pipeline

We take a scientifically driven approach to designing ProTides, which we believe have the potential to result in highly efficacious cancer therapies with improved tolerability. Our pipeline of product candidates in clinical development and their current development stage is summarised below.



NuCana is currently developing a portfolio of new medicines to address a broad range of cancers, but we do not have any approved products. As further described in “Our Strategy”, our current intention is to build a sales and marketing capability in the United States and Europe in order to commercialise our ProTides. We may also consider partnerships, co-promotion agreements or other commercial arrangements, in certain geographic areas or otherwise, in order to most effectively address our market opportunities.

review of the business

Since our inception, we have incurred significant net losses and negative cash flows from operations. To date, we have financed our operations primarily through placements of equity securities, an initial public offering, a follow-on public offering and research and development tax credits.

DEVELOPMENT AND PERFORMANCE DURING THE PERIOD

Research and Development Expenses

Research and development expenses were £36.8 million for the year ended 31 December 2021 as compared to £25.9 million for the year ended 31 December 2020, an increase of £10.9 million. The increase resulted primarily from higher expenses incurred related to clinical studies of £20.4 million in 2021, compared with £12.5 million in 2020. Manufacturing costs in 2021 were £3.3 million compared to £3.2 million in 2020. Patent costs increased by £1.3 million in 2021 compared with 2020 primarily due to increased patent defence activity. Other research and development costs increased in 2021 by £1.6 million primarily due to higher personnel costs and share-based payment expenses incurred during the year, partially offset by lower non-clinical costs. The following table gives a breakdown of the research and development costs incurred by product for the years ended 31 December 2020 and 2021:

	Year ended 31 December	
	2021	2020
	(in thousands)	
Acelarin	£ 22,800	£ 13,927
NUC-3373	7,303	6,305
NUC-7738	4,029	3,746
Other	2,702	1,921
	£ 36,834	**£ 25,899**

Administrative Expenses

Administrative expenses were £8.5 million for the year ended 31 December 2021 as compared to £7.1 million for the year ended 31 December 2020, an increase of £1.4 million. The increase was primarily related to higher insurance, professional fees and share-based payment expenses.

Impairment of Intangible Assets

On 2 March 2022 we announced that the Phase 3 clinical study of Acelarin for patients with advanced biliary tract cancer was being discontinued following a pre-planned futility analysis by the study's Independent Data Monitoring Committee ("IDMC"). Management concluded that this was an indication of impairment and hence reviewed the assets associated with both the clinical study and Acelarin. Based on this review, an impairment charge of £2.8 million was recognised, representing the full aggregate carrying value of the patents relating to Acelarin as at 31 December 2021. The announcement is an adjusting event, as the data that supported the recommendation of the IDMC to discontinue the clinical study existed at 31 December 2021, although this data had not been compiled, analysed or communicated to the IDMC at that time.

Net Foreign Exchange Gains (Losses)

For the year ended 31 December 2021, we reported a net foreign exchange gain of £0.3 million as compared to a net foreign exchange loss of £3.5 million for the year ended 31 December 2020. In 2021 the gain primarily arose from cash balances held in U.S. dollars and the U.S. dollar appreciating relative to the U.K. pound sterling and conversely in 2020 the loss arose from cash balances held in U.S. dollars and the U.S. dollar depreciating relative to the U.K. pound sterling.

Finance Income

Finance income represents bank interest and was £0.1 million for the year ended 31 December 2021 and £0.2 million for the year ended 31 December 2020.

Income Tax Credit

The income tax credit, which is largely comprised of research and development credits, amounted to £7.3 million for the year ended 31 December 2021 and £5.5 million for the year ended 31 December 2020.

In the United Kingdom, research and development credits are currently obtained at a maximum rate of 33.35% of our qualifying research and development expenses. The increase in the income tax credit was primarily attributable to an increase in our eligible research and development expenses.

POSITION OF GROUP AT YEAR END

Liquidity and Capital Resources

Overview

Since our inception, we have incurred significant operating losses and negative operating cash flows. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and administrative expenses will increase in connection with conducting clinical studies and seeking marketing approval for our product candidates, as well as costs associated with operating as a public company. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity financings, debt financings, research funding, collaborations, contract and grant revenue or other sources.

As of 31 December 2021 and 31 December 2020, we had cash and cash equivalents of £60.3 million and £87.4 million, respectively. We do not currently have any approved products and have never generated any revenue from product sales. To date we have financed our operations primarily through the issuances of our equity securities.

In October 2018, we entered into an "at-the-market" (ATM) sales agreement with Cowen and Company, LLC, or Cowen, pursuant to which we could sell from time to time, ADSs having an aggregate offering price of up to $100.0 million through Cowen, acting as our agent. Sales of our ADSs

pursuant to this ATM program were subject to certain conditions specified in the sales agreement. Sales under the ATM program were registered on a shelf registration statement on Form F-3 that we filed with the US Securities and Exchange Commission (SEC) in October 2018, and which permitted the offering, issuance and sale by us of up to a maximum aggregate offering price of $400.0 million of our securities, inclusive of our ADSs sold under the ATM program. During 2020, we sold and issued 774,511 ADSs, representing 774,511 ordinary shares, under the ATM program, raising gross proceeds of £3.7 million. The ATM sales agreement with Cowen was terminated in August 2021.

In August 2021, we entered into an ATM sales agreement with Jefferies LLC, or Jefferies, pursuant to which we may sell from time to time, ADSs having an aggregate offering price of up to $100.0 million through Jefferies, acting as our agent. Sales of our ADSs pursuant to this ATM program are subject to certain conditions specified in the sales agreement. Sales under the ATM program are registered on a shelf registration statement on Form F-3 that we filed with the SEC in August 2021, and which permits the offering, issuance and sale by us of up to a maximum aggregate offering price of $400.0 million of our securities, inclusive of our ADSs sold under the ATM program. We did not sell or issue any ADSs under the ATM program in 2021.

Cash Flows

The following table summarises the results of our cash flows for the years ended 31 December 2021 and 2020.

	Year ended 31 December	
	2021	**2020**
	(in thousands)	
Net cash used in operating activities	£ (23,824)	£ (21,619)
Net cash used in investing activities	(3,561)	(1,313)
Net cash (used in) from financing activities	(98)	61,800
Net (decrease) increase in cash and cash equivalents	**£ (27,483)**	**£ 38,868**

Operating Activities

Net cash used in operating activities was £23.8 million in 2021 as compared to £21.6 million in 2020, reflecting a net increase in cash outflows of £2.2 million. Operating loss cash flows were higher by £10.1 million in 2021, primarily reflecting higher research and development costs. The increase in operating loss cash flows was partially offset by working capital inflows of £4.1 million in 2021 as compared to working capital inflows of £1.9 million in 2020. Also, tax refunds of £9.9 million were received in 2021 compared to £4.2 million in 2020.

Investing Activities

Net cash used in investing activities was £3.6 million in 2021 as compared with £1.3 million in 2020, reflecting a net increase in outflows of £2.3 million. Interest received in 2021 was £0.1 million compared with £0.3 million in 2020, a decrease of £0.2 million. In 2021, cash used to acquire property, plant and equipment was lower by £0.3 million than in 2020, and cash used to acquire intangible assets was £0.3 million lower. 2021 included payments for other non-current assets of £2.6 million with no similar payments in 2020.

Financing Activities

Net cash used in financing activities was £0.1 million in 2021 as compared to £61.8 million from financing activities in 2020. In 2021 the Company generated net proceeds from the issue of share capital on exercise of share options of £0.2 million, as compared to £62.1 million in 2020, which included proceeds from the follow-on public offering in September 2020.

main business trends and factors

NUC-3373 is currently in a Phase 1b/2 clinical study for patients with advanced colorectal cancer. NUC-7738 is currently in a Phase 1/2 clinical study for patients with advanced solid tumours. We have retained worldwide rights to these lead product candidates as well as our preclinical product candidates, all of which we refer to as ProTides. The key business trends affecting our development and performance during and at the period ended 31 December 2021 are detailed above.

In addition to these internal trends that have impacted our financial results, we may also in the future face competition for our products if they are approved. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy, immunotherapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer, including many which are administered in combination to enhance efficacy. We believe that our product candidates, if approved, will principally face competition from other chemotherapies, immunotherapy and targeted drug therapies. In the field of chemotherapy, our competitors include companies that manufacture off-patent chemotherapies, including 5-FU, as well as companies that have developed new or improved chemotherapies. In addition, our product candidates, if approved, may face competition from cancer therapies developed by other companies using phosphoramidate chemistry, as well as other approved drugs or drugs that may be approved in the future for indications for which we may develop our product candidates.

The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our products. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Many of the companies against which we may compete have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical studies, obtaining regulatory approvals and marketing approved products than we do.

Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs.

key performance indicators

As a measurement of liquidity, we review our total liquidity position (including cash and cash equivalents), as well as our operating cash flow. At 31 December 2021, the total liquidity position was £60.3 million (at 31 December 2020: £87.4 million). Net cash used in operating activities was £23.8 million for the year ended 31 December 2021 (year ended 31 December 2020: £21.6 million).

Total liquidity position

£60.3 million (at 31 December 2021)

£87.4 million (at 31 December 2020)

Net cash used in operating activities

£23.8 million (for the year ended 31 December 2021)

£21.6 million (for the year ended 31 December 2020)

principal risks and uncertainties

In common with other pharmaceutical development companies NuCana faces a number of risks and uncertainties. Internal controls are in place to help identify, manage and mitigate these risks. Further details of risk factors considered by NuCana for the year ended 31 December 2021 are included on Form 20-F filed with the SEC on 27 April 2022.

Financial

We have incurred significant operating losses since our inception. We incurred net losses of £40.5 million for the year ended 31 December 2021 and £30.7 million for the year ended 31 December 2020. As of 31 December 2021, we had an accumulated deficit of £149.7 million. Our product candidate NUC-3373 is currently in a Phase 1b/2 clinical study for patients with advanced colorectal cancer. Our product candidate NUC-7738 is currently in a Phase 1/2 clinical study for patients with advanced solid tumours. It may be several years, if ever, before we have a product candidate ready for commercialisation. To date, we have financed our operations primarily through public and private placements of our equity securities. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter.

We expect our expenses to increase with our ongoing activities, particularly as we conduct larger-scale clinical studies of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialisation expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we will continue to incur costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we fail to obtain additional financing, we may be unable to complete the development and commercialisation of our product candidates or continue our development programmes.

Dependence on Clinical Candidates

We do not currently generate any revenues from sales of any products, and we may never be able to develop or commercialise a marketable product. We have invested substantially all of our efforts and financial resources to date in the development of NUC-3373 and NUC-7738, as well as Acelarin, for which we discontinued the NuTide:121 clinical study in March 2022. Our ability to generate product revenues, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development and eventual commercialisation of these product candidates, if approved, which may never occur. Each of NUC-3373 and NUC-7738 will require additional clinical development, management of clinical, preclinical and manufacturing activities, regulatory approval in multiple jurisdictions, procurement of manufacturing supply, commercialisation, substantial additional investment and significant marketing efforts before we generate any revenues from product sales, if at all. We are not permitted to market or promote any product candidates in the United States, Europe or other countries before we receive regulatory approval from the FDA, the European Medicines Agency (EMA) or comparable foreign regulatory authorities, and we may never receive such regulatory approval for NUC-3373, NUC-7738 or any future product candidate. We have not submitted a New Drug Application, or NDA, to the FDA, a Marketing Authorisation Application, or MAA, to the EMA or comparable applications to other regulatory authorities for any of our product candidates and do not expect to be in a position to do so in the foreseeable future.

Manufacturing

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third parties for the manufacture and shipment of our product candidates for preclinical studies and clinical studies, as well as for the commercial manufacture of our drugs if any of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialisation efforts.

BREXIT

On 31 January 2020, the United Kingdom left the European Union. The terms of a withdrawal agreement, provided for a "Transition Period" during which E.U. rules continued to apply in the United Kingdom until 31 December 2020. The Trade and Cooperation Agreement (the "TCA"), which governs the future relationship between the United Kingdom and the European Union, was agreed in December 2020 and implemented in the United Kingdom through the European Union (Future Relationship) Act 2020, which came into force when the Transition Period ended. The TCA provides for zero tariff/zero quota trade in goods (including medicinal products) between the United Kingdom and E.U. member states, and includes commitments from the United Kingdom and the European Union to maintain common high standards across a number of areas, such as intellectual property, competition and taxation, as well as a number of other benefits, such as the U.K.'s continued access to the Horizon Europe research program. However, the United Kingdom's departure from the European Union single market has resulted in substantial changes for U.K. businesses, including an end to the free movement of persons, goods and services between the United Kingdom and the European Union, and the loss of a number of other benefits afforded to citizens and businesses in the United Kingdom and the European Union prior to the withdrawal, such as the mutual recognition of professional qualifications, or passporting for financial services. Furthermore, as the United Kingdom is no longer subject to European Union law, or the jurisdiction of the European Court of Justice, there will be increasing scope for divergence between United Kingdom and E.U. member states' laws and regulations, including the application, interpretation and enforcement of the body of European Union law which has been retained by the United Kingdom.

These developments, and continued uncertainty around how the United Kingdom's legal, political and economic relationship with the European Union will evolve following the withdrawal, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. These developments may also have a significant effect on our ability to attract and retain employees, including scientists and other employees who are important for our and our collaborators' research and development efforts.

COVID-19

Public health crises such as pandemics or similar outbreaks could adversely impact our business. The coronavirus, SARS-CoV-2, which causes COVID-19, and its variants have spread to every country in the world and throughout the United States and the United Kingdom. Many countries, as well as most states of the United States, reacted by instituting quarantines, "lockdowns" and other public health restrictions on leisure activities, work and travel. Although pandemic-related restrictions have been eased or removed in certain geographies, our business remains subject to pandemic-related controls, which may become more restrictive at any time. We rely on third-party manufacturers, distributors, information technology and software service providers, law and accounting firms, contract research organisations (CROs), and consultants who are subject to, or may become subject to, pandemic-related controls. COVID-19 may also affect employees of third-party CROs located in affected geographies that we rely upon to carry out clinical studies. If these third parties cannot perform the services we require in a timely way and we cannot successfully implement replacements or workarounds, our business, results of operations, and financial condition could be harmed. As a result of the COVID-19 pandemic, or potential future pandemics, we have experienced and may in the future experience disruptions that could severely impact our business, preclinical studies and clinical studies, including:

- delays or difficulties in enrolling patients in our clinical studies;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or disruptions in preclinical experiments and investigational new drug application-enabling good laboratory practice standard toxicology studies due to unforeseen circumstances at CROs and vendors along their supply chain;
- increased rates of patients withdrawing from our clinical studies following enrolment as a result of contracting COVID-19, being forced to quarantine, or not wanting to attend hospital visits;
- diversion of healthcare resources away from the conduct of clinical studies, including the diversion of hospitals serving as our clinical study sites and hospital staff supporting the conduct of our clinical studies;
- interruption of key clinical study activities, such as clinical study site data monitoring, due to limitations on travel imposed or recommended by national, state or local governments, employers and others or interruption of clinical study subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA, EMA or other foreign regulatory agencies, which may impact approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organisations due to staffing shortages, production slowdowns or stoppages and disruptions in our supply chain or distribution vendors' ability to ship product candidates; and
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical studies, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home or mass transit disruptions.

These and other factors arising from the COVID-19 pandemic could worsen in countries that are already afflicted with COVID-19, could continue to spread to additional countries, or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct clinical studies and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading prices for our ADSs and for the securities of other biopharmaceutical companies have been highly volatile during certain periods as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our ADSs or such sales may be on unfavourable terms. The COVID-19 pandemic continues to evolve. The extent to which this pandemic may impact our business, preclinical studies and clinical studies will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the emergence, severity and spread of new variants of the disease, the duration of the pandemic and any outbreak of future variants, the potential imposition of travel restrictions and actions to contain the pandemic and any future outbreaks, such as social distancing and quarantines or lockdowns in the United Kingdom, the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United Kingdom, the United States and other countries to contain and treat the disease.

Commercialisation

We currently have no marketing capability or sales force, but we intend to commercialise or participate in the commercialisation of our product candidates for which we receive regulatory approval in major markets, such as the United States and Europe. This may necessitate building a specialised sales force and other commercial capabilities in such markets. To achieve commercial success for any approved product candidate for

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

Regulation

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

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes several years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent us from commercialising the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have limited experience in planning and conducting the clinical studies required for marketing approvals, and we expect to rely on third-party CROs to assist us in this process. Obtaining marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process, and in many cases the inspection of manufacturing facilities by the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the new drug approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies or clinical studies. Our product candidates could be delayed in receiving, or fail to receive, marketing approval.

Intellectual Property

If we are unable to obtain and maintain intellectual property protection for our technology and products, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could commercialise technology and products similar or identical to ours, and our ability to successfully commercialise our technology and products may be impaired. In addition, if we infringe the valid patent rights of others, we may be prevented from making, using or selling our products or may be subject to damages or penalties. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. We may become involved in administrative adversarial proceedings in the United States Patent and Trademark Office (USPTO) or in the patent offices of foreign countries brought by a third party to attempt to cancel or invalidate our patent rights, which could be expensive, time consuming and cause a loss of patent rights. We may have to file one or more lawsuits in court to prevent a third party from selling a product or using a product in a manner that infringes our patent, which could be expensive, time consuming and unsuccessful, and ultimately result in the loss of our proprietary market. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could hurt our business. We may not be able to effectively enforce our intellectual property rights throughout the world. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements. Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors. We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. Our proprietary information, or that of our suppliers and any future collaborators, may be lost or we may suffer security breaches. Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

In 2018, we were granted a European patent from the European Patent Office (EPO), EP 2955190, that covers the composition of matter of a small genus of phosphoramidate nucleotide compounds that includes sofosbuvir, sold under the brand name Sovaldi®, a leading drug for the treatment of hepatitis C sold by Gilead Sciences, Inc. Sofosbuvir and our drug Acelarin share a similar chemical structure, and sofosbuvir is covered by the claims in our patent, which predates Gilead's patent on sofosbuvir by several years. Later in 2018, Gilead filed an Opposition to our patent at the EPO in an attempt to revoke it. In February 2021, the Opposition Division of the European Patent Office, or EPO, upheld our European Patent 2955190 in an amended form. In June 2021, the decision by the Opposition Division to uphold our European Patent 2955190 was appealed by Gilead to the EPO Technical Boards of Appeal. We also filed an appeal to the EPO Technical Boards of Appeal against the decision by the Opposition Division to only allow the patent in an amended form. Subsequent to the decision of the Opposition Division, but also in February 2021, Gilead Sciences, Inc. and Gilead Sciences Limited filed a lawsuit against us in the Patents Court of the High Court of Justice of England and Wales requesting revocation of the U.K. part of that same European patent. In March 2021, we filed a counterclaim against Gilead Sciences, Inc. and Gilead Sciences Limited alleging infringement of our patent resulting from acts including the sale of Sovaldi®, as well as its combination products Harvoni®, Vosevi® and Epclusa®, in the United Kingdom. In April 2021, we initiated legal proceedings against Gilead Sciences Ireland UC and Gilead Sciences GmbH in the German Regional Court of Dusseldorf for patent infringement for the sale of Sovaldi® as well as its combination products Harvoni®, Vosevi® and Epclusa® in Germany. There can be no assurance as to the outcome of any such proceedings or litigation. The appeal of the decision upholding our patent by the EPO Opposition Division, the litigation in the U.K. Patents Court with Gilead, and potential future infringement or validity litigation in Europe with Gilead may subject us to significant legal expense and may be a distraction to management.

