Advanced Oncotherapy plc

Annual Report 2021

Democratising Proton Therapy
Advancing cancer treatment with innovative, cost-effective technology

ADVANCED ONCOTHERAPY

What we do

Advanced Oncotherapy plc ("AVO") is a British company active in the field of cancer treatment. Following the acquisition of ADAM SA, a CERN spin-off radiation therapy company, AVO aims to capitalise on the know-how and infrastructure that CERN has provided to build an innovative linear accelerator for proton therapy, LIGHT. Its purpose is to deploy globally affordable proton therapy machines with clinical superior benefits to cyclotron and synchrotron alternatives.

Its development strategy and unique business model are designed to maximise product differentiation and value creation whilst seeking to minimise regulatory and execution risk.

"LIGHT will democratise access to healthcare globally and make proton therapy accessible to cancer patients regardless of their location and financial wealth. Put simply, we are seeking to remove the current bottlenecks and put LIGHT in the hands of most healthcare institutions so that a majority, not a minority, of cancer patients benefit from the latest innovation in proton therapy and have the right tools to defeat cancer."

Nicolas Serandour
Chief Executive Officer

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Information about Advanced Oncotherapy: www.avoplc.com

INVESTMENT CASE

Advanced Oncotherapy is a specialist developer and provider of a breakthrough proton therapy system, the LIGHT system, which is the result of 25 years of work at CERN and ADAM. Our focus is on developing and supplying technologies to maximise the destructive effect of radiation on tumours whilst minimising damage to the patient's healthy tissues. We strive to defeat cancer and democratise proton therapy across the globe.

1.

Story with a clear ethical purpose and true social impact

With our LIGHT system, we have the ambition and the means to democratise proton therapy by treating patients not only at proximity to their family but also at a more affordable price for payers: proton therapy for all, not just the lucky ones. This is particularly beneficial for children, and we are proud to be working with partners who share this vision by going the extra mile for them.

2.

Revolutionary CERN technology applied to address the current shortcomings in radiation therapy

Our LIGHT system – created at the world-renowned physics and engineering institute, CERN – is designed to offer the most precise and fastest proton beam for cancer treatment whilst providing significant cost savings for payers. Due to its modularity and its ability to be installed into existing buildings, LIGHT is the first proton therapy equipment that can be leased, which is expected to dramatically accelerate the adoption curve, replicating the success of other breakthrough medical equipment such as MRI or CT scanners.

3.

Growing market opportunity with strong unmet need due to current costs

In the cancer market, an area with significant needs, we provide the latest technological advancement in proton therapy – a more targeted radiation therapy sparing up to 60% of healthy tissue. With the introduction of our LIGHT system, we expect to substantially increase the global availability of proton therapy, well above today's global capacity of 87,000 patients a year.

4.

Broad industrialisation ecosystem in place with high-quality partners

Our manufacturing processes are outsourced to leading manufacturers, further de-risking our business model, creating leaner operations, and laying out the foundations for cost optimisation, accelerated lead times and high-volume production. We work with world-class partners and assemble our LIGHT systems in partnership with a UK-government body, the Science and Technology Facilities Council (STFC).

5.

Rigorous process-driven approach allowing the company to deliver on its plan

With all the critical parts of LIGHT manufactured and delivered to our assembly site as well as our ISO13485 certification, we are focused on the lower-risk parts of our project and on completing the Verification and Validation of LIGHT, a process aimed at ensuring the specification and user requirements are met. Therefore, we are uniquely positioned to fulfil a pipeline of interest already established in the UK, Europe, the US and across Asia and become the undisputed leader for proton therapy.

6.

Business model with complementary and strong sustainable revenue streams and a leasing model that is unique in proton therapy

Our ability to dismantle and move our LIGHT system is the foundation of our business model. We can lease LIGHT to prospective customers, which reduces their upfront considerations. Furthermore our partnership with Kineo is an opportunity to fund our working capital requirements. The low treatment cost per patient and the ability of operators to service the debt due to the attractive financial profile of a proton therapy centre provide us with a further opportunity to take economic interest in the operations of the clinical facility whilst accelerating the pipeline ramp-up.

7.

Experienced management team with great track-record and supported by high-profile industry experts

The management team has significant experience in developing and launching radiation and proton-based equipment with extensive regulatory and commercial expertise. It is supported by experts and advisors whose reputation is unquestionable.

Our Project in Numbers

34,000+

LIGHT and its supporting equipment has more than 34,000 items, of which roughly half are commercially off the shelf

The product complexity of LIGHT is a strong barrier to entry, given the need to document the design records (e.g. product requirements, product architecture, Bill of Materials, design reports, product risk analysis, etc.)