Conduct of Clinical Studies

We rely on, and expect to continue to rely on, third parties to conduct our clinical studies for our product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialise our product candidates, and our business could be substantially harmed. We do not have the ability to independently conduct clinical studies. Nevertheless, we will be responsible for ensuring that each of our clinical studies are conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards.

Employees
We currently have a limited number of employees, and our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel. We are a clinical development-stage group, and, as of 31 December 2021, had 33 employees, including four executive officers. We are highly dependent on the research and development, clinical and business development expertise of Hugh Griffith, our Chief Executive Officer, as well as the other principal members of our management team and our collaborators' scientific and clinical teams. Recruiting and retaining qualified scientific, clinical, manufacturing, finance, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialisation objectives and seriously harm our ability to successfully implement our business strategy.

environmental matters

We currently outsource our research, development and manufacturing activities.

Our leased offices in the United Kingdom, used solely for administrative purposes, drive the majority of our carbon emissions. The building currently has a current Energy Performance Certificate, with a Building Energy Performance Rating of "C" (between 31 to 45 $kgCO_2$ per m^2 per year). This rating remains unchanged from the rating indicated in NuCana's previous annual accounts and reports for the financial years ended 31 December 2019 and 31 December 2020. The certificate has been produced under the Energy Performance of Buildings (Scotland) Regulations 2008 from data lodged to the Scottish EPC register. The building energy performance rating is a measure of the effect of a building on the environment in terms of carbon dioxide CO_2 emission, with ratings ranging between "A+" (net zero carbon) to "G" (very poor). The better the rating, the less impact on the environment. The current rating is based upon an assessor's survey of the building, using EPCgen, V4.1.e.5. The main heating fuel: Grid Supplied Electricity; the Building Environment: Air Conditioning; Renewable Energy Source: Heat pumps.

Our report on greenhouse gas emissions is included in our Directors' Report on page 15 of this Annual Report.

employees

The number of employees by function and geographic location as of the end of the period for our fiscal years ended 31 December 2021 and 2020 was as follows:

	2021	2020
By Function:		
Research and development	27	23
Management and administrative	6	6
Total	**33**	**29**
By Geography:		
United Kingdom and Crown Dependencies	30	27
North America	3	2
Total	**33**	**29**

As of 31 December 2021, we had 31 full-time employees and 2 part-time employees. We have never had a work stoppage and none of our employees are covered by collective bargaining agreements or represented by a labour union. We believe our employee relations are good.

Diversity
We make appointments based on merit according to the balance of skills and experience offered by prospective candidates. Whilst acknowledging the benefits of diversity, individual appointments are made irrespective of personal characteristics such as sex, race, disability, gender, sexual orientation, religion or age.

A breakdown of the statistics as at 31 December 2021 is as follows:

Position	Male	Female	Total
Company Director	8	-	8
Senior Manager	7	7	14
Other Employees	11	7	18
Total Employees[1]	**19**	**14**	**33**

(1) Total Employees includes one Executive Director.

employee consultation and human rights

We place considerable value on the involvement of our employees. 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 Group through share option schemes (see note 16 to the financial statements). We endeavour to impact positively on the communities in which we operate. We do not, at present, have a specific policy on human rights. However, we have several policies that promote the principles of human rights, including our Anti-Slavery and Human Trafficking Policy, which governs our zero-tolerance approach to modern slavery and our commitment to acting ethically and with integrity in all our business dealings; and an Anti-Corruption and Bribery Policy in order to reflect our policy to conduct our business in an honest and ethical manner. Our Health & Safety policy sets out our commitment to provision of a safe working environment for our employees. Furthermore, our Equal Opportunities Policy promotes the right of every employee to be treated with dignity and respect and not to be harassed or bullied on any grounds. Accordingly, we have a policy framework in place to ensure that 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. This report does not contain information relating to social or community matters as such information is not relevant in understanding our development, performance or position.

section 172(1) statement

Section 172 of the Companies Act 2006 requires each of directors to act in the way he or she considers, 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, have regard (amongst other matters) to:

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

The directors continue to have regard to the interests of our key stakeholders, including our shareholders, holders of ADSs, and employees. The Board recognises its responsibility to take into consideration the needs and concerns of all our stakeholders as part of our discussion and decision-making processes.

Details of our interactions and engagement with shareholders, ADSs holders and analysts are summarised below.

Interests – issues and factors which are most important to shareholders, ADSs holders and analysts	• Successful R&D pipeline development • Sufficient cash and cash equivalents on hand to fund our anticipated operations
Engagement – examples of engagement in 2021	• Annual General Meeting in June 2021 within COVID-19 restrictions • Directors and senior management meet investors and analysts • Quarterly financial results and regular press releases • Investor outreach programme, including regular investor conferences and events
Outcomes – any actions which resulted	• Helped to inform the objectives and strategy of the business, as outlined in the Our Strategy section of this Strategic Report on page 5 • Attracted new investors in the Group

Our engagement and consultation with employees are outlined in the Employee Consultation and Human Rights section of this Strategic Report on page 13.

The consideration and impact of our operations on the environment are contained in the Environmental Matters section of this Strategic Report on page 12.

The Strategic Report was approved by the Board on 16 May 2022.

On behalf of the Board

Hugh S. Griffith
Chief Executive Officer

directors' report

directors' report

Company registration
NuCana plc is registered in England and Wales with the registered number 03308778.

Results and dividends
The loss for the year after taxation amounted to £40.5 million (2020: £30.7 million). The directors do not recommend a final dividend (2020: £nil).

Principal activities
NuCana is a rapidly growing, clinical-stage biopharmaceutical Group developing a portfolio of new medicines (ProTides) to treat patients with cancer. The unique feature of ProTides is their ability to overcome the key limitations associated with many widely used anti-cancer medicines.

Future developments
The future developments have been set out in the Strategic Report on page 2.

Research and development activities
NuCana's research and development strategy and activities have been set out in the Strategic Report on pages 2 to 13.

Directors
The directors who served the Company during the year and up to the date of this report were as follows:

Hugh Griffith
Andrew Kay
Adam George
Martin Mellish
Cyrille Leperlier
Bali Muralidhar
Elliott Levy (appointed 1 November 2021)
Rafaèle Tordjman (retired 28 September 2021)
James Healy (retired 27 April 2022)

Financial instruments
Details of financial instruments are set out in note 18 to the financial statements on page 65.

Charitable and political contributions
No charitable contributions were paid during the 2021 financial year (2020: £nil).
No donations were made during the 2021 financial year to political organisations (2020: £nil).

Structure of group's capital
Details of the structure of the Group's capital are set out in note 14 to the financial statements on page 58.

Directors' insurance and indemnities
The directors have the benefit of the indemnity provisions contained in the Company's Articles of Association, and the Company has maintained throughout the year directors' and officers' liability insurance for the benefit of the Company, the directors and its officers. The Company has entered into qualifying third-party indemnity arrangements for the benefit of all its directors in a form and scope which comply with the requirements of the Companies Act 2006 and which were in force throughout the year and remain in force.

Overseas branches
The Company has no overseas branches.

Environmental matters
The Group measures and reports its greenhouse gas emissions.

As 2020 was the first year of reporting, it is reported as the baseline year against which future performance is measured.

Quantification and reporting methodology
This report was compiled by management. The 2019 U.K. Government Environmental Reporting Guidelines and the GHG Protocol Corporate Accounting and Reporting Standard (revised edition) were followed to ensure the Streamlined Energy and Carbon Reporting ("SECR") requirements were met.

The energy data was collated using existing reporting mechanisms for the Group's leased offices in the United Kingdom, where the majority of the Group's employees work. These methodologies provided a continuous record of electricity use.

The energy data was converted to carbon emissions using the 2021 U.K. Government GHG Conversion Factors for Company Reporting. The associated emissions are divided into the combustion of fuels and the operation of facilities (scope 1), purchased electricity, heating and cooling (scope 2) and indirect emissions that occur as a consequence of company activities (scope 3). During the year the Group only had emissions relating to scope 2.

Estimations
The electricity use was compiled from invoices and meter readings.

	2021	2020
Energy used by the company (in KWH)	128,699	164,026
Emissions associated with the reported energy use (tCO_2e)	27	38

Intensity Ratio
The chosen primary intensity ratio is total gross emissions in metric tonnes CO_2e (mandatory emissions) per employee.

	2021	2020
Tonnes of CO_2e per employee	1.01	1.37

Energy efficiency action during current financial year
We will continue to monitor our carbon emissions and look for cost-effective improvements of energy performance.

Energy consumption is expected to increase this year as we adopt a blended approach to working, with a mix of remote and office working. The COVID-19 pandemic has shown that more flexible working policies have not had a detrimental impact on the day-to-day function of the business. It is therefore expected that our energy consumption will be lower relative to pre-pandemic levels.

As a result of the COVID-19 restrictions, there has been an increase in the use of video conferencing for meetings, reducing the need for travel. The emission savings resulting from these activities has not been quantified, but this practice has resulted in behavioural changes that are expected to continue for the foreseeable future.

Climate change
The Group relies on third parties to manufacture and ship our product candidates for preclinical studies and clinical studies, as well as conducting the associated preclinical and clinical studies. As a result, the Group's direct operational footprint is such that it does not expect any material impact on their operations and financial position as a result of climate change.

The Audit Committee makes recommendations to the Board on the principal risks of relevance to the business. Climate-related issues are considered in terms of potential for contribution to these principal risks. The issues considered include both the risk of physical disruption to the business from climate change, and the risks and opportunities as the global economy transitions to significantly lower carbon emissions. In the current period, the Audit Committee concluded that climate-related risks did not rise to the level of a principal risk.

Events after the reporting period
Details of important events affecting the Group, which have occurred since 31 December 2021, are set out in note 19 to the financial statements on page 66.

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 auditor in connection with preparing its report, of which the auditor is unaware. Having made enquiries of fellow directors and the Group's auditor, each director has taken all the steps that they are obliged to take as directors in order to make themselves aware of any relevant audit information and to establish that the auditor is aware of that information.

Auditors
Resolutions to re-appoint Ernst & Young LLP as auditor of the Company and to authorise the Board to set its remuneration will be proposed at the Company's forthcoming annual general meeting ("AGM").

The Directors' Report was approved by the Board on 16 May 2022.

On behalf of the Board

Hugh S. Griffith
Director

directors' remuneration report

remuneration committee chair's annual statement

The information provided in this part of the Directors' Remuneration Report is not subject to audit.

On behalf of the Board of Directors of NuCana plc, I am pleased to present the Directors' Remuneration Report for the year ended 31 December 2021.

With shareholder attendance being limited due to ongoing COVID-19 challenges voting at our 2021 AGM was conducted on a poll of the proxy vote. At the meeting, the resolution to approve the 2020 Directors' Remuneration Report was approved as follows:

- Resolution 8 regarding approval of the Directors' Remuneration Report: 48,530,497 votes for and 979,261 votes against which equates to over 98% of the proxy vote being in favour of the resolution. 2,179,406 votes were withheld.

At the 2020 AGM, the resolution to approve the 2019 Directors' Remuneration Policy was approved as follows:

- Resolution 6 regarding approval of the Directors' Remuneration Policy: 29,488,397 votes for and 959,483 votes against which equates to over 96% of the proxy vote in favour of the resolution. 1,463,007 votes were withheld.

A copy of the Directors' Remuneration Policy (approved to take effect from 25 June 2020) is available for inspection at the Global Headquarters of the Company at 3 Lochside Way, Edinburgh, EH12 9DT, United Kingdom, and is also available on pages 22 to 26 of our 2019 Annual Report, which is on our website at http://www.nucana.com.

Remuneration committee

The Remuneration Committee consists of two independent Non-Executive Directors, Bali Muralidhar (Chair from 27 April 2022 and Member since 5 February 2021), and Elliott Levy (Member since 6 May 2022). Rafaèle Tordjman was Chair and Member until 5 February 2021. James Healy was Chair and Member until 27 April 2022.

The Remuneration Committee is responsible for reviewing and establishing our executive remuneration policy and philosophy, including reviewing the performance of the senior executive officers and setting the scale and structure of their remuneration and the basis of their service agreements with due regard to the interests of the shareholders. It is the policy of the Remuneration Committee that no individual can participate in discussions or decisions concerning his or her own remuneration.

The Directors' Remuneration Report that follows is for the year from 1 January 2021 to 31 December 2021 except where otherwise stated.

The Directors' Remuneration Policy is designed to:

- Increase shareholder value;
- Reward senior executive officers for their contribution to the Company's development and value creation;
- Recognise individual initiative, leadership, achievement, and other contributions; and
- Provide competitive compensation that will attract and retain qualified executives.

Activities and major decisions

During the year ended 31 December 2021, the Committee undertook the following activities and major decisions:

- Commissioned an updated benchmarking review of director and senior executive officer compensation, which was undertaken to ensure that remuneration for our directors and senior executive officers remains competitive for the retention and engagement of key talent. The Committee engaged Radford (an Aon Hewitt company) as independent advisors to:
  - Provide an assessment of director and senior executive officer annual cash compensation, including base salary and annual bonuses as compared to the market; and
  - Provide an assessment of the annual grants of options for directors and senior executive officers as compared to the market.

  As a result of a Radford benchmarking study completed in early 2022, the Chief Financial Officer (CFO) received an increased base salary award at a level that is aligned with the peer group comparator data. For our CFO, this resulted in a base salary award of $490,611 effective from 1 January 2022. Our Chief Executive Officer (CEO) elected to forego an inflationary increase in his base salary award and has maintained his 2021 base salary of £531,193.
- Awarded share options to selected employees in January, February, August, September and December 2021.

2022 Annual General Meeting

On behalf of the Board, I wish to thank our shareholders for their input and support during the year ended 31 December 2021. The Remuneration Committee and the Board of Directors welcome feedback from our shareholders on the Directors' Remuneration Report. We look forward to receiving the support of our shareholders for the Directors' Remuneration Report at our Annual General Meeting to be held on 23 June 2022.

Bali Muralidhar
Non-Executive Director & Chair of Remuneration Committee

16 May 2022

report on remuneration

The information provided in this part of the Directors' Remuneration Report is subject to audit.

The Remuneration Committee presents the Report on Remuneration for the year ended 31 December 2021, which will be put to shareholders for a non-binding vote at the Annual General Meeting to be held on 23 June 2022.

Single Total Figure for Remuneration of each Director

The following table shows the remuneration received by the directors for the years ended 31 December 2021 and 31 December 2020.

Name of director		Salary & Fees[1] £	Taxable Benefits[2] £	Annual Bonus[3] £	Share Options[4] £	Pension Benefit[5] £	Total £	Total Fixed Remuneration[6] £	Total Variable Remuneration[7] £
Executive Directors[8]									
Hugh Griffith	YE 31 Dec 2021	531,193	3,506	318,716	1,251,582	53,119	2,158,116	587,818	1,570,298
	YE 31 Dec 2020	551,425	2,982	309,433	789,133	56,210	1,709,183	610,617	1,098,566
Christopher Wood[9]	YE 31 Dec 2021	-	-	-	-	-	-	-	-
	YE 31 Dec 2020	80,822	2,167	-	-	-	82,989	82,989	-
Non-Executive Directors									
Andrew Kay[10]	YE 31 Dec 2021	58,860	-	-	-	-	58,860	58,860	-
	YE 31 Dec 2020	1,773	-	-	-	-	1,773	1,773	-
Adam George	YE 31 Dec 2021	45,574	-	-	54,100	-	99,674	45,574	54,100
	YE 31 Dec 2020	47,420	-	-	34,137	-	81,557	47,420	34,137
Martin Mellish	YE 31 Dec 2021	38,299	-	-	54,100	-	92,399	38,299	54,100
	YE 31 Dec 2020	39,697	-	-	34,137	-	73,834	39,697	34,137
Cyrille Leperlier	YE 31 Dec 2021	38,299	-	-	54,100	-	92,399	38,299	54,100
	YE 31 Dec 2020	34,660	-	-	34,137	-	68,797	34,660	34,137
Bali Muralidhar[11]	YE 31 Dec 2021	42,840	-	-	54,100	-	96,940	42,840	54,100
	YE 31 Dec 2020	8,959	-	-	-	-	8,959	8,959	-
Isaac Cheng[12]	YE 31 Dec 2021	-	-	-	-	-	-	-	-
	YE 31 Dec 2020	7,542	-	-	-	-	7,542	7,542	-
Elliot Levy[13]	YE 31 Dec 2021	6,383	-	-	12,799	-	19,182	6,383	12,799
	YE 31 Dec 2020	-	-	-	-	-	-	-	-
Rafaèle Tordjman[14]	YE 31 Dec 2021	24,663	-	-	-	-	24,663	24,663	-
	YE 31 Dec 2020	47,420	-	-	34,137	-	81,557	47,420	34,137
James Healy[15]	YE 31 Dec 2021	44,653	-	-	54,100	-	98,753	44,653	54,100
	YE 31 Dec 2020	37,766	-	-	34,137	-	71,903	37,766	34,137
Total	**YE 31 Dec 2021**	**830,764**	**3,506**	**318,716**	**1,534,881**	**53,119**	**2,740,986**	**887,389**	**1,853,597**
	YE 31 Dec 2020	**857,484**	**5,149**	**309,433**	**959,818**	**56,210**	**2,188,094**	**918,843**	**1,269,251**

(1) The majority of the remuneration was set and paid in pounds sterling (£). For the purposes of this table, the fees paid in any other currency in which remuneration was paid have been converted into pounds sterling based on the currency/pounds sterling average exchange rate for the period the costs relate to. All of the figures in the table above are in pounds sterling.
(2) The amount for taxable benefits represents the Company's contribution to medical insurance.
(3) The annual bonus amounts shown for the year ended 31 December 2021 represent the total bonus payments that related to performance in 2021, which was paid in early 2022.
(4) These options only have service conditions attached. There are no performance conditions. The values of these share option awards are therefore recorded in this table at the date of grant. Where the options have vested before the date of this report the value is based on the market value of the shares at the date of vesting, less the exercise price. Where the options have not vested the market value of the options at the date of vesting is not ascertainable. Therefore, the value included in this table is based on the average market value of the shares over the three months to 31 December 2021 and 31 December 2020 respectively, less the applicable exercise price.
(5) The amount for pension benefit represents the Company's contribution into a money purchase plan.
(6) Total fixed remuneration includes salary and fees, taxable benefits and pension benefit.
(7) Total variable remuneration includes annual bonus and share options.
(8) Changes to the compensation for our Executive Directors take effect from 1 January in each year.
(9) Christopher Wood retired from the Board on 25 June 2020.
(10) Andrew Kay appointed to the Board on 21 December 2020.
(11) Bali Muralidhar appointed to the Board on 30 September 2020.
(12) Isaac Cheng retired from the Board on 11 March 2020.
(13) Elliott Levy appointed to the Board on 1 November 2021.
(14) Rafaèle Tordjman retired from the Board on 28 September 2021.
(15) James Healy retired from the Board on 27 April 2022.

Annual bonus

Our Executive Directors are eligible for an annual bonus at the discretion of the Remuneration Committee. Bonus awards are reviewed at the end of each calendar year and any such awards are determined by the performance of the individual and the company as a whole, based upon the achievement of strategic objectives set at the beginning of the year. In determining Executive Director compensation for the year ended 31 December 2021, the Remuneration Committee considered achievement of specific performance measures which had been previously approved by the Remuneration Committee to be achieved by the executive team during 2021. These are considered to be commercially sensitive and will not be disclosed in detail, but are linked to our business strategies which include to:

- Rapidly develop NUC-3373 to replace 5-FU as the standard of care for the treatment of patients with colorectal cancer;
- Identify additional indications for development of NUC-3373;
- Rapidly develop NUC-7738 as a treatment for patients with solid tumours;
- Leverage our proprietary ProTide technology platform to develop additional product candidates; and
- Continue to protect and strengthen our intellectual property position.