3 billion

The electromagnetic field inside the LIGHT accelerator changes sign 3 billion times per second

Protons are charged particles and can be accelerated if placed in an electro-magnetic field. The strength and direction of the magnetic field is constantly changing so that the north pole becomes the south pole and vice-versa

1/3 millimetre

The accurate evaluation of the beam energy requires measurement of time differences to picosecond precision; a picosecond being the time it takes light to travel one third of a millimetre

Protons can go as fast as 60% speed of light. Measuring the time protons travel between two spots of the machine is crucial to deliver the right treatment for patients

650 million

Protons travelling at a speed of 650 million km/hour will damage a tumour located at a depth of 32 cm

Accelerated protons get “energised”; the higher their energy and their speed, the deeper in the body the radiation damage will be made. There is a direct relationship between the energy of protons and their speed

4,400

Almost 4,400 documents have been needed to support the certification of LIGHT through the quality management system

As an ISO13485-certified company, Advanced Oncotherapy must provide meaningful data evidence of effective quality controls. Data quality and availability are critical to the success of a quality management system framework to drive continuous improvement and preventative quality control activities

1,045

1,045 work applications were submitted in 2021 from people willing to join Advanced Oncotherapy

The Company employs 174 employees as of end of 2021

200

Approx. 200 separate registered IP assets have been filed in more than 35 countries

Advanced Oncotherapy has a dedicated IP department to manage and grow its IP portfolio and to identify, assess and manage IP risks. The Company uses a range of approaches and strategies, depending on the type and content of property and its relation to the overall company strategy as defined by the Board

5

The deposition of proton pulses can be varied and occur once every 5 milliseconds

This ultra-fast change makes LIGHT ideally suited for suited for the treatment of moving targets

CHAIRMAN AND CEO LETTER

Dr Michael Sinclair
Executive Chairman

Dear shareholders,

Despite the unknowns brought by COVID-19 over the period, the Company's objectives and purpose remained consistent with our vision of democratising proton therapy and guided our employees and partners to overcome moments that, at times, seemed insurmountable. We are now pleased and proud to say that Advanced Oncotherapy is on the verge of doing something that has never been done before – building a sustainable and value-enhancing platform to democratise access to proton therapy. We continue to be centre stage in the transformation of cancer care and the deployment of proton therapy, and what we do in this critical phase will define us for decades.

From C to Sea

20 years ago, when family members had cancer, they would often call it the C word and it was hard to blame them: cancer was largely a death sentence for those who were unfortunate enough to get it. Few people can say their lives have not been touched by the disease, either personally or through friends and family. However, the combination of advances in cancer treatments, improved awareness and diagnosis, has changed the trajectory and prognosis of cancer.

Cancer mortality rates have plummeted over the past years, with four out of five of those diagnosed with childhood cancer set to survive for more than five years after diagnosis. While this is great news, much more remains to be done. An estimated ten million people die from cancer each year, and about 75% of cancer survivors have one or more health problems, often as a side-effect of the treatments they received, ranging from heart failure due to chemotherapy, to secondary malignancies as a result of radiotherapy. Chronic problems are also associated with surgeries to remove cancers. These methods have influenced an 'innovation' mindset that is focused on improving clinical outcomes and patients' quality of life. This is best exemplified by the development of more targeted cancer modalities, arguably the most important paradigm treatment shift in cancer care over the last decade.

Proton therapy – as an effective proven radiation therapy with limited long-term side effects due to its high precision – has a key role to play in transforming cancer treatment. Yet, with only 114 proton therapy centres currently across the globe, only circa 87,000 cancer patients can be treated in one year at a cost which is often out of the reach of individual patients and is clearly unsustainable for healthcare systems. This situation is unsatisfactory and, as such, access to proton therapy needs to be democratised. We believe this can be achieved through our 'blue ocean' strategy which relies on the following '5S' principles:

Nicolas Serandour
Chief Executive Officer

- ***Solving*** customers' needs: Our LIGHT solution consists of a breakthrough linear accelerator, an integrated imaging and positioning system and the latest software advancement, which when taken together provide a medically superior solution that is easier to install and can be fitted in existing structures, and more accessible, resulting in a significantly lower treatment cost for payors. This is not only value-enhancing for our customers, but also for the Company's shareholders;
- ***Supporting*** customers through long-term servicing agreements;
- ***Scaling*** our infrastructure to deliver a fast-growing pipeline, further reduce costs and lead times;
- ***Sharing*** our vision with all stakeholders through a long-term interest alignment. We intend to expand the market opportunity through a uniquely designed business model built upon a joint risk / reward sharing policy as evidenced by the profit-sharing arrangements agreed with customers; and
- ***Sustaining*** our competitive advantage by leveraging our proprietary LIGHT platform through a continuous commitment to innovate, attracting top talent and making a positive impact on wider society and the environment.

Executing our global strategy

In a highly regulated industry, we must continue to demonstrate our ability to adapt to our environment and remain agile by accelerating the speed at which we execute our strategy to deliver improved returns. In 2021, the executive team made significant progress in overseeing the assembly of the LIGHT system at our assembly and integration site located in Daresbury, UK, as well as laying out the groundwork for a potential successful market approval.