Share options awarded during the financial year

The table below shows, for each director, the total number of options awarded in the year ended 31 December 2021. The face value of the award is calculated as the share price at date of grant, in pounds sterling, multiplied by the number of options granted. The options granted have no performance conditions, only service conditions.

We periodically grant share options to employees, directors and consultants to enable them to share in our successes and to reinforce a corporate culture that aligns their interests with that of our shareholders.

Name of director	Type of plan	Number of options granted	Exercise price £	Share price at date of grant £	Value at date of grant £	Performance period end	Date of expiry
Executive Directors							
Hugh Griffith	2020 Long-Term Incentive Plan	393,850	4.53	4.53[2]	1,784,141	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	196,925	0.04	4.53[3]	892,070	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	815,800	1.71	1.71[4]	1,395,018	15 September 2025	15 September 2031
	2020 Long-Term Incentive Plan	408,000	0.04	1.71[5]	697,680	15 September 2025	15 September 2031
Non-Executive Directors							
Andrew Kay	2020 Long-Term Incentive Plan	200,000	3.92	3.92[6]	784,000	13 January 2025	13 January 2031
Adam George	2020 Long-Term Incentive Plan	23,100	4.53	4.53[2]	104,643	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	11,550	0.04	4.53[3]	52,322	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	29,700	1.71	1.71[4]	50,787	15 September 2025	15 September 2031
	2020 Long-Term Incentive Plan	14,850	0.04	1.71[5]	25,394	15 September 2025	15 September 2031
Martin Mellish	2020 Long-Term Incentive Plan	23,100	4.53	4.53[2]	104,643	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	11,550	0.04	4.53[3]	52,322	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	29,700	1.71	1.71[4]	50,787	15 September 2025	15 September 2031
	2020 Long-Term Incentive Plan	14,850	0.04	1.71[5]	25,394	15 September 2025	15 September 2031
Cyrille Leperlier	2020 Long-Term Incentive Plan	23,100	4.53	4.53[2]	104,643	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	11,550	0.04	4.53[3]	52,322	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	29,700	1.71	1.71[4]	50,787	15 September 2025	15 September 2031
	2020 Long-Term Incentive Plan	14,850	0.04	1.71[5]	25,394	15 September 2025	15 September 2031
Bali Muralidhar	2020 Long-Term Incentive Plan	23,100	4.53	4.53[2]	104,643	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	11,550	0.04	4.53[3]	52,322	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	29,700	1.71	1.71[4]	50,787	15 September 2025	15 September 2031
	2020 Long-Term Incentive Plan	14,850	0.04	1.71[5]	25,394	15 September 2025	15 September 2031
Elliott Levy	2020 Long-Term Incentive Plan	90,000	1.72	1.72[7]	154,800	15 December 2025	15 December 2031
Rafaèle Tordjman[1]	2020 Long-Term Incentive Plan	23,100	4.53	4.53[2]	104,643	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	11,550	0.04	4.53[3]	52,322	10 February 2025	10 February 2031
James Healy	2020 Long-Term Incentive Plan	23,100	4.53	4.53[2]	104,643	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	11,550	0.04	4.53[3]	52,322	10 February 2025	10 February 2031
	2020 Long-Term Incentive Plan	29,700	1.71	1.71[4]	50,787	15 September 2025	15 September 2031
	2020 Long-Term Incentive Plan	14,850	0.04	1.71[5]	25,394	15 September 2025	15 September 2031

(1) Options granted to Rafaèle Tordjman in 2021 have lapsed.
(2) The share options were granted on 10 February 2021.
(3) The share options were granted on 10 February 2021. The exercise price of these share options are at the nominal value of our ordinary shares of £0.04 rather than at the share price at the date of grant of £4.53. The exercise price of the share options has not changed since the date of the grant.
(4) The share options were granted on 15 September 2021.
(5) The share options were granted on 15 September 2021. The exercise price of these share options are at the nominal value of our ordinary shares of £0.04 rather than at the share price at the date of grant of £1.71. The exercise price of the share options has not changed since the date of the grant.
(6) The share options were granted on 13 January 2021.
(7) The share options were granted on 15 December 2021.

Statement of directors' shareholdings and share interests

The table below shows, for each director, the total number of shares owned, the total number of share options held and the number of share options vested as at 31 December 2021. The table only reflects shares held individually by each director, or in a family investment vehicle, and does not include shares held by any investment fund with which the director is affiliated.

Name of director	Shares owned	Share options Vested not yet exercised[1]	Share options Unvested with performance conditions[1]	Share options Exercised during the year	Total (Shares and Share Options)
Executive Directors					
Hugh Griffith	1,180,121	2,574,564	3,024,072	155,000	6,778,757
Non-Executive Directors					
Andrew Kay	-	-	200,000	-	200,000
Adam George	-	42,600	139,999	-	182,599
Martin Mellish	2,392	70,208	134,749	2,392	207,349
Cyrille Leperlier	-	42,600	139,999	-	182,599
Bali Muralidhar[2]	540	-	79,200	-	79,740
Elliott Levy	-	-	90,000	-	90,000
Rafaèle Tordjman[3]	-	72,600	-	-	72,600
James Healy[4]	48,142	24,458	134,749	2,392	207,349

(1) All share options that were outstanding as at 31 December 2021 use time-based vesting and are not subject to performance targets other than continued service until the date of vesting.

(2) Consists of 540 ADSs. Excludes 3,333,333 ADSs held by Abingworth Bioventures VII, LP ("Abingworth VII"). Abingworth VII (acting by its general partner Abingworth Bioventures VII GP LP, acting by its general partner Abingworth General Partner VII LLP) has delegated to Abingworth LLP ("Abingworth"), all investment and dispositive power over the securities held by Abingworth VII. Abingworth holds the reported securities indirectly through Abingworth VII. Bali Muralidhar is a managing partner and investment committee member of Abingworth and disclaims beneficial ownership of the ADSs held by Abingworth VII.

(3) Rafaèle Tordjman retired from the Board on 28 September 2021. All unvested share options lapsed on the date of her retirement.

(4) Consists of 48,142 ordinary shares held in the Healy Family Trust, for which James Healy's spouse is the trustee. Excludes 5,777,777 ordinary shares owned of record by Sofinnova Venture Partners VIII, L.P. ("SVP VIII") and 2,222,222 ordinary shares owned of record by Sofinnova Venture Partners X, L.P. ("SVP X"). James Healy, together with Michael F. Powell, are the managing members of Sofinnova Management VIII, L.L.C., the general partner of SVP VIII, and as such, may be deemed to share voting and investment power with respect to such shares. James Healy, together with Michael F. Powell and Maha Katabi, are the managing members of Sofinnova Management X, L.L.C., the general partner of SVP X, and as such, may be deemed to share voting and investment power with respect to such shares. James Healy disclaims beneficial ownership with regard to the 5,777,777 shares owned by SVP VIII and the 2,222,222 shares owned by SVP X, except to the extent of his proportionate pecuniary interest therein. James Healy retired from the Board on 27 April 2022.

Policy on shareholding requirements

We do not currently have a policy requiring our directors to hold a certain number or value of our shares.

Directors' equity-based awards held at 31 December 2021

The table below presents the interests of the directors in options to acquire our ordinary shares with a nominal value of £0.04 per share as at 31 December 2021. A total of 2,535,225 options were granted to directors during the year ended 31 December 2021. Three of our directors exercised options during the year ended 31 December 2021.

Name of director	Options held	Grant date	Start date for vesting	Earliest date of potential exercise of any options[1]	Date of expiry
Executive Directors					
Hugh Griffith	124,999	21-Sep-2012	21-Sep-2012	21-Sep-2013	21-Sep-2022
	125,000	28-Jun-2013	28-Jun-2013	28-Jun-2014	28-Jun-2023
	124,999	27-Jan-2014	27-Jan-2014	27-Jan-2015	27-Jan-2024
	625,000	27-Mar-2014	27-Mar-2014	27-Mar-2014	27-Mar-2024
	1,028,533	15-Sep-2017	15-Sep-2017	15-Sep-2017	15-Sep-2027
	428,600	15-May-2019	15-May-2019	15-May-2020	15-May-2029
	1,105,775	10-Jun-2020	10-Jun-2020	10-Jun-2021	10-Jun-2030
	221,155	9-Sep-2020	9-Sep-2020	9-Sep-2021	9-Sep-2030
	590,775	10-Feb-2021	10-Feb-2021	10-Feb-2022	10-Feb-2031
	1,223,800	15-Sep-2021	15-Sep-2021	15-Sep-2022	15-Sep-2031
Total	**5,598,636**				
Non-Executive Directors					
Andrew Kay	200,000	13-Jan-2021	13-Jan-2021	13-Jan-2022	13-Jan-2031
Total	**200,000**				
Adam George	21,000	11-Apr-2018	11-Apr-2018	11-Apr-2019	11-Apr-2028
	25,000	15-May-2019	15-May-2019	15-May-2020	15-May-2029
	47,832	10-Jun-2020	10-Jun-2020	10-Jun-2021	10-Jun-2030
	9,567	9-Sep-2020	9-Sep-2020	9-Sep-2021	9-Sep-2030
	34,650	10-Feb-2021	10-Feb-2021	10-Feb-2022	10-Feb-2031
	44,550	15-Sep-2021	15-Sep-2021	15-Sep-2022	15-Sep-2031
Total	**182,599**				
Martin Mellish	15,000	21-Sep-2012	21-Sep-2012	21-Sep-2013	21-Sep-2022
	7,500	28-Jun-2013	28-Jun-2013	28-Jun-2014	28-Jun-2023
	23,250	16-May-2017	28-Oct-2016	28-Oct-2017	16-May-2027
	25,000	15-May-2019	15-May-2019	15-May-2020	15-May-2029
	47,832	10-Jun-2020	10-Jun-2020	10-Jun-2021	10-Jun-2030
	7,175	9-Sep-2020	9-Sep-2020	9-Sep-2021	9-Sep-2030
	34,650	10-Feb-2021	10-Feb-2021	10-Feb-2022	10-Feb-2031
	44,550	15-Sep-2021	15-Sep-2021	15-Sep-2022	15-Sep-2031
Total	**204,957**				
Cyrille Leperlier	21,000	11-Apr-2018	11-Apr-2018	11-Apr-2019	11-Apr-2028
	25,000	15-May-2019	15-May-2019	15-May-2020	15-May-2029
	47,832	10-Jun-2020	10-Jun-2020	10-Jun-2021	10-Jun-2030
	9,567	9-Sep-2020	9-Sep-2020	9-Sep-2021	9-Sep-2030
	34,650	10-Feb-2021	10-Feb-2021	10-Feb-2022	10-Feb-2031
	44,550	15-Sep-2021	15-Sep-2021	15-Sep-2022	15-Sep-2031
Total	**182,599**				
Bali Muralidhar	34,650	10-Feb-2021	10-Feb-2021	10-Feb-2022	10-Feb-2031
	44,550	15-Sep-2021	15-Sep-2021	15-Sep-2022	15-Sep-2031
Total	**79,200**				
Elliott Levy	90,000	15-Dec-2021	15-Dec-2021	15-Dec-2022	15-Dec-2031
Total	**90,000**				

cont

Name of director	Options held	Grant date	Start date for vesting	Earliest date of potential exercise of any options[1]	Date of expiry
Rafaèle Tordjman[2]	45,750	15-Sep-2017	15-Sep-2017	15-Sep-2018	15-Sep-2027
	12,500	15-May-2019	15-May-2019	15-May-2020	15-May-2029
	11,958	10-Jun-2020	10-Jun-2020	10-Jun-2021	10-Jun-2030
	2,392	9-Sep-2020	9-Sep-2020	9-Sep-2021	9-Sep-2030
Total	**72,600**				
James Healy[3]	25,000	15-May-2019	15-May-2019	15-May-2020	15-May-2029
	47,832	10-Jun-2020	10-Jun-2020	10-Jun-2021	10-Jun-2030
	7,175	9-Sep-2020	9-Sep-2020	9-Sep-2021	9-Sep-2030
	34,650	10-Feb-2021	10-Feb-2021	10-Feb-2022	10-Feb-2031
	44,550	15-Sep-2021	15-Sep-2021	15-Sep-2022	15-Sep-2031
Total	**159,207**				

(1) All share options awarded to directors that were outstanding as at 31 December 2021 use time-based vesting and are not subject to performance targets other than continued service until the date of vesting.
(2) Rafaèle Tordjman retired from the Board on 28 September 2021. All unvested share options lapsed on the date of her retirement.
(3) James Healy retired from the Board on 27 April 2022.

The closing market price of our ADSs on 31 December 2021 was $2.38. One ADS represents one ordinary share.

Payments made to past directors
During the year ended 31 December 2021, no payments were made to former directors of the Company.

Payments for loss of office
During the year ended 31 December 2021, no payments were made with respect to a director's loss of office.

Policy on payments for loss of office
Our approach to payments in the event of termination of an Executive Director is to take account of the individual circumstances including the reason for termination, individual performance, contractual obligations and the terms of the share option scheme in which the Executive Director participates.

Payment obligations would include base salary, target bonus and benefits. In addition, our option scheme rules allow some or all of the options held by our Executive Directors and senior executive officers to vest in certain circumstances upon the event of a change of control.

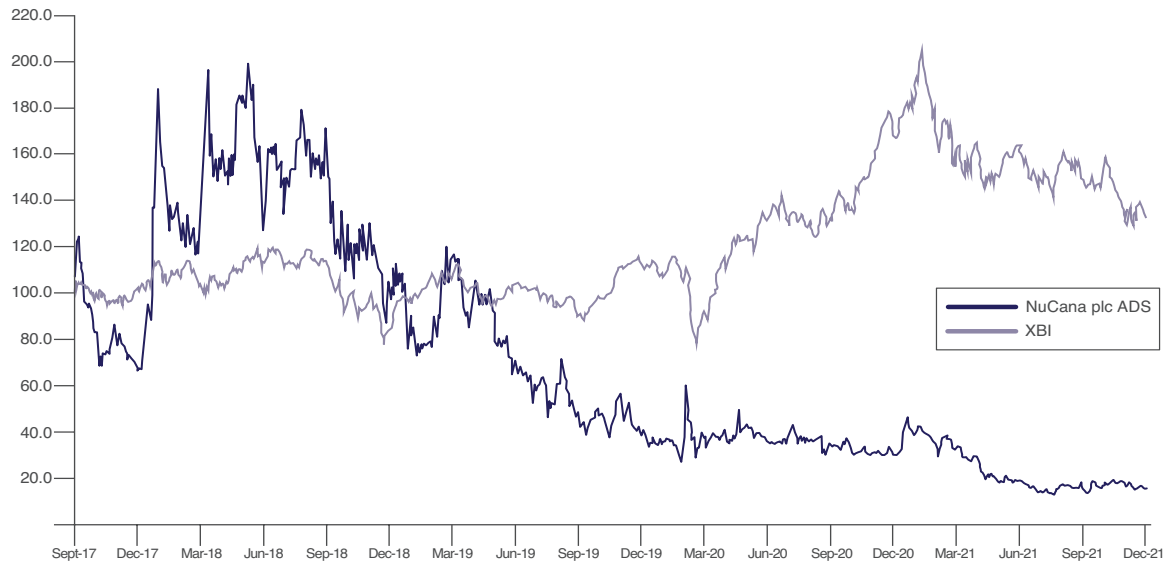
There are no contractual provisions agreed prior to 27 June 2012 that could impact on the quantum of the payment.

We will comply with applicable disclosure and reporting requirements of the Securities and Exchange Commission with respect to remuneration arrangements with a departing Executive Director.

Illustration of total shareholder return

The information provided in this part of the Directors' Remuneration Report is not subject to audit.

The graph below shows the daily movements by 31 December 2021, of $100 invested in NuCana plc ADS at our IPO price on 28 September 2017 compared with the value of $100 invested in the SPDR Series Trust SPDR S&P Biotech ETF (XBI). We believe this graph reflects our relative performance against a group of similarly situated comparator companies.



Chief executive officer historical remuneration

The table below sets out total remuneration delivered to the Chief Executive Officer over the last six years valued using the methodology applied to the single total figure of remuneration. The Remuneration Committee does not believe that the remuneration payable in its earlier years as a private company bears any comparative value to that paid in its later years and therefore the Remuneration Committee has chosen to disclose remuneration only for the six most recent financial years.

Period	Single total figure of remuneration £	Annual bonus payout against maximum opportunity	Long term incentive vesting rates against maximum opportunity
Year ended 31 December 2021(1)	2,158,116	100%	100%
Year ended 31 December 2020(1)	1,709,183	100%	100%
Year ended 31 December 2019	827,586	95%	100%
Year ended 31 December 2018	786,311	97%	n/a
Year ended 31 December 2017(1)	11,033,025	100%	100%
Year ended 31 December 2016	407,533	100%	100%

(1) The years ended 31 December 2021, 31 December 2020 and 31 December 2017 include unrealised gains on share options, which have not been exercised.

Change in director remuneration compared to other employees

The following table below shows the percentage change in the remuneration of directors and the average change per employee from 2020 onwards.

Percentage change in Remuneration				
		Salary & Fees %	Taxable Benefits %	Annual Bonus %
Executive Directors				
Hugh Griffith	2020 to 2021	(3.7)	17.6	3.0
	2019 to 2020	10.8	24.7	9.6
Christopher Wood(1)	2020 to 2021	-	-	-
	2019 to 2020	(49.7)	(47.9)	(100.0)
Non-Executive Directors(2)				
Andrew Kay(3)	2020 to 2021	3,219.8	-	-
	2019 to 2020	-	-	-
Adam George	2020 to 2021	(3.9)	-	-
	2019 to 2020	(1.1)	-	-
Martin Mellish	2020 to 2021	(3.5)	-	-
	2019 to 2020	22.8	-	-
Cyrille Leperlier	2020 to 2021	10.5	-	-
	2019 to 2020	7.2	-	-
Bali Muralidhar(4)	2020 to 2021	378.2	-	-
	2019 to 2020	-	-	-
Isaac Cheng(5)	2020 to 2021	-	-	-
	2019 to 2020	(76.7)	-	-
Elliott Levy(6)	2020 to 2021	-	-	-
	2019 to 2020	-	-	-
Rafaèle Tordjman(7)	2020 to 2021	(48.0)	-	-
	2019 to 2020	7.7	-	-
James Healy	2020 to 2021	18.2	-	-
	2019 to 2020	16.8	-	-
Employees(8)	2020 to 2021	8.9	(1.3)	14.3
	2019 to 2020	12.8	4.3	25.4

(1) Christopher Wood retired from the Board on 25 June 2020. The percentage change compares a full year with a part year until Christopher's retirement.
(2) Fees for Non-Executive Directors are set in US dollars and converted to pounds sterling (£) at the average rate for each year. Fees paid also reflect membership of various sub-committees, such as the Audit, Remuneration or Nominations Committee, in each respective year.
(3) Andrew Kay was appointed to the Board on 21 December 2020. The percentage change compares a full year with a part year from Andrew's appointment.
(4) Bali Muralidhar was appointed to the Board on 30 September 2020. The percentage change compares a full year with a part year from Bali's appointment.
(5) Isaac Cheng retired from the Board on 11 March 2020. The percentage change compares a full year with a part year until Dr. Cheng's retirement date.
(6) Elliott Levy was appointed to the Board on 1 November 2021.
(7) Rafaèle Tordjman retired from the Board on 28 September 2021. The percentage change compares a full year with a part year until Rafaèle's retirement.
(8) The employee group comprises employees of the Company. The percentage change compares the average annualised costs for all employees employed by the Company in a specific year.

Relative importance of spend on pay

The following table sets forth the total amounts spent by the Group on remuneration for the year ended 31 December 2021 and the year ended 31 December 2020. The comparator chosen to reflect the relative importance of the Group's spend on pay is the Group's research and development expenses as shown in its consolidated income statement on page 37 of its Annual Report and Financial Statements for the year ended 31 December 2021. Dividend distribution and share buy-back comparators have not been included as the Group has no history of such transactions.

Period	Year ended 31 December 2021	Year ended 31 December 2020
	£ (in thousands)	£ (in thousands)
Total spend on remuneration[1]	12,832	9,985
Research and development expenses	36,834	25,899

(1) The total spend on remuneration includes the value of equity-based awards as recognised in the financial statements in accordance with International Financial Reporting Standard 2 "Share-Based Payments".

statement of implementation of the directors' remuneration policy in financial year ending 31 December 2022

The Company does not anticipate any changes in the implementation of the Directors' Remuneration Policy approved and adopted at the 2020 AGM. The following activities and decision were taken in the current financial year:

- In January 2022, the Remuneration Committee considered the extent to which the 2021 calendar year objectives were achieved by the executive team and determined the level of bonus incentive awards payable in respect of the 2021 calendar year. The awards made to our CEO and senior executive officers recognised that, against the backdrop of the COVID-19 pandemic, almost all of our corporate objectives for 2021 had been achieved, with our CEO and senior executive officers receiving bonus awards at 100% of the potential target bonus amount. These target bonus amounts had also been benchmarked against peer group comparative data as provided by Radford, an Aon Hewitt company.
- The Committee also met to consider the award of share options to the directors and senior executive officers in respect of services provided and performance attained during 2021, in accordance with the Remuneration Policy. Details are provided in this 2021 Annual Report.
- In March 2022, the Committee approved the objectives to be achieved by the executive team during 2022. These are considered to be commercially sensitive and will not be disclosed in detail, but are linked to our business strategies which include to:
    - Rapidly develop NUC-3373 to replace 5-FU as the standard of care for the treatment of patients with colorectal cancer;
    - Identify additional indications for development of NUC-3373;
    - Rapidly develop NUC-7738 as a treatment for patients with solid tumours;
    - Leverage our proprietary ProTide technology platform to develop additional product candidates; and
    - Continue to protect and strengthen our intellectual property position.

The remuneration committee

The Remuneration Committee consists of two independent Non-Executive Directors, Bali Muralidhar and Elliott Levy. James Healy was a member of the Remuneration Committee until 27 April 2022.

Each of these Non-Executive Director members is a non-employee director as defined in Rule 166-3 under the Exchange Act and an outside director as defined in Section 162(m) of the Internal Revenue Code of 1986, as amended. Bali Muralidhar serves as Chair of the Remuneration Committee. The Remuneration Committee reviews, among other things, the performance of the senior executive officers and sets the scale and structure of their remuneration and the basis of their service agreements with due regard to the interests of the shareholders.

It is a policy of the Remuneration Committee that no individual participates in discussions or decisions concerning his or her own specific remuneration (although the members of the Remuneration Committee do consider the remuneration generally of the Non-Executive Directors as a class).

All members have continued to serve until the date of this Report on Remuneration, with the exception of James Healy who was a member of the Remuneration Committee until 27 April 2022. The terms of reference of the Remuneration Committee is set forth on our website at http://www.nucana.com.

Advice provided to the remuneration committee

The Remuneration Committee retained Radford, an Aon Hewitt company, to provide independent advice and consultation with respect to remuneration arrangements for the directors and senior executive officers. The Committee selected Radford based on the fact that Radford are global remuneration consultants with a well-established reputation for the design and implementation of remuneration programmes, including the design and implementation of equity-based award programmes. Radford have no other connection to, or business relationship with, NuCana. Based on Radford's extensive experience with similar assignments and the fact that Radford have no other connections to, or business relationships, with NuCana, the Remuneration Committee believes the advice received from Radford is objective and independent. For the year ended 31 December 2021, the cost of advice from Radford that was expensed in the year was £16,499 (2020: £48,158).

In addition to Radford, the Remuneration Committee solicited and received input from the CEO concerning the remuneration of employees other than himself. The CEO provided recommendations with respect to annual cash bonuses to be paid to these persons for service in the year ending 31 December 2021 and base salary awards effective from 1 January 2022. Finally, the CEO also provided input to the Remuneration Committee regarding the implementation of equity-based remuneration as an element of all other employees' remuneration.

Approval

This report was approved by the Board of Directors on 16 May 2022 and signed on its behalf by:

Bali Muralidhar
Non-Executive Director & Chair of Remuneration Committee

16 May 2022

statement of directors' responsibilities

statement of directors' responsibilities

The directors are responsible for preparing the Strategic Report, the Directors' Report, the Directors' Remuneration Report and the financial statements in accordance with applicable United Kingdom law and regulations. Company law requires the directors to prepare financial statements for each financial year. Under that law the directors have elected to prepare the financial statements in accordance with U.K.-adopted international accounting standards, International Financial Reporting Standards (IFRS), in conformity with the requirements of the Companies Act 2006.

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

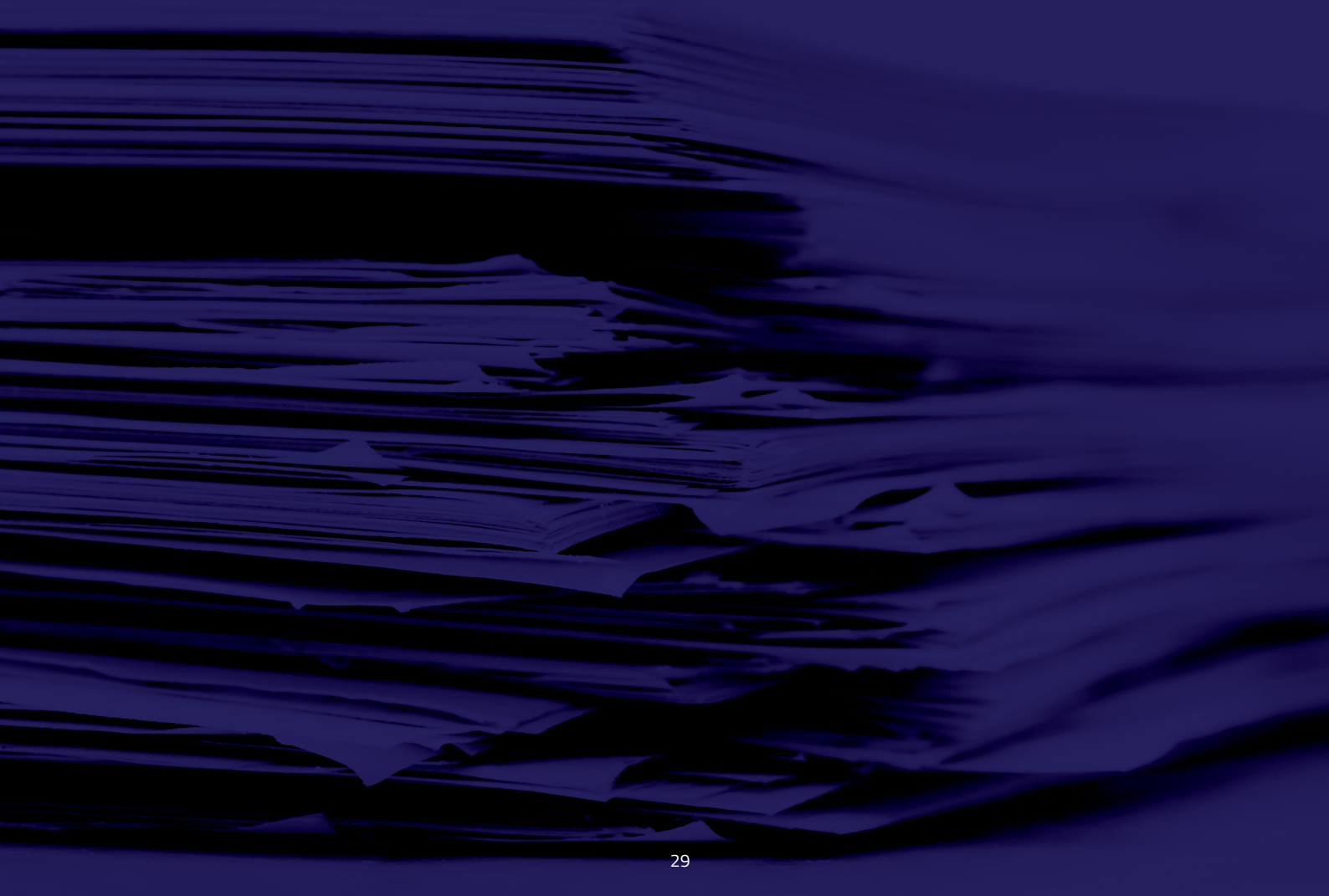
- present fairly the financial position, financial performance and cash flows of the Group and Company for that period;
- select suitable accounting policies in accordance with IAS 8: Accounting Policies, Changes in Accounting Estimates and Errors and then apply them consistently;
- present information, including accounting policies, in a manner that provides relevant, reliable, comparable and understandable information;
- provide additional disclosures when compliance with the specific requirements in IFRSs is insufficient to enable users to understand the impact of particular transactions, other events and conditions on the Group's and Company's financial position and financial performance;
- state that the Group and Company have complied with IFRSs, subject to any material departures disclosed and explained in the financial statements; and
- make judgements and estimates that are reasonable and prudent.

The directors are responsible for keeping adequate accounting records that are sufficient to show and explain the Group's and Company's transactions and disclose with reasonable accuracy at any time the financial position of the Group and Company and enable them to ensure that the financial statements comply with the Companies Act 2006. They are also responsible for safeguarding the assets of the Group and the Company and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The directors are responsible for the maintenance and integrity of the corporate and financial information included on the Company's website.

The names of the directors are set out on page 15 of this report.

independent auditor's report to the members of NuCana plc



opinion

In our opinion:

- NuCana 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 for the year then ended;
- the Group financial statements have been properly prepared in accordance with U.K. adopted international accounting standards;
- the Parent Company financial statements have been properly prepared in accordance with U.K. adopted international accounting standards as applied in accordance with section 408 of the Companies Act; and
- the financial statements have been prepared in accordance with the requirements of the Companies Act 2006.

We have audited the financial statements of NuCana plc (the 'Parent Company') and its subsidiaries (the 'Group') for the year ended 31 December 2021 which comprise:

Group	Parent Company
Group statement of financial position as at 31 December 2021	Company statement of financial position as at 31 December 2021
Group income statement for the year then ended	Company statement of changes in equity for the year then ended
Group statement of comprehensive loss for the year then ended	Company statement of cash flows for the year then ended
Group statement of changes in equity for the year then ended	Related notes 1 to 19 to the financial statements including a summary of significant accounting policies
Group statement of cash flows for the year then ended	
Related notes 1 to 19 to the financial statements, including a summary of significant accounting policies	

The financial reporting framework that has been applied in their preparation is applicable law and U.K. adopted international accounting standards and as regards to the Parent Company financial statements, as applied in accordance with section 408 of the Companies Act 2006.

basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) (ISAs (UK)) and applicable law. Our responsibilities under those standards are further described in the Auditor's responsibilities for the audit of the financial statements section of our report. We are independent of the Group and Parent Company in accordance with the ethical requirements that are relevant to our audit of the financial statements in the U.K., including the FRC's Ethical Standard as applied to listed entities, and we have fulfilled our other ethical responsibilities in accordance with these requirements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

conclusions relating to going concern

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. Our evaluation of the directors' assessment of the Group and Parent Company's ability to continue to adopt the going concern basis of accounting included:

- In conjunction with our walkthrough of the Group's financial close process, we confirmed our understanding of management's going concern assessment process and engaged with management early to ensure all key factors were considered in their assessment.
- We obtained management's going concern assessment, including cash forecast and models for the going concern period ending 30 June 2023. The Group projects that their cash holdings from shareholder funding are adequate to fund operations and all planned research activity in the period under review.
- We verified year end and reporting date actual cash positions against bank statements and assessed the accessibility restrictions of these funds.
- We considered the available cash balances against the forecast cash expenditure required in the going concern period and assessed whether the business has sufficient cash resources to operate under adverse expenditure scenarios.
- We have assessed the reasonableness of the underlying cash utilisation assumptions on current and planned research activities based on our expectations and understanding of the business. This involved reviewing the status of each of the clinical studies with the operational team and senior management to understand the spend trajectory on each research program.
- In order to assess management's forecasting accuracy, we have compared the prior year budgets against actual.
- We reviewed the ability management have to manage their available cash resources by reviewing mitigating actions, such as managing timelines associated with clinical study spend and re-assessing timing of discretionary spend, to intervene if mitigating actions are required.
- We reviewed the appropriateness and completeness of the Group's going concern disclosures included in the annual report and assessed that the disclosures were in conformity with the reporting standards.

The activities of the Group have not been significantly impacted by the COVID-19 pandemic and are not expected to be significantly impacted by COVID-19 in the going concern assessment period. At 31 December 2021 the Group had total cash resources (being cash and short-term deposits) of £60.3 million, which is the basis of their going concern conclusion.

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 and Parent Company's ability to continue as a going concern for the going concern period ending 30 June 2023.

Our responsibilities and the responsibilities of the directors with respect to going concern are described in the relevant sections of this report. However, because not all future events or conditions can be predicted, this statement is not a guarantee as to the Group's ability to continue as a going concern.

overview of our audit approach

Audit scope	• We performed an audit of the complete financial information of two components. • The components where we performed full or specific audit procedures accounted for 100% of Loss before tax and 100% of Total assets.
Key audit matters	• Research and development cost accruals and prepayments (clinical study NuTide:121). • Management override of controls.
Materiality	• Overall Group materiality of £745,000 which represents 2% of operating expenses.

an overview of the scope of the Parent Company and Group

Tailoring the scope

Our assessment of audit risk, our evaluation of materiality and our allocation of performance materiality determine our audit scope for each Company within the Group. Taken together, this enables us to form an opinion on the consolidated financial statements. In assessing the risk of material misstatement to the Group financial statements, and to ensure we had adequate quantitative coverage of significant accounts in the financial statements, we performed audit procedures on the two reporting components that make up the Group.

We performed an audit of the complete financial information of both components ("full scope components") based on their size or risk characteristics. No components were untested during the financial year.

The reporting components where we performed audit procedures accounted for 100% (2020: 100%) of the Group's Operating expenses (adjusted for share-based payments as defined in 'Our application of materiality' section of this report), and 100% (2020: 100%) of the Group's Total assets.

Changes from the prior year

There have been no changes in audit approach from the prior year.

Involvement with component teams

All audit work performed for the purposes of the audit was undertaken by the Group audit team.

Climate change

The Group has determined that there are no future impacts from climate change on their operations. This is explained on page 16 in the directors' report which forms part of the "Other information," rather than the audited financial statements. Our procedures on these disclosures therefore consisted solely of considering whether they are materially inconsistent with the financial statements or our knowledge obtained in the course of the audit or otherwise appear to be materially misstated.

Our audit effort in considering climate change was focused on evaluating management's assessment that there is no impact of climate change risk, the adequacy of the disclosures in the financial statements and the conclusion that no issues were identified that would impact carrying values of assets with indefinite and long lives or have any other impact on the financial statements. We also challenged the directors' considerations of climate change in their assessment of going concern and associated disclosures.

key audit matters

Key audit matters are those matters that, in our professional judgment, were of most significance in our 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) that we identified. These matters included 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 were addressed in the context of our audit of the financial statements as a whole, and in our opinion thereon, and we do not provide a separate opinion on these matters.

Risk	Our response to the risk	Key observations communicated to the Audit Committee
Management override of controls *The risk has not changed from the prior year.* The UK Auditing Standards (ISA 240) require that we consider fraud risk due to management being in a unique position to perpetrate fraud. Management has the primary responsibility to prevent and detect fraud; our responsibility is to plan and perform our audit to obtain reasonable assurance that the financial statements, as a whole are free of material misstatements, whether caused by error or fraud. The nature of operations are such that the business holds significant cash balances and due to the limited staff resources compared to larger organisations there is an increased risk of misappropriation of cash. Given that the entity does not yet generate any revenues, the risk of improper revenue recognition has been rebutted. We have assessed the completeness and accuracy of the disclosures.	**Our principal audit procedures included:** • Through inquiry of management, completion of our walkthrough procedures, review of the established entity level controls, we considered areas that may be more susceptible to management override and designed procedures to address the risks identified. • Testing all major cash and bank transactions during the year and post year end, recognising the existing controls over senior management's ability to transfer funds. This included agreeing all payments over the testing threshold to supporting documentation and, as appropriate, verifying against the payment approval matrix. • Analysed material manual journal entries posted during the year, with a focus of those in relation to cash. • Enquired of management and those charged with governance of any instances of suspected or actual fraud during the year. • Considered the instances of significant estimates in the preparation of financial statements such as research and development accruals and prepayments related to clinical study NuTide:121 and challenged basis for these assumptions. • Assessed and evaluated the financial statements and underlying ledgers for any unusual transactions. • We performed full scope audit procedures over this risk area.	**We communicated to the Audit Committee that:** As a result of procedures performed, no instances of management override were identified. We also concluded that disclosures in the financial statements were free from material misstatement.
Research & development cost accruals and prepayments *Refer to Accounting policies (page 43) and note 12 of the financial statements (page 57).* *This risk has changed from prior year, as the risk has moved to specifically cover clinical study NuTide:121 as opposed to all clinical studies.* The completeness of estimates of accruals and the existence of prepayment amounts for clinical studies and manufacturing contracts on the largest clinical study (NuTide:121) has been deemed a significant risk. The Company estimates the costs of services received through the reporting date less amounts invoiced to determine the appropriate accrual. In certain circumstances the Company may make payments in advance and consequently record a prepayment in respect of these amounts. A significant risk has been associated with clinical study NuTide:121 as result of the size of the study, i.e., 125 study sites and 828 patients being recruited. The business held material accrual (£6.6 million) and prepayment (£0.8 million) balances on this clinical study at 31 December 2021.	**Our principal audit procedures included:** • Reviewing management's assessment of clinical study (NuTide:121) and agree information to supporting information (contracts, contract amendments, invoices, press releases and other communications). • Assessing terms and conditions of all significant new contracts entered into during the year, and challenging accounting adopted. • We agreed unpaid costs at year end to creditors and/or accrual balances or, in respect of the contract for which a prepayment has been made in prior years, to the calculation of the remaining prepayment amount. • Agreeing values for stages of completion to the signed contracts and the calculation of total costs incurred as at the year end and agreeing the stage of completion of the services under contract to information from the third parties and agreeing payments made to invoices from the third party. • Challenging management on the accounting adopted on clinical and manufacturing projects through independent review of contracts and through engagement with the operational teams (such as stage of completion for contracts with milestone payments). We held discussions with project managers, the Director of Finance, the Senior VP of Clinical Operations and the senior executive management including the CFO. • We tested material payments after year end through the reporting date to determine completeness of accruals. • We have reviewed the completeness and accuracy of the related disclosures.	**We communicated to the audit committee that:** As a result of our procedures, we identified an under accrual below our materiality related to the accrual of reimbursable costs at 31 December. Management have subsequently adjusted for this under accrual.

In the prior year, our auditor's report also included a key audit matter in relation to management override of controls and research and development cost accruals and prepayments. In the current year, the research and development cost accrual and prepayment risk has been associated specifically to clinical study NuTide:121.

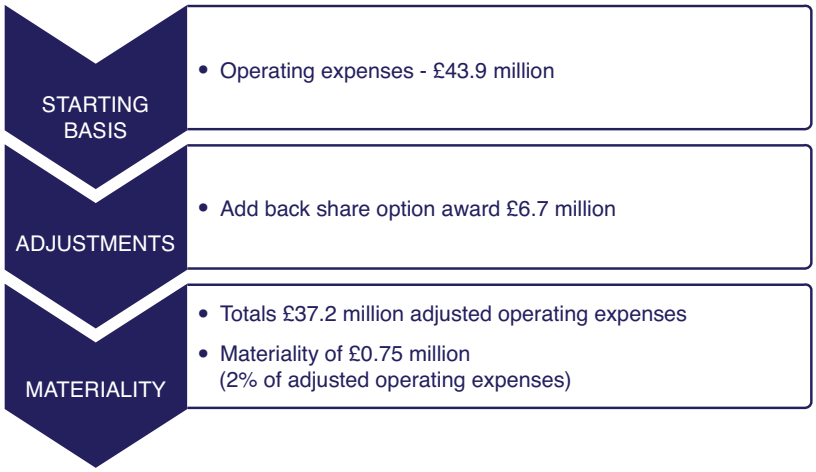
our application of materiality

We apply the concept of materiality in planning and performing the audit, in evaluating the effect of identified misstatements on the audit and in forming our audit opinion.

Materiality

The magnitude of an omission or misstatement that, individually or in the aggregate, could reasonably be expected to influence the economic decisions of the users of the financial statements. Materiality provides a basis for determining the nature and extent of our audit procedures.

We determined materiality for the Group and Parent Company to be £0.75 million (2020: £0.57 million), which is 2% (2020: 2%) of operating expenses excluding share-based payment expense and before any audit adjustments. We believe that operating costs provides us with an appropriate basis for determining materiality since the Group is in the development stage of its life cycle and is investing in research and development, with no operating income to date. Furthermore, we have based materiality on this measure due to our understanding of the perspective of the users of the financial statements. The increase from prior year reflects the increased level of activity of the Group.



Performance materiality

The application of materiality at the individual account or balance level. It is set at an amount to reduce to an appropriately low level the probability that the aggregate of uncorrected and undetected misstatements exceeds materiality.

On the basis of our risk assessments, together with our assessment of the Group's overall control environment, our judgement was that performance materiality was 75% (2020: 75%) of our planning materiality, namely £0.56 million (2020: £0.43 million). We have set performance materiality at this percentage due various considerations including the past history of misstatements, our ability to assess the likelihood of misstatements, the effectiveness of the internal control environment and other factors affecting the entity and its financial reporting.

Audit work at component locations for the purpose of obtaining audit coverage over significant financial statement accounts is undertaken based on a percentage of total performance materiality. The performance materiality set for each component is based on the relative scale and risk of the component to the Group as a whole and our assessment of the risk of misstatement at that component. In the current year, the range of performance materiality allocated to components was £0.15 million to £0.56 million (2020: £0.09 million to £0.43 million).

Reporting threshold

An amount below which identified misstatements are considered as being clearly trivial.

We agreed with the Audit Committee that we would report to them all uncorrected audit differences in excess of £45,000 (2020: £29,000), which is set at 5% of planning materiality, as well as differences below that threshold that, in our view, warranted reporting on qualitative grounds.

We evaluate any uncorrected misstatements against both the quantitative measures of materiality discussed above and in light of other relevant qualitative considerations in forming our opinion.

other information

The other information comprises the information included in the annual report set out on pages 2 to 28 other than the financial statements and our auditor's report thereon. The directors are responsible for the other information contained within annual report.

Our opinion on the financial statements does not cover the other information and, except to the extent otherwise explicitly stated in this report, we do not express any form of assurance conclusion thereon.

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 course of the audit or otherwise appears to be materially misstated. If we identify such material inconsistencies or apparent material misstatements, we are required to determine whether this gives rise to a material misstatement in the financial statements themselves. If, based on the work we have performed, we conclude that there is a material misstatement of the other information, we are required to report that fact.

We have nothing to report in this regard.

opinions on other matters prescribed by the Companies Act 2006

In our opinion, the part of the directors' remuneration report to be audited has been properly prepared in accordance with the Companies Act 2006.

In our opinion, based on the work undertaken in the course of the audit:

- the information given in the strategic report and the directors' report for the financial year for which the financial statements are prepared is consistent with the financial statements; and
- the strategic report and directors' report have been prepared in accordance with applicable legal requirements.

matters on which we are required to report by exception

In the light of the knowledge and understanding of the Group and the Parent Company and its environment obtained in the course of the audit, we have not identified material misstatements in the strategic report or the directors' report.

We have nothing to report in respect of the following matters in relation to which the Companies Act 2006 requires us to report to you if, in our opinion:

- 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
- 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; or
- certain disclosures of directors' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit.

responsibilities of directors

As explained more fully in the directors' responsibilities statement set out on page 28, the directors are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view, and for such internal control as the directors 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 and 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.

auditor's 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 auditor's 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.

Explanation as to what extent the audit was considered capable of detecting irregularities, including fraud

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

However, the primary responsibility for the prevention and detection of fraud rests with both those charged with governance of the Company and management.

- We obtained an understanding of the legal and regulatory frameworks that are applicable to the Group and determined that the most significant are those that are directly relevant to specific assertions in the financial statements are those that relate to the reporting framework (IFRS and the Companies Act 2006), and the relevant tax compliance regulations in the jurisdictions in which the Group operates. In addition, we concluded that there are certain significant laws and regulations in relation to health and safety, employee matters and anti- bribery and corruption practices.
- We understood how the Group is complying with those frameworks by making enquiries of management, those responsible for legal and compliance procedures and the Company Secretary. We corroborated our enquiries through our review of board minutes, papers provided to the Audit Committee.
- We assessed the susceptibility of the Group's financial statements to material misstatement, including how fraud might occur by meeting with management, including within various parts of the business, to understand where they considered there was susceptibility to fraud. We also considered performance targets and their propensity to influence reports made by management to manage earnings or influence the perceptions of analysts. Where the risk was considered higher, we performed specific procedures including testing of manual journals to provide reasonable assurance that the financial statements were free from fraud and error. Further details of the procedures performed, and our observations are included in the Key audit matters section of this report.
- Based on this understanding we designed our audit procedures to identify non-compliance with such laws and regulations. Our procedures included review of board minutes, review of management reports made to the Audit Committee, enquiries of external legal counsel, enquiries of management as well as the application of data analytical tools with a focus on manual journals and transactions that have heightened risk by nature.

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

use of our report

This report is made solely to the Company's members, as a body, in accordance with Chapter 3 of Part 16 of the Companies Act 2006. Our audit work has been undertaken so that we might state to the Company's members those matters we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the Company and the Company's members as a body, for our audit work, for this report, or for the opinions we have formed.

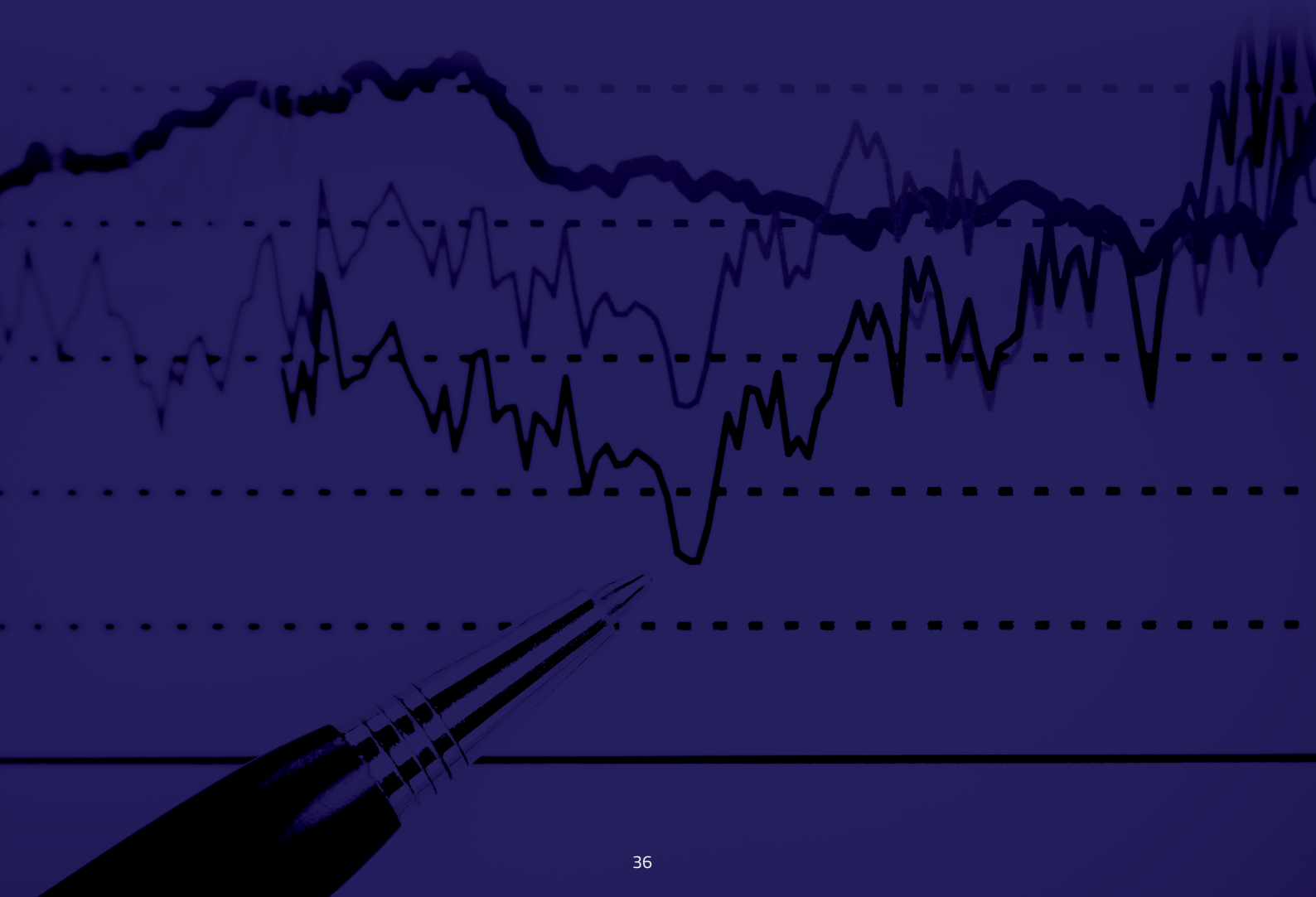
Ernst & Young LLP

Paul Copland (Senior statutory auditor)

for and on behalf of Ernst & Young LLP, Statutory Auditor
Edinburgh

18 May 2022

financial statements



group income statement

for the year ended 31 December 2021

	Notes	*2021*	*2020*
		(in thousands)	
		£	£
Research and development expenses		(36,834)	(25,899)
Administrative expenses		(8,529)	(7,050)
Impairment of intangible assets	7	(2,809)	-
Net foreign exchange gains (losses)		267	(3,472)
Operating loss		**(47,905)**	**(36,421)**
Finance income		103	246
Loss before tax	3	**(47,802)**	**(36,175)**
Income tax credit	4	7,269	5,493
Loss for the year		**(40,533)**	**(30,682)**
Attributable to:			
Equity holders of the Company		**(40,533)**	**(30,682)**
		£	£
Basic and diluted loss per share	5	(0.78)	(0.81)

group statement of comprehensive loss

for the year ended 31 December 2021

	2021	*2020*
	(in thousands)	
	£	£
Loss for the year	**(40,533)**	**(30,682)**
Other comprehensive income (expense):		
Items that may be reclassified subsequently to profit or loss:		
Exchange differences on translation of foreign operations	5	(12)
Other comprehensive income (expense) for the year	5	(12)
Total comprehensive loss for the year	**(40,528)**	**(30,694)**
Attributable to:		
Equity holders of the Company	**(40,528)**	**(30,694)**

group statement of financial position

at 31 December 2021

	Notes	*2021*	*2020*
		(in thousands)	
		£	£
Assets			
Non-current assets			
Intangible assets	7	2,410	4,753
Property, plant and equipment	8	851	1,189
Deferred tax asset	4	60	44
Other non-current assets	9	2,540	-
		5,861	**5,986**
Current assets			
Prepayments, accrued income and other receivables	12	4,161	4,628
Current income tax receivable	4	7,188	9,822
Cash and cash equivalents	13	60,264	87,356
		71,613	**101,806**
Total assets		**77,474**	**107,792**
Equity and liabilities			
Capital and reserves			
Share capital and share premium	14	143,137	142,937
Other reserves	15	72,137	66,887
Accumulated deficit		(149,726)	(110,594)
Total equity attributable to equity holders of the Company		**65,548**	**99,230**
Non-current liabilities			
Provisions		46	46
Lease liabilities	17	164	367
		210	**413**
Current liabilities			
Trade payables		1,829	2,257
Payroll taxes and social security		170	177
Accrued expenditure		9,510	5,437
Lease liabilities	17	207	278
		11,716	**8,149**
Total liabilities		**11,926**	**8,562**
Total equity and liabilities		**77,474**	**107,792**

On behalf of the Board

Hugh S. Griffith
Director
16 May 2022

company statement of financial position

at 31 December 2021

		2021	*2020*
		(in thousands)	
Assets	Notes	£	£
Non-current assets			
Intangible assets	7	2,410	4,753
Property, plant and equipment	8	786	1,080
Investment in subsidiaries	10	–	–
Loan receivable from subsidiary	11	389	385
Other non-current assets	9	2,540	–
		6,125	**6,218**
Current assets			
Prepayments, accrued income and other receivables	12	4,096	4,565
Current income tax receivable	4	7,185	9,818
Cash and cash equivalents	13	60,230	87,284
		71,511	**101,667**
Total assets		**77,636**	**107,885**
Equity and liabilities			
Capital and reserves			
Share capital and share premium	14	143,137	142,937
Other reserves	15	72,493	67,248
Accumulated deficit		(150,136)	(110,916)
Total equity		**65,494**	**99,269**
Non-current liabilities			
Provisions		46	46
Lease liabilities	17	164	316
		210	**362**
Current liabilities			
Trade payables		1,814	2,251
Payroll taxes and social security		169	175
Loan payable to subsidiary	11	512	334
Accrued expenditure		9,284	5,270
Lease liabilities	17	153	224
		11,932	**8,254**
Total liabilities		**12,142**	**8,616**
Total equity and liabilities		**77,636**	**107,885**

The Company's loss for the year is £40.6 million (2020: £30.7 million)

On behalf of the Board

Hugh S. Griffith
Director
16 May 2022

group statement of changes in equity

for the year ended 31 December 2021

	Share capital	Share premium	Own share reserve	Share option reserve	Foreign currency translation reserve	Capital reserve	Accumulated deficit	Total equity attributable to equity holders of the Company
	(in thousands)							
	£	£	£	£	£	£	£	£
Balance at 1 January 2020	**1,299**	**79,541**	**(339)**	**20,620**	**(10)**	**42,466**	**(80,055)**	**63,522**
Loss for the year	–	–	–	–	–	–	(30,682)	(30,682)
Other comprehensive expense for the year	–	–	–	–	(12)	–	–	(12)
Total comprehensive loss for the year	–	–	–	–	(12)	–	(30,682)	(30,694)
Share-based payments	–	–	–	4,305	–	–	–	4,305
Exercise of share options	1	14	–	(68)	–	–	68	15
Lapse of share options	–	–	–	(75)	–	–	75	–
Issue of share capital	747	65,834	–	–	–	–	–	66,581
Share issue expenses	–	(4,499)	–	–	–	–	–	(4,499)
Balance at 31 December 2020	**2,047**	**140,890**	**(339)**	**24,782**	**(22)**	**42,466**	**(110,594)**	**99,230**
Loss for the year	–	–	–	–	–	–	(40,533)	(40,533)
Other comprehensive income for the year	–	–	–	–	5	–	–	5
Total comprehensive loss for the year	–	–	–	–	5	–	(40,533)	(40,528)
Share-based payments	–	–	–	6,664	–	–	–	6,664
Exercise of share options	40	160	–	(1,222)	–	–	1,204	182
Lapse of share options	–	–	–	(197)	–	–	197	–
Balance at 31 December 2021	**2,087**	**141,050**	**(339)**	**30,027**	**(17)**	**42,466**	**(149,726)**	**65,548**

company statement of changes in equity

for the year ended 31 December 2021

	Share capital	Share premium	Share option reserve	Capital reserve	Accumulated deficit	Total equity attributable to equity holders of the Company
			(in thousands)			
	£	£	£	£	£	£
Balance at 1 January 2020	**1,299**	**79,541**	**20,620**	**42,466**	**(80,320)**	**63,606**
Loss for the year	–	–	–	–	(30,739)	(30,739)
Other comprehensive expense for the year	–	–	–	–	–	–
Total comprehensive loss for the year	–	–	–	–	(30,739)	(30,739)
Share-based payments	–	–	4,305	–	–	4,305
Exercise of share options	1	14	(68)	–	68	15
Lapse of share options	–	–	(75)	–	75	–
Issue of share capital	747	65,834	–	–	–	66,581
Share issue expenses	–	(4,499)	–	–	–	(4,499)
Balance at 31 December 2020	**2,047**	**140,890**	**24,782**	**42,466**	**(110,916)**	**99,269**
Loss for the year	–	–	–	–	(40,621)	(40,621)
Other comprehensive expense for the year	–	–	–	–	–	–
Total comprehensive loss for the year	–	–	–	–	(40,621)	(40,621)
Share-based payments	–	–	6,664	–	–	6,664
Exercise of share options	40	160	(1,222)	–	1,204	182
Lapse of share options	–	–	(197)	–	197	–
Balance at 31 December 2021	**2,087**	**141,050**	**30,027**	**42,466**	**(150,136)**	**65,494**

group and company statement of cash flows

for the year ended 31 December 2021

	Group		Company	
	2021	*2020*	*2021*	*2020*
	(in thousands)			
	£	£	£	£
Cash flows from operating activities				
Loss for the year	(40,533)	(30,682)	(40,621)	(30,739)
Adjustments for:				
Income tax credit	(7,269)	(5,493)	(7,255)	(5,494)
Amortisation and depreciation	942	890	886	832
Impairment of intangible assets	2,809	–	2,809	–
Finance income	(103)	(246)	(106)	(250)
Interest expense on lease liabilities	18	26	16	24
Share-based payments	6,664	4,305	6,664	4,305
Net foreign exchange (gains) losses	(335)	3,481	(334)	3,477
	(37,807)	(27,719)	(37,941)	(27,845)
Movements in working capital:				
Decrease (increase) in prepayments, accrued income and other receivables	473	(9)	476	(1)
Decrease in trade payables	(428)	(155)	(437)	(147)
Increase in payroll taxes, social security, accrued expenditure and payable to subsidiary	4,050	2,112	4,170	2,182
Movements in working capital	4,095	1,948	4,209	2,034
Cash used in operations	**(33,712)**	**(25,771)**	**(33,732)**	**(25,811)**
Net income tax received	9,888	4,152	9,888	4,152
Net cash used in operating activities	**(23,824)**	**(21,619)**	**(23,844)**	**(21,659)**
Cash flows from investing activities				
Interest received	101	319	101	319
Payments for property, plant and equipment	(64)	(361)	(57)	(361)
Payments for intangible assets	(1,001)	(1,271)	(1,001)	(1,271)
Payments for other non-current assets	(2,597)	–	(2,597)	–
Net cash used in investing activities	**(3,561)**	**(1,313)**	**(3,554)**	**(1,313)**
Cash flows from financing activities				
Payments of lease liabilities	(296)	(297)	(239)	(238)
Proceeds from issue of share capital - exercise of share options	198	15	198	15
Proceeds from issue of share capital	–	66,581	–	66,581
Share issue expenses	–	(4,499)	–	(4,499)
Net cash (used in) from financing activities	**(98)**	**61,800**	**(41)**	**61,859**
Net (decrease) increase in cash and cash equivalents	(27,483)	38,868	(27,439)	38,887
Cash and cash equivalents at beginning of year	**87,356**	**51,962**	**87,284**	**51,856**
Effect of exchange rate changes on cash and cash equivalents	391	(3,474)	385	(3,459)
Cash and cash equivalents at end of year	**60,264**	**87,356**	**60,230**	**87,284**

notes to the financial statements

for the year ended 31 December 2021

1. Authorisation of financial statements

The financial statements of NuCana plc ("Company") and together with its subsidiaries ("Group") for the year ended 31 December 2021 were authorised for issue by the board of directors on 16 May 2022.

The Group is a clinical-stage biopharmaceutical company developing a portfolio of new medicines to treat patients with cancer. We are harnessing the power of phosphoramidate chemistry to generate new medicines called ProTides. These compounds have the potential to improve cancer treatment by enhancing the efficacy and safety of several current standards of care.

On 29 August 2017 the Company re-registered as a public limited company and changed its name from NuCana BioMed Limited to NuCana plc.

The Company has had American Depository Shares ("ADSs") registered with the US Securities and Exchange Commission ("SEC") and has been listed on Nasdaq since 2 October 2017. The Company is incorporated in England and Wales and domiciled in the United Kingdom (registration number 03308778) and is limited by shares.

The address of its registered office and principal place of business are disclosed in the introduction to the report and financial statements.

2. Significant accounting policies

Basis of preparation

The financial statements have been prepared in accordance with U.K.-adopted international accounting standards, International Financial Reporting Standards ("IFRS"), in conformity with the requirements of the Companies Act 2006. As permitted by section 408 of the Companies Act 2006, no Income Statement is presented for the Company.

The Group financial statements comprise the financial statements of the Company and its subsidiaries at 31 December 2021. The financial statements are presented in Pounds Sterling, which is also the Company's functional currency. All values are rounded to the nearest thousand, except where otherwise indicated.

In preparing the financial statements, management has considered the impact of the physical and transition risks of climate change and identified this as an emerging risk as set out on page 16 but have concluded that it does not have a material impact on the recognition and measurement of the assets and liabilities in these financial statements as at 31 December 2021.

Going concern

In common with many companies in the biopharmaceutical sector, the Group incurs significant expenditure in its early years as it researches and develops its potential products for market.

The Group's board of directors, having reviewed the operating budgets and development plans for the 18 month period to 30 June 2023, considers that the Group has adequate resources to continue in operation for the foreseeable future. The board of directors is therefore satisfied that it is appropriate to adopt the going concern basis of accounting in preparing the financial statements. The Group believes that its cash and cash equivalents of £60.3 million at 31 December 2021 will be sufficient to fund its current operating plan for at least the next 12 months. Further, following the announcement on 2 March 2022 that the Group's Phase 3 clinical study of Acelarin for patients with advanced biliary tract cancer was being discontinued, the directors have conducted an assessment on the going concern status of the Group and have concluded that it will have a positive impact on the cash outflows of the Group over the period assessed for going concern purposes.

As the Group continues to incur losses, the transition to profitability is dependent upon the successful development, approval and commercialisation of its product candidates and achieving a level of revenues adequate to support its cost structure. The Group may never achieve profitability, and unless and until it does, it will continue to need to raise additional capital. There can be no assurances, however, that additional funding will be available on acceptable terms.

COVID-19

In response to the COVID-19 pandemic, the majority of the Group's employees continue to work from home with limited attendance at the Group's offices.

During the early months of the pandemic the Group announced that there was some temporary interruption to the enrolment of new patients in the Group's ongoing clinical studies. In May 2020, the Group further announced that enrolment of new patients in the Group's clinical studies had re-commenced. While the Group continues to evaluate the impact of COVID-19 on its operations, the Group believes that this pandemic will inevitably cause some delays to the timing of initiation and completion of its clinical studies. The Group is continuing to monitor the impact of COVID-19.

COVID-19 has had no impact on the judgements and estimates used in the preparation of these financial statements.

Judgements and estimates

The preparation of the financial statements requires management to make judgements, estimates and assumptions that affect the amounts reported for assets and liabilities at the balance sheet date and the amounts reported for revenue and expenses during the year. The nature of estimations means that actual outcomes could differ from those estimates.

The following judgements have had the most significant effect on the amounts recognised in the financial statements:

Research and development expenses

The Group recognises research and development expenses in the income statement in the period in which they are incurred. When development activities reach the advanced stage, as set out in the specific criteria of International Accounting Standard ("IAS") 38, *Intangible Assets*, there will be a requirement to capitalise such costs as intangible assets. Management will continue to exercise judgement in the appropriate treatment of research and development costs.

Taxation

Management judgement is required to determine the amount of deferred tax assets that should be recognised, based upon the likely timing and level of future taxable profits. Further details are contained in note 4.

The following estimates have had the most significant effect on the amounts recognised in the financial statements:

Recognition of clinical study expenses
As part of the process of preparing our consolidated financial statements, we may be required to estimate accrued or prepaid expenses related to our clinical studies. In order to obtain reasonable estimates, we review open contracts and master service agreements. In addition, we communicate with applicable personnel in order to identify services that have been performed, but for which we have not yet been invoiced, and services not yet performed for which we have been invoiced in advance. In most cases, our vendors provide us with monthly invoices in arrears for services performed. The following are examples of our accrued expenses:

- fees paid to CROs for services performed on clinical studies; and
- pass-through costs for activities at clinical study investigator sites.

Accruals for clinical study expenses, including estimated amounts recognised consistent with the above policy, were £7.2 million at 31 December 2021 as compared to £3.5 million at 31 December 2020.

Prepayments for clinical study expenses, including estimated amounts recognised consistent with the above policy, were £1.5 million at 31 December 2021 as compared to £2.2 million at 31 December 2020. These amounts include sums that are expected to be realised over the period of the associated studies, which in some cases could be greater than one year.

Recognition of contracted manufacturing expenses
As part of the process of preparing our consolidated financial statements, we may be required to estimate accrued or prepaid expenses related to our contracted manufacturing expenses. In order to obtain reasonable estimates, we review open contracts and master service agreements. In addition, we consult with applicable personnel in order to identify services that have been performed and which have not yet been invoiced, and services not yet performed for which we have been invoiced in advance.

Accruals for contracted manufacturing expenses, including estimated amounts recognised consistent with the above policy, were £0.1 million at 31 December 2021 as compared to £0.1 million at 31 December 2020.

Prepayments for contracted manufacturing expenses, including estimated amounts recognised consistent with the above policy, were £0.1 million at 31 December 2021 as compared to £nil at 31 December 2020.

Share-based payments
Estimating fair value for share-based payment transactions requires determination of the most appropriate valuation model, which depends on the terms and conditions of the grant. This estimate also requires determination of the most appropriate inputs to the valuation model, including the expected life of the share option, historical volatility of the share price, dividend yield and assumptions about them, and the actual market value of an ordinary share in the Company at the date of grant. For the measurement of the fair value of equity-settled transactions at the grant date, the Company uses the Black-Scholes model. The assumptions used for estimating fair value for share-based payment transactions are detailed in note 16.

Basis of consolidation
The Group financial statements comprise the financial statements of the Company and its subsidiaries.

Subsidiaries are consolidated from the date of acquisition, being the date on which the Company obtains control, and continue to be consolidated until the date when such control ceases. The financial statements of the subsidiaries are prepared for the same reporting period as the parent company, using consistent accounting policies. All intra-group balances, transactions, unrealised gains and losses resulting from intra-group transactions and dividends are eliminated in full.

Assets, liabilities, income and expenses of a subsidiary acquired or disposed of during the year are included in the Group financial statements from the date the Company gains control until the date the Company ceases to control the subsidiary.

Foreign currencies
The Group's consolidated financial statements are presented in pounds sterling, which is also the parent company's functional currency. For each group entity, the Group determines the functional currency and items included in the financial statements of each entity are measured using that functional currency.

Transactions and balances
Transactions in foreign currencies are initially recorded by the Group's entities at their respective functional currency spot rates at the date the transaction first qualifies for recognition.

Monetary assets and liabilities denominated in foreign currencies are translated at the functional currency spot rates of exchange at the reporting date. Differences arising on settlement or translation of monetary items are recognised in the Group income statement.

Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rates at the dates of the initial transactions.

Group companies
On consolidation, the assets and liabilities of foreign operations are translated into pounds sterling at the rate of exchange prevailing at the reporting date and their income statements are translated at the average exchange rate for the financial period in which those transactions occur. The exchange differences arising on translation for consolidation are recognised in the group statement of comprehensive income or loss.

Segment reporting
The Group operates in one operating segment. Operating segments are reported in a manner consistent with the internal reporting provided to the Group's chief operating decision maker ("the CODM"). The Group's CODM, its Chief Executive Officer, views the Group's operations and manages its business as a single operating segment, which is the business of developing and commercialising ProTides for use in Oncology. The Group's principal operations and decision-making functions are located in the United Kingdom from where global decisions are made.

Share issue expenses
Incremental costs incurred and directly attributable to the issuance of shares are deducted from the related proceeds of the issuance. The net amount is recorded as contributed shareholders' equity in the period when such shares were issued. Costs that are not incremental and directly attributable to issuing new shares, are recorded as an expense in the Group income statement.

Property, plant and equipment
Property, plant and equipment is stated at cost, net of accumulated depreciation and accumulated impairment losses, if any. There are no restrictions on title to assets nor equipment pledged as security for liabilities.

Depreciation is provided on property, plant and equipment over their expected useful economic life as follows:

Asset class	Depreciation method and period
Office and computer equipment	Straight-line over 3 years
Fixtures and fittings	Straight-line over 5 years, or, for non–removable items, the remaining term of an associated lease, whichever is shorter
Right of use assets	Straight-line over the lease term, which are between two and five years, or the estimated useful lives of the assets, whichever is shorter

Intangible assets
Intangible assets are stated at cost, net of accumulated amortisation and accumulated impairment losses, if any. Cost in relation to patents includes registration, documentation and other legal fees associated with obtaining the patent. Computer software cost represents the initial purchase price of the asset.

The amortisation method and amortisation period for the principal categories of intangible assets are as follows:

Asset class	Amortisation method and period
Patents	Straight-line over 20 years
Computer software	Straight-line between 3 and 5 years

The Group's primary patents each have a life of 20 years. Further patents are granted in various jurisdictions to extend the territorial coverage of the primary patent. These patents are granted up to the period of the related primary patent. Costs are thus amortised over the remaining life of the relevant primary patent. The amortisation expense on intangible assets with finite lives is recognised in the Group income statement as an administrative expense. The amortisation method and the amortisation period for an intangible asset with a finite useful life are reviewed at least at each financial year end. Changes in the expected useful economic life or the expected pattern of consumption of future economic benefits embodied in the asset are accounted for by changing the amortisation period or method, as appropriate.

Intangible assets are tested for impairment when there is an indicator of impairment.

Cash and cash equivalents
Cash and cash equivalents in the statement of financial position include cash at banks with deposit maturity terms of less than three months, which is subject to an insignificant risk of changes in value.

Other non-current assets
The Group initiated legal proceedings against a third party for patent infringement in Germany. The court supported the request by the defendants that the Group provide them with a security to cover their legal costs in the event that the Group is unsuccessful in the final outcome of the legal proceedings. The Group subsequently provided a fixed euro deposit to the court in accordance with the court order. The sum deposited is a monetary asset and is currently expected to be held for greater than 12 months. Further details are contained in note 9.

Research and development
Research and development expenses are currently recognised in the income statement in the year in which they are incurred. Development expenses on an individual project will be recognised as an intangible asset when the Group can demonstrate:

- the technical feasibility of completing the intangible asset so that the asset will be available for use or sale;
- its intention to complete and its ability and intention to use or sell the asset;
- how the asset will generate future economic benefits;
- the availability of resources to complete the asset; and
- the ability to measure reliably the expenditure during development.

Investments in subsidiaries
Investments in subsidiaries are carried at cost less accumulated impairment losses in the Company's statement of financial position.

Income taxes
Current income tax
Current income tax assets and liabilities are measured at the amount expected to be recovered from or paid to the taxation authorities. The tax rates and tax laws used to compute the amounts are those that are enacted or substantively enacted at the reporting date in the countries where the Group operates within the tax regime.

Deferred income tax
Deferred income tax is provided in full, using the liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the Group's financial statements. However, the deferred income tax is not accounted for if it arises from initial recognition of an asset or liability in a transaction other than a business combination that at the time of the transaction affects neither accounting nor taxable profit or loss. Deferred income tax is determined using tax rates and laws that have been enacted or substantially enacted by the year end date and are expected to apply when the related deferred income tax asset is realised or the deferred tax liability is settled. Deferred tax assets are recognised to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilised.

Income tax credit
The Group benefits from the U.K. and U.S. research and development tax credit regimes. In the U.K. a portion of the Company's losses can currently be surrendered for a cash rebate of up to 33.35% of eligible expenditures. In the U.S. the Group is able to offset the research and development credits against corporation tax payable. Such credits are accounted for within the tax provision, in the year in which the expenditures are incurred.

Leases
The Group assesses, at contract inception, whether a contract is, or contains, a lease. That is, if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration.

The Group applies a single recognition and measurement approach for all leases, except for short-term leases and leases of low-value assets. The Group recognises lease liabilities to make lease payments and right of use assets representing the right to use the underlying assets.

Right of use assets
The Group recognises right of use assets at the commencement date of the lease (i.e. the date the underlying asset is available for use). Right of use assets are measured at cost, less any accumulated depreciation and impairment losses, and adjusted for any remeasurement of lease liabilities. The cost of right of use assets includes the amount of lease liabilities recognised, initial direct costs incurred, and lease payments made at or before the commencement date less any lease incentives received. Right of use assets, which relate solely to office space, are depreciated on a straight–line basis over the shorter of the lease terms, which are between two and five years, or the estimated useful lives of the assets.

Lease liability
At the commencement date of the lease, the Group recognises a lease liability measured at the present value of lease payments to be made over the lease term. The lease payments include fixed payments less any lease incentives receivable, and any variable lease payments that depend on an index.

In calculating the present value of lease payments, the Group uses its incremental borrowing rate at the lease commencement date because the interest rate implicit in the lease is not readily determinable. After the commencement date, the amount of the lease liability is increased to reflect the accretion of interest and reduced for the lease payments made. In addition, the carrying amount of the lease liability is remeasured if there is a modification, a change in the lease term or a change in the lease payments.

The Group determines the lease term as the non-cancellable term of the lease, together with any periods covered by an option to extend the lease if it is reasonably certain to be exercised, or any periods covered by an option to terminate the lease, if it is reasonably certain not to be exercised.

The Group has a number of lease contracts that include extension and termination options. The Group applies judgement in evaluating whether it is reasonably certain whether or not to exercise the option to renew or terminate the lease. That is, it considers all relevant factors that create an economic incentive for it to exercise either the renewal or termination. After the commencement date, the Group reassesses the lease term if there is a significant event or change in circumstances that is within its control and affects its ability to exercise or not to exercise the option to renew or to terminate, such as the construction of significant leasehold improvements.

Refer to note 17 for information on potential future rental payments relating to periods following the exercise date of extension options that are not included in the lease liability.

Impairment of non-financial assets
The Group assesses, at each reporting date, whether there is an indication that an asset may be impaired. If any indication exists, the Group estimates the recoverable amount of the asset.

An impairment loss is recognised whenever the carrying amount of an asset or its cash-generating unit exceeds its recoverable amount. Impairment losses are recognised in the Group income statement.

A cash-generating unit is the smallest identifiable group of assets that generates cash inflows that are largely independent of the cash inflows from other assets or groups of assets.

Calculation of recoverable amount
The recoverable amount of assets and cash-generating units is the higher of their fair value less costs to sell and value in use. In assessing value in use, the estimated future cash flows are discounted to their present value using a pre-tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset. For an asset that does not generate largely independent cash inflows, the recoverable amount is determined for the cash-generating unit to which the asset belongs.

Reversal of impairment
An assessment is made at each reporting date as to whether there is an indication that a previously recognised impairment loss may no longer exist or may have decreased. If such an indication exists the recoverable amount is estimated.

A previously recognised impairment loss is reversed only if there has been a change in the estimates used to determine the recoverable amount since the last impairment loss was recognised. If that is the case, the carrying value is increased to its recoverable amount. An impairment loss is reversed only to the extent that the asset's carrying amount does not exceed the carrying amount that would have been determined, net of depreciation or amortisation, if no impairment loss had been recognised.

Share-based payments
Employees, directors and consultants of the Group receive remuneration in the form of share options, whereby individuals render services as consideration for equity instruments and the cost is recognised as share-based payments under IFRS 2.

Under IFRS 2 *Share-based Payment*, equity share-based payments are measured at the fair value of the equity instruments at the grant date. Details regarding the determination of fair value of equity settled share-based transactions are set out in note 16.

The fair value determined at the grant date of equity settled share-based payments, after adjusting for an assumed forfeiture rate, is expensed on a straight-line basis over the vesting period, with a corresponding increase in equity to the share option reserve.

Fair value measurement
The fair value of the financial assets and liabilities is included at the amount at which an instrument could be exchanged in a current transaction between willing parties, other than in a forced liquidation or sale.

Fair value is based on the price that would be received from the sale of an asset or that would be paid to transfer a liability in an orderly transaction between market participants at the measurement date. In order to increase consistency and comparability in fair value measurements, IFRS 13 establishes a fair value hierarchy that prioritises observable and unobservable inputs used to measure fair value into three broad levels, which are described as follows:

Level 1: Quoted (unadjusted) prices in active markets for identical assets or liabilities.

Level 2: Other techniques for which all inputs that have a significant effect on the recorded fair value are observable, either directly or indirectly.

Level 3: Techniques that use inputs that have a significant effect on the recorded fair value that are not based on observable market data.

The fair values of cash and cash equivalents, other receivables and trade payables approximate their carrying amounts largely due to the short-term maturities of these instruments.

Accounting standards

In preparing these financial statements, the Group has applied all relevant IAS, IFRS and International Financial Reporting Interpretations Committee ("IFRIC") Interpretations as of the date of approval of these financial statements and which are mandatory for the financial year ended 31 December 2021.

The following amendments have been adopted as of or after 1 January 2021 in these financial statements and have not had a material impact on the Group's accounts in the period of initial application, but may impact the accounting for future transactions:

- Amendments to IFRS 9, IAS 39, IFRS 7, IFRS 4 and IFRS 16 – Interest Rate Benchmark Reform, Phase 2 (effective from 1 January 2021)
- Amendment to IFRS 16 – Covid-19-Related Rent Concessions beyond 30 June 2021 (effective from 1 April 2021)

The International Accounting Standards Board ("IASB") and IFRIC have issued the following standards and amendments with an effective date after the date of these financial statements:

- Amendments to IFRS 3 – Reference to the Conceptual Framework (effective from 1 January 2022)
- Amendments to IAS 16 Property, Plant and Equipment – Proceeds before Intended Use (effective from 1 January 2022)
- Amendments to IAS 37 – Onerous Contracts: Costs of Fulfilling a Contract (effective from 1 January 2022)
- IFRS 17 Insurance Contracts (effective from 1 January 2023)
- Amendments to IAS 1 Presentation of Financial Statements – Classification of Liabilities as Current or Non-Current (effective from 1 January 2023)
- Amendments to IAS 1 Presentation of Financial Statements and IFRS Practice Statement 2 – Disclosure of Accounting Policies (effective from 1 January 2023)
- Amendments to IAS 8 Accounting Policies, Changes in Accounting Estimates and Errors – Definition of Accounting Estimates (effective from 1 January 2023)
- Amendments to IAS 12 – Deferred Tax related to Assets and Liabilities arising from a Single Transaction (effective from 1 January 2023)

The IASB has also issued the following amendments from the 2018-2020 annual improvement cycles with an effective date after the date of these financial statements:

- IFRS 1 - First-time Adoption of International Financial Reporting Standards - Subsidiary as a first–time adopter (effective from 1 January 2022)
- IFRS 9 Financial Instruments - Fees in the '10 per cent' test for derecognition of financial liabilities (effective from 1 January 2022)
- IAS 41 Agriculture - Taxation in fair value measurements (effective from 1 January 2022)

The Group will adopt the above standards and amendments on their effective date, although the Group has reviewed the above standards and amendments and considers that they either do not apply to the Group or will not have a material impact in future periods.

3. Loss before tax

Loss before tax is stated after charging:

	2021	2020
	(in thousands)	
	£	£
Amortisation and depreciation		
Owned assets	676	622
Right of use assets under IFRS 16	266	268
Interest expense on lease liabilities (included in administrative expenses) under IFRS 16	18	26
Share-based payments	6,664	4,305

(a) Auditors remuneration

	2021	2020
	(in thousands)	
	£	£
Audit of the financial statements	295	271
Other fees:		
Audit-related fees[1]	193	210
	488	**481**

[1] Audit-related fees are primarily for quarterly reviews and services related to SEC filings.

(b) Staff costs and directors' emoluments

Group

	2021	2020
	(in thousands)	
Included in research and development expenses:	£	£
Wages and salaries	3,931	3,492
Social security costs	465	430
Pension costs	189	189
Share-based payments	3,833	2,412
	8,418	6,523

	2021	2020
	(in thousands)	
Included in administrative expenses:	£	£
Wages and salaries	1,407	1,387
Social security costs	136	135
Pension costs	40	47
Share-based payments	2,831	1,893
	4,414	3,462
Total employee benefit expense	**12,832**	**9,985**

	2021	2020
The average number of staff employed under contracts of service were:	(number)	
Research and development activities	25	24
Administrative activities	5	6
	30	**30**

Company	*2021*	*2020*
	(in thousands)	
Included in research and development expenses:	£	£
Wages and salaries	3,468	3,246
Social security costs	444	417
Pension costs	185	189
Share-based payments	3,833	2,412
	7,930	6,264

	2021	*2020*
	(in thousands)	
Included in administrative expenses:	£	£
Wages and salaries	1,035	1,003
Social security costs	127	124
Pension costs	37	42
Share-based payments	2,831	1,893
	4,030	3,062
Total employee benefit expense	**11,960**	**9,326**

	2021	*2020*
The average number of staff employed under contracts of service were:	(number)	
Research and development activities	23	23
Administrative activities	5	5
	28	**28**

Directors' remuneration

Company	*2021*	*2020*
	(in thousands)	
	£	£
Directors' remuneration in respect of qualifying services	1,153	1,172
Pension	53	56
	1,206	**1,228**

The number of directors who exercised share options in 2021 was 3 (2020: nil). The gain on exercise of these options was £0.7 million (2020: £nil).

During the year the number of directors who were receiving benefits was as follows:

	2021	*2020*
	(number)	
Accruing benefits under money purchase pension scheme	1	1

4. Income Tax Credit

(a) Tax on loss on ordinary activities:

	2021	*2020*
	(in thousands)	
	£	£
Current tax:		
In respect of current year U.K.	7,185	5,516
In respect of current year U.S.	–	–
In respect of prior year U.K.	69	(22)
Total current tax	**7,254**	**5,494**
Deferred tax:		
In respect of the current year U.S.	15	–
In respect of the prior year U.S.	–	(1)
Total deferred tax	**15**	**(1)**
Income tax credit	**7,269**	**5,493**
Current income tax receivable:		
U.K. tax	7,185	9,818
U.S. tax	3	4
Current income tax receivable	**7,188**	**9,822**
Deferred tax:		
U.S. tax	**60**	**44**

(b) Reconciliation of the total income tax credit:

The credit for the year can be reconciled to the loss per the income statement as follows:

	2021	*2020*
	(in thousands)	
	£	£
Loss before tax	**(47,802)**	**(36,175)**
Tax on loss at standard U.K. tax rate of 19% (2020: 19%)	(9,082)	(6,873)
Effects of:		
Expenses not deductible	4,757	3,972
Deduction for R&D	(9,415)	(7,228)
Losses surrendered for R&D tax credit	9,415	7,228
Deferred tax - prior year adjustment	–	1
Overseas tax payable - current year	–	–
R&D tax credit - U.S.	(15)	–
R&D tax credit - current year	(7,185)	(5,516)
R&D tax credit - prior years	(69)	22
Deferred tax asset not recognised	4,325	2,901
Income tax credit	**(7,269)**	**(5,493)**

(c) Deferred tax

In the United Kingdom, the Group has not recognised a deferred tax asset in respect of tax losses carried forward or temporary differences on share-based payment arrangements as at 31 December 2021 on the basis that the timing during which tax losses or temporary differences could be regarded as recoverable against future taxable profits cannot be determined with reasonable certainty. In the United States, a deferred tax asset, which relates to research & development tax credits, has been recognised to the extent that management consider that adequate future taxable profits will be available to realise the deferred tax asset.

Temporary differences and cumulative carry forward tax losses for which deferred tax has not been recognised amount to £74.4 million (2020: £57.5 million), comprising temporary differences on share-based payment arrangements of £4.1 million (2020: £9.9 million) and cumulative carry forward tax losses of £70.3 million (2020: £47.6 million).

(d) Factors affecting future tax

In March 2021, the U.K. Government announced that from 1 April 2023 the corporation tax rate would increase to 25% for U.K. companies with annual profits of £250,000 or higher. This was substantively enacted on 24 May 2021.

5. Basic and diluted loss per share

	2021	*2020*
	(in thousands, except per share data)	
	£	£
Loss for the year	**(40,533)**	**(30,682)**
Basic and diluted weighted average number of shares	52,041	37,882
	£	£
Basic and diluted loss per share	**(0.78)**	**(0.81)**

Basic loss per share is calculated by dividing the loss for the year attributable to the equity holders of the Company by the weighted average number of shares outstanding during the year.

The dilutive effect of potential shares through equity settled transactions were considered to be anti-dilutive as they would have decreased the loss per share and were therefore excluded from the calculation of diluted loss per share.

6. Capital commitments and contingencies

Other commitments
Collaboration and License Agreements
Cardiff University License

In August 2009, we entered into a research, collaboration and license agreement with Cardiff University and University College Cardiff Consultants Ltd., or Cardiff Consultants, which we refer to as the Cardiff Agreement.

At the end of 2021 we took the decision not to further extend the Cardiff Agreement. In December 2021 we served notice on Cardiff University and Cardiff Consultants to extend the licence of the ProTide-related intellectual property owned or controlled by Cardiff University as of the date of the Cardiff Agreement or owned or controlled by Cardiff University during the term of that Agreement, which we refer to as the Cardiff Intellectual Property, granted to NuCana under the Cardiff Agreement for a period of three months from expiry of the Cardiff Agreement on 31 December 2021 whilst we continue evaluating additional ProTides generated under the Cardiff Agreement.

Under the Cardiff Agreement, we collaborated with Cardiff University in the design, synthesis, characterisation and evaluation of phosphoramidate prodrugs, which we refer to as ProTides, based on certain nucleosides. Cardiff University and Cardiff Consultants, which is a holder of intellectual property developed by Cardiff University, have assigned to us all rights in the results of the research under the Cardiff Agreement.

Upon our completion of the evaluation of the ProTides, we have the right to select one or more of the evaluated ProTides as candidates for potential development of a commercial product. Cardiff University and Cardiff Consultants have granted us an exclusive worldwide license to use for all purposes the Cardiff intellectual property in respect of the nucleoside family of our selected ProTides. This licence survives expiration of the Cardiff Agreement. During the license period Cardiff University and Cardiff Consultants may not undertake any research for any competing third party on nucleoside families of interest to us where such research would make use of the Cardiff intellectual property, or to grant rights in the Cardiff intellectual property to any third party for use in connection with nucleosides of interest to us.

On our filing, or that of a sublicensee, of patent applications resulting from research under the Cardiff Agreement, we will owe Cardiff Consultants certain payments. If we or our sublicensees develop and commercialise a product resulting from such research, we will owe Cardiff Consultants clinical development milestone payments of up to £1,875,000, provided that such milestone payments are due only with respect to the first product within each nucleoside family to achieve the milestone. We will also owe Cardiff Consultants royalties equal to a low-single digit percentage on our sales of a product resulting from such research. Should we sublicense our right to commercialise a product resulting from the research, we will owe Cardiff Consultants a high-single digit percentage of payments received in consideration of the sublicense.

Cardiff ProTides Agreement

In October 2009, we entered into a license and collaboration agreement with Cardiff ProTides Ltd., or Cardiff ProTides, which agreement was subsequently amended and restated as an assignment, license and collaboration agreement in March 2012 and was further amended in May 2012, which we refer to as the ProTides Agreement. Under the ProTides Agreement, we collaborated with Cardiff ProTides in the discovery, drug design and *in vitro* screening of purine and pyrimidine-based nucleosides as potential drug candidates. We funded certain work at Cardiff ProTides, and Cardiff ProTides has assigned to us all rights in the results of its research under the ProTides Agreement. Cardiff ProTides also assigned to us patents related to certain compounds of interest, including with respect to Acelarin, and granted us an exclusive, worldwide license, including the right to grant sublicenses, to rights in and technical information related to certain unpatented compounds for all therapeutic, diagnostic, prognostic and prophylactic applications.

If we or a sublicensee develop one or more products covered by a valid claim of an assigned patent or patent resulting from Cardiff ProTides' research, such as Acelarin, we will owe Cardiff ProTides up to approximately $4.5 million in development and approval milestone payments in the aggregate for the first such product. Additional development and approval milestones would be payable for the first additional product in a new nucleoside series covered by a valid claim of an assigned patent or a patent resulting from Cardiff ProTides' research, although the maximum potential value of such milestone payments is approximately half the value of the milestone payments associated with the first product. We will also owe Cardiff ProTides royalties equal to a percentage in mid to high single-digits on sales of such products, subject to reduction under certain circumstances. Royalties on sales by sublicensees are set by formula, which formula would be likely to result in a royalty in the mid-single digits.

The ProTides Agreement expires, on a country-by-country basis, on the later of the expiration, invalidity, abandonment, lapsing or rejection of the last valid claim of an assigned patent or patent resulting from Cardiff ProTides' research, or, if certain technical information licensed from Cardiff ProTides remains confidential or the product is covered by a period of data exclusivity, ten years from the date of first commercial sale of a product in such country. The ProTides Agreement may be sooner terminated on an uncured material breach, bankruptcy of a party or, by Cardiff ProTides, if we challenge, or assist in a challenge, of the validity or ownership of an assigned patent or patent resulting from Cardiff ProTides' research, or fail to pay amounts payable under the ProTides Agreement. It may also be sooner terminated where sums payable by us remain unpaid for 45 days after we receive a notice from Cardiff ProTides that the relevant sums are overdue. Upon a termination of the ProTides Agreement, our license rights will terminate except where the breach results from certain breaches by Cardiff ProTides, in which case our license rights continue on a non-exclusive basis, subject to reduced payment obligations. Upon termination of the ProTides Agreement, including as a result of our breach, we will be under an obligation to assign back to Cardiff ProTides the patents which Cardiff ProTides originally assigned to us.

CROs and manufacturing commitments

We have agreed to make payments to CROs and manufacturers under various CRO and manufacturing agreements. We have not included further details on such contingent payment obligations as the amount, timing and likelihood of such payments are not fixed or determinable.

Other Contingencies

Under the U.K. share-based payment plan, the Company granted unapproved share options that have fully vested. If and when these share options are exercised, the Company will be liable for the Employer Class 1 National Insurance payable to HMRC in the U.K. This contingent liability will be determined based on the market value of the shares on exercise less the exercise price paid by the option holders, at the prevailing rate of Employer National Insurance (currently 13.8%). Based on the closing share price of ADSs on the Nasdaq Global Select Market on 31 December 2021, the last trading day of the period to which these financial statements relate, and assuming full exercise of all outstanding and vested unapproved share options on that date, the Employer National Insurance contingent liability would have been £0.4 million (31 December 2020: £0.8 million).

As referenced in note 9, during 2021 the Group provided a security of €3.0 million to cover the legal costs of Gilead Sciences Ireland UC and Gilead Sciences GmbH in the event that the Group is unsuccessful in the final outcome of the patent infringement litigation in Germany. Any cost reimbursement by the Group to the defendants is dependent on a range of potential outcomes, and the timing of those outcomes, with respect to the litigation, which are currently indeterminable. Therefore, no provision has been recognised with respect to these legal costs as the Group does not consider it probable that the litigation will be unsuccessful.

7. Intangible assets

Group and Company

	Patents	*Computer software*	*Total*
		(in thousands)	
	£	£	£
Cost:			
At 31 December 2019	4,523	374	4,897
Additions	1,262	9	1,271
At 31 December 2020	**5,785**	**383**	**6,168**
Accumulated amortisation:			
At 31 December 2019	806	131	937
Charge for the year	383	95	478
At 31 December 2020	**1,189**	**226**	**1,415**
Net book value:			
At 31 December 2020	**4,596**	**157**	**4,753**
At 31 December 2019	3,717	243	3,960
Cost:			
At 31 December 2020	5,785	383	6,168
Additions	999	2	1,001
At 31 December 2021	**6,784**	**385**	**7,169**
Accumulated amortisation:			
At 31 December 2020	1,189	226	1,415
Charge for the year	441	94	535
Impairment	2,809	–	2,809
At 31 December 2021	**4,439**	**320**	**4,759**
Net book value:			
At 31 December 2021	**2,345**	**65**	**2,410**
At 31 December 2020	4,596	157	4,753

On 2 March 2022 the Group announced that the Phase 3 clinical study of Acelarin for patients with advanced biliary tract cancer was being discontinued following a pre-planned futility analysis by the study's Independent Data Monitoring Committee ("IDMC"). Management concluded that this was an indication of impairment and hence reviewed the assets associated with both the clinical study and Acelarin. Based on this review, an impairment charge of £2.8 million was recognised, representing the full aggregate carrying value of the patents relating to Acelarin as at 31 December 2021.

8. Property, plant and equipment

Group

	Right of use assets	*Office and computer equipment*	*Fixtures and fittings*	*Total*
		(in thousands)		
	£	£	£	£
Cost:				
At 31 December 2019	982	236	418	1,636
Additions	–	90	291	381
Re-measurement	115	–	–	115
Effect of foreign currency exchange differences	(10)	–	–	(10)
At 31 December 2020	**1,087**	**326**	**709**	**2,122**
Depreciation:				
At 31 December 2019	191	160	176	527
Charge for the year	268	61	83	412
Effect of foreign currency exchange differences	(6)	–	–	(6)
At 31 December 2020	**453**	**221**	**259**	**933**
Net book value:				
At 31 December 2020	**634**	**105**	**450**	**1,189**
At 31 December 2019	791	76	242	1,109
Cost:				
At 31 December 2020	1,087	326	709	2,122
Additions	–	59	6	65
Re-measurement	4	–	–	4
Disposals	–	(6)	–	(6)
Effect of foreign currency exchange differences	2	–	–	2
At 31 December 2021	**1,093**	**379**	**715**	**2,187**
Depreciation:				
At 31 December 2020	453	221	259	933
Charge for the year	266	34	107	407
Disposals	–	(6)	–	(6)
Effect of foreign currency exchange differences	2	–	–	2
At 31 December 2021	**721**	**249**	**366**	**1,336**
Net book value:				
At 31 December 2021	**372**	**130**	**349**	**851**
At 31 December 2020	634	105	450	1,189

Company

	Right of use assets	*Office and computer equipment*	*Fixtures and fittings*	*Total*
		(in thousands)		
	£	£	£	£
Cost:				
At 31 December 2019	873	231	418	1,522
Additions	–	90	291	381
At 31 December 2020	**873**	**321**	**709**	**1,903**
Depreciation:				
At 31 December 2019	138	155	176	469
Charge for the year	211	61	82	354
At 31 December 2020	**349**	**216**	**258**	**823**
Net book value:				
At 31 December 2020	**524**	**105**	**451**	**1,080**
At 31 December 2019	735	76	242	1,053
Cost:				
At 31 December 2020	873	321	709	1,903
Additions	–	51	6	57
Disposals	–	(6)	–	(6)
At 31 December 2021	**873**	**366**	**715**	**1,954**
Depreciation:				
At 31 December 2020	349	216	258	823
Charge for the year	211	33	107	351
Disposals	–	(6)	–	(6)
At 31 December 2021	**560**	**243**	**365**	**1,168**
Net book value:				
At 31 December 2021	**313**	**123**	**350**	**786**
At 31 December 2020	524	105	451	1,080

9. Other non-current assets

Group and Company

	2021	*2020*
	(in thousands)	
	£	£
Other non-current assets	2,540	–
	2,540	**–**

During 2021, the Group initiated legal proceedings against Gilead Sciences Ireland UC and Gilead Sciences GmbH for patent infringement in Germany. The Group was requested by the court to provide the defendants with a security of €3.0 million (£2.6 million) to cover the legal costs of the defendants in the event that the Group is unsuccessful in the final outcome of the legal proceedings. Subsequently, the Group provided the security in accordance with the court order by depositing €3.0 million with the court.

The extent to which the sum deposited will be reimbursed to the Group is dependent on a range of potential outcomes, and the timing of those outcomes, with respect to the patent infringement litigation in Germany, which is currently indeterminable.

10. Investments in subsidiaries

	2021	*2020*
	£	£
Unlisted investments at cost and net book value	155	69

The increase in investments in subsidiaries reflects the incorporation of a subsidiary in Ireland (NuCana Limited) during 2021.

Details of Group undertakings:

Name	Principal activity	Country of incorporation	Registered office	Proportion of ownership
NuCana, Inc.	Development and administrative support	U.S.	2711 Centerville Road, Suite 400, Wilmington, Delaware, 19808	100%
NuCana BioMed Trustee Company Limited	Dormant	U.K.	3 Lochside Way, Edinburgh, EH12 9DT	100%
NuCana BioMed Employee Benefit Trust	Employee benefit trust	U.K.	3 Lochside Way, Edinburgh, EH12 9DT	100%
NuCana Limited	Development and administrative support	IE	70 Sir John Rogerson's Quay, Dublin 2, Ireland	100%

11. Related party disclosures

The following table provides the total amount of transactions that have been entered into with related parties for the relevant financial year.

Subsidiaries of NuCana plc	Purchases from related parties	Advances to related parties	Amounts due to related parties	Amounts owed by related parties	Interest Income from related parties
			(in thousands)		
	£	£	£	£	£
NuCana, Inc.					
31 December 2021	1,056	878	512	–	–
31 December 2020	865	797	334	–	–
NuCana BioMed Employee Benefit Trust					
31 December 2021	–	–	–	389	4
31 December 2020	–	–	–	385	4
NuCana Limited					
31 December 2021	–	–	–	–	–
31 December 2020	–	–	–	–	–

Terms and conditions of transactions with related parties

The sales to and purchases from related parties are made on terms equivalent to those that prevail in arm's length transactions. Cash advances are made available to NuCana, Inc. in order to fund the activities which are subsequently recharged on an arm's length basis. The amounts advanced are repayable on demand. Outstanding balances at the year end with NuCana, Inc. are unsecured, interest free and settlement occurs in cash. The NuCana BioMed Employee Benefit Trust balances are subject to interest at RBS base rate plus 1%. There have been no guarantees provided or received for any related party receivables or payables. For the year ended 31 December 2021, the Group has not recorded any impairment of receivables relating to amounts owed by related parties (2020: £nil). This assessment is undertaken each financial year through examining the financial position of the related party and the market in which the related party operates.

Compensation of key management personnel of the Group

	2021	*2020*
	(in thousands)	
	£	£
Short-term employee benefits	2,165	1,658
Pension and other benefits	104	79
Share-based payments	5,637	3,377
	7,906	**5,114**

Compensation of key management personnel of the Company

	2021	*2020*
	(in thousands)	
	£	£
Short-term employee benefits	1,417	1,167
Pension and other benefits	73	61
Share-based payments	4,368	2,583
	5,858	**3,811**

The amounts disclosed in the tables above are the amounts recognised as an expense during the reporting year.

12. Prepayments, accrued income and other receivables

Group

	2021	*2020*
	(in thousands)	
	£	£
Prepayments - manufacturing and clinical	1,598	2,177
Prepayments - other	1,551	1,625
Accrued income	5	4
VAT	998	813
Other receivables	9	9
	4,161	**4,628**

Company

	2021	*2020*
	(in thousands)	
	£	£
Prepayments - manufacturing and clinical	1,598	2,177
Prepayments - other	1,495	1,571
Accrued income	5	4
VAT	998	813
	4,096	**4,565**

13. Cash and cash equivalents

Group	*2021*	*2020*
	(in thousands)	
	£	£
Cash and cash equivalents	60,264	87,356

Company	*2021*	*2020*
	(in thousands)	
	£	£
Cash and cash equivalents	60,230	87,284

Cash and cash equivalents comprise cash at banks with deposit maturity terms of three months or less, which is subject to insignificant risk of changes in value. Cash at banks earns interest at fixed or variable rates based on the terms agreed for each account.

Liquidity risk is minimal and is managed using deposits with immediate and varied fixed term dates.

14. Share capital and share premium

Group and Company	*2021*	*2020*
	(in thousands)	
	£	£
Share capital	2,087	2,047
Share premium	141,050	140,890
	143,137	**142,937**

Group and Company	*2021*	*2020*
	Number	Number
	(in thousands)	
Issued share capital comprises:		
Ordinary shares of £0.04 each	**52,180**	**51,175**

Group and Company	Number of shares	Share capital	Share premium
		(in thousands)	
Fully paid shares:		£	£
Balance at 31 December 2019	**32,479**	**1,299**	**79,541**
Exercise of share options	33	1	14
Issue of share capital	18,663	747	61,335
Balance at 31 December 2020	**51,175**	**2,047**	**140,890**
Exercise of share options	1,005	40	160
Balance at 31 December 2021	**52,180**	**2,087**	**141,050**

Ordinary shares
Holders of ordinary shares are entitled to one vote for each share held of record on all matters submitted to a vote of shareholders and do not have cumulative voting rights.

Capital management
For the purpose of the Group's capital management, capital includes issued capital, share premium and all other equity reserves attributable to the equity holders of the Company. The purpose of the Group's capital management is to maximise shareholder value and ensure adequate capital is available to meet the medium-term operating plan. Review of operations and commitments is key to identifying future capital management and a full review is undertaken on a quarterly basis.

No changes were made in the objectives, policies or processes for managing capital during the years ending 31 December 2021 or 2020.

15. Other reserves

Group	*2021*	*2020*
	(in thousands)	
	£	£
Own share reserve	(339)	(339)
Foreign currency translation reserve	(17)	(22)
Capital reserve	42,466	42,466
Share option reserve		
Balance at beginning of year	24,782	20,620
Share-based payments	6,974	4,823
Exercise of share options	(1,222)	(68)
Forfeiture of share options	(310)	(518)
Lapse of share options	(197)	(75)
Balance at end of year	30,027	24,782
Total other reserves	**72,137**	**66,887**

Company	*2021*	*2020*
	(in thousands)	
	£	£
Share option reserve	30,027	24,782
Capital reserve	42,466	42,466
Total other reserves	**72,493**	**67,248**

Foreign currency translation reserve
The foreign currency translation reserve is used to record exchange differences arising from the translation of the financial statements of foreign operations.

Own share reserve
The own share reserve represents the cost of 500,000 shares of NuCana plc purchased by NuCana Employee Benefit Trust and that may, at the discretion of the trustee, be used to satisfy future exercise of options under the Company's share options plan.

Capital reserve
The capital reserve balance arose from the reduction of the share premium account and corresponding increase to the capital reserve account reflected as of 30 June 2017 in connection with the Company's re-registration as a public limited company, as further described in note 1.

Share option reserve
The share option reserve is used to recognise the value of equity-settled share-based payments provided to employees, directors and consultants as part of their remuneration. Refer to note 16 for further details of these plans.

16. Share-based payments

The Company has six share-based payment plans for employees, directors and consultants. The share options granted under these plans will be settled in equity. Options granted under each of the six plans have a maximum life of 10 years.

2020 options

In 2020, share options were granted under the following share-based payment plans:

U.K. share-based payment plans

Options granted under these plans will vest if the option holder remains under their respective contract of employment or contract of service for the agreed vesting period. The share options granted under these plans will vest equally over a period of four years.

Upon vesting, each option allows the holder to purchase one ordinary share at a specified option price determined at grant date.

2020 Long-Term Incentive Plan

Options granted under this plan will vest if the option holder remains under their respective contract of employment or contract of service for the agreed vesting period. The share options granted under this plan will vest equally over a period of four years.

Upon vesting, each option allows the holder to purchase one ordinary share at a specified option price determined at grant date. Options granted as RSU-style options are automatically exercised on vesting. If the Company determines, and at its discretion, an arrangement may be made under the 2020 Long-Term Incentive Plan to substitute the right to acquire shares with a cash alternative of equivalent value.

2021 options

In 2021, share options were granted under the following share-based payment plan:

2020 Long-Term Incentive Plan

Options granted under this plan will vest if the option holder remains under their respective contract of employment or contract of service for the agreed vesting period. The share options granted under this plan will vest equally over a period of four years.

Upon vesting, each option allows the holder to purchase one ordinary share at a specified option price determined at grant date. Options granted as RSU-style options are automatically exercised on vesting. If the Company determines, and at its discretion, an arrangement may be made under the 2020 Long-Term Incentive Plan to substitute the right to acquire shares with a cash alternative of equivalent value.

Share options and weighted average exercise prices are as follows for the reporting periods presented:

Group and Company	Number of shares	Weighted average exercise price per share
		£
Outstanding at 31 December 2019	**5,298,840**	**3.91**
Granted	2,665,639	4.03
Forfeited	(192,750)	10.89
Lapsed	(14,438)	7.42
Exercised[1]	(32,500)	0.45
Outstanding at 31 December 2020	**7,724,791**	**3.78**
Granted	4,329,913	1.91
Forfeited	(193,949)	5.26
Lapsed	(42,750)	11.21
Exercised[2]	(1,014,939)	0.20
Outstanding at 31 December 2021[3]	**10,803,066**	**3.32**
Vested and exercisable at 31 December 2021	**4,138,803**	**3.51**
Vested and exercisable at 31 December 2020	4,176,281	2.07

(1) The weighted average share price at the date of exercise of these options was £4.63.
(2) The weighted average share price at the date of exercise of these options was £3.77.
(3) The exercise price of outstanding share options ranges from £0.04 to £18.05.

The weighted average remaining contractual life of the share options outstanding as at 31 December 2021 is 7.59 years (2020: 5.77 years).

The following principal assumptions were used in the valuation for 2020 share options:

Grant date	10-June-2020	9-Sept-2020	9-Sept-2020	9-Dec-2020
Vesting dates	10-June-2021	9-Sept-2021	9-Sept-2021	9-Dec-2021
	10-June-2022	9-Sept-2022	9-Sept-2022	9-Dec-2022
	10-June-2023	9-Sept-2023	9-Sept-2023	9-Dec-2023
	10-June-2024	9-Sept-2024	9-Sept-2024	9-Dec-2024
Volatility	76.59%	82.98%	87.21%	81.26%
Dividend yield	0%	0%	0%	0%
Risk-free investment rate	0.003%	(0.08)%	(0.08)%	(0.03)%
Fair value of option at grant date	£2.76	£4.24	£4.24	£2.10
Fair value of share at grant date	£4.78	£4.28	£4.28	£3.48
Exercise price at date of grant	£4.78	£0.04	£0.04	£3.48
Lapse date	10-June-2030	9-Sept-2030	–	9-Dec-2030
Expected option life (years)	4.50	3.50	2.50	4.50
Number of options granted	2,186,780	290,356	108,503	80,000

The fair values of options granted were determined using the Black-Scholes model that takes into account factors specific to the share incentive plan such as the assumption that the options will be exercised at a point in time up to 2 years after vesting. This has been incorporated into the measurement by means of actuarial modelling. As NuCana plc was unlisted until 2 October 2017, it is not possible to derive historical volatility from the Company's ADSs prior to October 2017. For options with an estimated life of greater than three years, the underlying expected volatility was determined by using the historical volatility of similar listed entities as a proxy. The volatility percentage applied to each tranche is the average of the historical volatility of comparable companies to the Company. Options granted with an estimated life of three years or less, have been valued using the Company's own historical volatility rates.

In the year ended 31 December 2020, an employee remuneration expense, all of which related to equity-settled share-based payments, of £4.3 million has been included in the Group income statement and credited to equity.

The following principal assumptions were used in the valuation for 2021 share options:

Grant date	13-Jan-2021	10-Feb-2021	10-Feb-2021
Vesting dates	13-Jan-2022	10-Feb-2022	10-Feb-2022
	13-Jan-2023	10-Feb-2023	10-Feb-2023
	13-Jan-2024	10-Feb-2024	10-Feb-2024
	13-Jan-2025	10-Feb-2025	10-Feb-2025
Volatility	81.42%	87.66%	81.45%
Dividend yield	0%	0%	0%
Risk-free investment rate	0.01%	0.01%	0.11%
Fair value of option at grant date	£2.37	£4.49	£2.74
Fair value of share at grant date	£3.92	£4.53	£4.53
Exercise price at date of grant	£3.92	£0.04	£4.53
Lapse date	13-Jan-2031	–	10-Feb-2031
Expected option life (years)	4.50	2.50	4.50
Number of options granted	200,000	91,888	872,775

Grant date	10-Feb-2021	11-Aug-2021	15-Sept-2021
Vesting dates	10-Feb-2022	11-Aug-2022	15-Sept-2022
	10-Feb-2023	11-Aug-2023	15-Sept-2023
	10-Feb-2024	11-Aug-2024	15-Sept-2024
	10-Feb-2025	11-Aug-2025	15-Sept-2025
Volatility	83.86%	81.07%	79.60%
Dividend yield	0%	0%	0%
Risk-free investment rate	0.05%	0.28%	0.21%
Fair value of option at grant date	£4.49	£0.95	£1.67
Fair value of share at grant date	£4.53	£1.57	£1.71
Exercise price at date of grant	£0.04	£1.57	£0.04
Lapse date	10-Feb-2031	11-Aug-2031	–
Expected option life (years)	3.50	4.50	2.50
Number of options granted	337,000	430,000	140,650

Grant date	15-Sept-2021	15-Sept-2021	15-Dec-2021
Vesting dates	15-Sept-2022	15-Sept-2022	15-Dec-2022
	15-Sept-2023	15-Sept-2023	15-Dec-2023
	15-Sept-2024	15-Sept-2024	15-Dec-2024
	15-Sept-2025	15-Sept-2025	15-Dec-2025
Volatility	82.06%	80.09%	81.80%
Dividend yield	0%	0%	0%
Risk-free investment rate	0.29%	0.36%	0.48%
Fair value of option at grant date	£1.67	£1.04	£1.05
Fair value of share at grant date	£1.71	£1.71	£1.72
Exercise price at date of grant	£0.04	£1.71	£1.72
Lapse date	15-Sept-2031	15-Sept-2031	15-Dec-2031
Expected option life (years)	3.50	4.50	4.50
Number of options granted	603,900	1,488,700	165,000

The fair values of options granted were determined using the Black-Scholes model that takes into account factors specific to the share incentive plan such as the assumption that the options will be exercised at a point in time of up to 2 years after vesting. This has been incorporated into the measurement by means of actuarial modelling. As NuCana plc was unlisted until 2 October 2017, it is not possible to derive historical volatility from the Company's ADSs prior to October 2017. For options with an estimated life of greater than four years, the underlying expected volatility was determined by using the historical volatility of similar listed entities as a proxy. The volatility percentage applied to each tranche is the average of the historical volatility of comparable companies to the Company. Options granted with an estimated life of four years or less, have been valued using the Company's own historical volatility rates.

In the year ended 31 December 2021, an employee remuneration expense, all of which related to equity-settled share-based payments, of £6.7 million (2020: £4.3 million) has been included in the Group income statement and credited to equity.

17. Leases

The Group has lease contracts solely for office space with lease terms of between two and five years. Generally, the Group is restricted from assigning and subleasing the leased assets. There are a number of lease contracts that include extension and termination options and variable lease payments, which are further discussed below.

Refer to note 8 for the carrying amounts of right of use assets recognised and the movements during the period.

The carrying amounts of lease liabilities and the movements during the period are as follows:

Group	*2021*	*2020*
	(in thousands)	
	£	£
At 1 January	**645**	**806**
Re-measurement of liability	4	115
Accretion of interest	18	26
Payments	(296)	(297)
Effect of foreign currency exchange differences	–	(5)
At 31 December	**371**	**645**
Classified as:		
Current	207	278
Non-current	164	367
	371	**645**

Company	*2021*	*2020*
	(in thousands)	
	£	£
At 1 January	**540**	**754**
Accretion of interest	16	24
Payments	(239)	(238)
At 31 December	**317**	**540**
Classified as:		
Current	153	224
Non-current	164	316
	317	**540**

The maturity analysis of lease liabilities is as follows:

Group	*2021*	*2020*
	(in thousands)	
	£	£
Contractual undiscounted payments		
Not later than 1 year	216	296
Later than 1 year and not later than 3 years	169	307
Later than 3 years and not later than 5 years	–	74
Total contractual undiscounted payments	**385**	**677**
Less: effect of discounting	(14)	(32)
Discounted lease liabilities	**371**	**645**

Company	*2021*	*2020*
	(in thousands)	
	£	£
Contractual undiscounted payments		
Not later than 1 year	161	240
Later than 1 year and not later than 3 years	169	255
Later than 3 years and not later than 5 years	–	74
Total contractual undiscounted payments	**330**	**569**
Less: effect of discounting	(13)	(29)
Discounted lease liabilities	**317**	**540**

Refer to note 3 for the amounts recognised in the Group income statement with respect to lease contracts.

The Group had total net cash outflows for leases of £0.3 million in 2021 (2020: £0.3 million).

The Group has one lease contract with variable payments where the lease costs after the first year of the lease are increased based upon a consumer price index. The lease liability for this lease was re-measured at 31 December 2021. All other lease contracts have fixed payments.

The Group has a number of lease contracts that include extension and termination options. These options are negotiated by management to provide flexibility in managing the leased asset portfolio and align it with the Group's business needs. None of the termination options have been exercised or are expected to be exercised. All of the extension options require a market rental review and the lease cost for the extension period will typically be set at the higher of either the current lease cost or the open market lease cost.

Based upon the current lease cost, the undiscounted future rental payments of potential extension options that are not included in the lease liability are as follows:

Group and Company	*2021*	*2020*
	(in thousands)	
	£	£
Extension options not expected to be exercised		
Not later than 5 years	830	591
Later than 5 years	148	387
Total	**978**	**978**

18. Financial instruments risk management

The Group is exposed to market risk arising from exposure to fluctuation in interest rates and currency exchange rates. These risks are managed by maintaining an appropriate mix of cash deposits in the two main currencies the Group operates in, placed with a variety of financial institutions for varying periods according to expected liquidity requirements.

Interest rate risk

As of 31 December 2021, the Group had cash and cash equivalents of £60.3 million. As of 31 December 2020, the Group had cash and cash equivalents of £87.4 million. Exposure to interest rate sensitivity is impacted primarily by changes in the underlying bank interest rates. The Group's surplus cash and cash equivalents are invested in interest bearing accounts and certificates of deposit from time to time which earn interest at fixed or variable rates based on the terms agreed for each account. The Group has not entered into investments for trading or speculative purposes.

Financial assets subject to fixed or variable interest rates are as follows:

Group	*2021*	*2020*
	(in thousands) Carrying amount	
	£	£
Financial assets at short-term fixed rates		
Cash and cash equivalents	24,515	48,432
Financial assets at variable rates		
Cash and cash equivalents	31,024	5,470
Non-interest bearing cash balances		
Cash and cash equivalents	4,725	33,454

An increase in the bank interest rates by 0.5 percentage points would increase the net annual interest income applicable to the cash and cash equivalents held on variable and short-term fixed rate deposits by £278,000 (2020: £270,000).

Currency risk

The Group's functional currency is U.K. pounds sterling, and our transactions are commonly denominated in that currency. However, a portion of expenses are incurred in other currencies, primarily U.S. dollars, and are exposed to the effects of this exchange rate.

Although the Group is based in the United Kingdom, it sources active pharmaceutical ingredients, raw materials, research and development, manufacturing, consulting and other services worldwide, including from the United States, the European Union and India. Any weakening of the pound sterling against the currencies of such other jurisdictions makes the purchase of such goods and services more expensive for the Group. The Group seeks to minimise this exposure by maintaining currency cash balances at levels appropriate to meet foreseeable short to mid-term expenses in these other currencies. The Group thus holds a significant portion of cash and cash equivalents in U.S. dollars and will therefore report the impact of exchange rates movements on these balances.

The Group does not use derivative instruments to manage exchange rate exposure.

Financial assets and liabilities in foreign currencies, primarily held in U.S. dollars, are as follows:

Group	*2021*	*2020*
	(in thousands) Carrying amount	
	£	£
Financial assets		
Prepayments, accrued income and other receivables	2,063	2,079
Current income tax receivable	4	4
Cash and cash equivalents	41,371	70,419
Financial liabilities		
Trade payables	773	409
Payroll taxes and social security	1	1
Lease liabilities	55	105
Accrued expenditure	915	926

A 1% increase in the value of the U.K. pound sterling relative to the U.S. dollar would reduce the carrying value of net financial assets and liabilities in foreign currencies by £417,000 (2020: £711,000).

Credit risk

The Group actively manages cash and cash equivalents across a number of banks and has deposits with different maturity dates. The Group monitors the credit rating of those banks.

All of the Group's cash and cash equivalents at 31 December 2021 were held at U.K. and U.S. financial institutions with short-term A-rated credit ratings, as assessed by recognised international credit rating agencies. As a result, no provision for expected credit losses has been recognised.

19. Events after the reporting period

On 2 March 2022, it was announced the Group's Phase 3 clinical study of Acelarin for patients with advanced biliary tract cancer was being discontinued following a pre-planned futility analysis by the study's IDMC. As disclosed in note 7, as a result of this announcement an impairment of intangible assets of £2.8 million has been recognised as at 31 December 2021. The announcement is an adjusting event, as the data that supported the recommendation of the IDMC to discontinue the clinical study existed at 31 December 2021, although this data had not been compiled, analysed or communicated to the IDMC at that time.

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This Annual Report contains forward-looking statements that reflect NuCana's current expectations regarding future events, including statements regarding financial performance and the timing, progress and results of clinical studies. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected in this Annual Report and depend on a number of factors, including (inter alia), the success of NuCana's clinical studies, its research programmes and the applicability of the discoveries made therein, the successful and timely resolution of uncertainties related to the regulatory process, and the acceptance of our products, if approved, by patients, medical professionals and payors. A further list and description of risks and uncertainties associated with an investment in NuCana can be found in NuCana's filings with the US Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. NuCana undertakes no obligation to update or revise the information contained in this Annual Report, whether as a result of new information, future events or circumstances or otherwise.

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