Execution of our '5S' strategy has also required a disciplined approach to how we invest in our assets. Over the last two years, we have made significant investments in our infrastructure. The trajectory of investment across our organisation is pivoting towards further cost optimisation for future machines and faster delivery times. The Board supports this approach and continues to encourage the executive team to shift their attention to rapid execution, with the key focus areas being the long-term financial benefits of making Advanced Oncotherapy the undisputed industry leader and innovator in the proton therapy field. This is crucial if we are to benefit from the versatility of the LIGHT platform and knowledge uniquely nurtured within our organisation as we pursue our various multi-year strategic goals.

In 2021, our execution plan and resilience as an organisation continued to be tested by COVID-19. While the pandemic has resulted in continual shifts and disruptions to normal business patterns – supply chain

functioning, fluctuating demand in certain areas, workplace operations – we continued to be focused on our LIGHT project. We instigated supply chain initiatives to identify and use alternative components and suppliers whilst complying to ISO standards and medical device requirements. We contracted with key suppliers to recruit additional installation and testing expertise and capacity. Most importantly, we kept our sights on our long-term objectives and our dynamic vision for the future of health. This confirmed the fortitude of our employees and dedication to the values that guide our behaviour every day and help us to build a business of the future. We are inspired by the abundant accounts of the extraordinary care, compassion and commitment of our employees as well as the strength of our organisation which has been resourceful and adaptable, able to anticipate, improvise, and draw on deep reserves of experience, relationships, and know-how.

The LIGHT system: a machine that will revolutionise cancer treatment

There is currently a significant unmet medical need in the treatment of cancer, and we believe the LIGHT system can play a key role in revolutionising cancer therapy. The modularity and movability of the LIGHT system allow us to lease machines to healthcare providers – a new business model in the proton therapy market – uniquely positioning the Company in the market and providing us the opportunity to play a key role in revolutionising proton therapy.

The accelerator, currently under final assembly, is driven by four inductive output tubes (IOTs) operating at 750 MHz, which generate the relevant power for the radiofrequency quadrupole (RFQ), and 13 klystrons operating at 3 GHz, which provide high radio-frequency power to the machine to accelerate the proton beam. The accelerator is cooled, kept under vacuum, and monitored by beam diagnostics and the Company's time-of-flight energy measurement algorithm. Our proprietary LIGHT Accelerator Control System integrates more than 300 separate devices and is driven from a control room where operators accelerate and steer the proton beam. Protons go through a gallery of accelerators moving as a 200Hz pulsed beam through the RFQ, the side-couple drift tube linacs (SCDTLs) and then through the 15 coupled cavity linacs (CCLs) accelerating up to a maximum energy of 230 MeV, the energy required to treat deep-seated tumours at a depth of 32cm. Patient treatment will take place in the treatment room which is located at the end of the accelerator where a state-of-the-art robot chair, with CT scanner and X-Ray panels for accurate patient positioning, has been installed.

During the period, the Company has continued to make significant progress with the commissioning of the LIGHT system. The machine installed at Daresbury has been successfully optimised to deliver a proton beam with a beam size smaller than 1 mm and a beam current of about 50 µA, equivalent to 500 million protons per pulse. As a result, the Company has made good progress in preparing data for the US Food and Drug Administration (FDA) regarding the stability, intensity and spot size of the proton beam. These new data sets demonstrate that the measurements of the quality of the beam match those from computer simulations. The Company can now proceed to finalise the integration of the remaining high energy accelerating modules of the LIGHT machine and further optimise the proton beam.

We have continued to work with our clinical collaborator (the University Hospitals Birmingham NHS Foundation Trust) and Clarivate, a global analytics company, to define the clinical protocol for treating the first patients. These discussions have been held in close coordination with the FDA, the UK Medicines and Healthcare products Regulatory Agency (MHRA) and the European Notified Body, which we consult with on a regular basis. As a result of these discussions, the Company has been requested to provide new measurement data to confirm that the beam performance is maintained within the required tolerances for the clinical use both in terms of energy (i.e. depth in the body) and intensity (i.e. number of protons per second). Although these measurements have not been conducted with the final configuration for 230MeV, they indicate that the beam stability is not a cause for concern in the planned final configuration, a key step which is expected to de-risk the overall certification process. This request originates from the fact that the key LIGHT components are now assembled in situ at Daresbury and the underlying parameters have been optimised in recent months as the Company performs the verification and validation activities, a key step in ensuring product certification.

Commercial momentum

Over the past year, we continued to build commercial momentum around the LIGHT system. During the period, we signed a lessor financing partnership with Kineo Finance (formerly known as DiaMedCare). Under the terms of the partnership agreement, Kineo Finance will acquire LIGHT systems from the Company and lease them to customers that are commissioning the LIGHT system for oncology treatments. As such, we will be able to offer customers easier access to the LIGHT system through a flexible financing solution that reduces the need for large initial upfront payments from customers.

During the period, we also signed a letter of intent with Saba Partners SA for the proposed purchase of a three-treatment room LIGHT system in Switzerland. The Company is working to obtain the applicable CE marking clearances and is working with Saba Partners to put in place a binding agreement and finalise the legal documentation. These agreements build on the commercial momentum for the LIGHT system from our earlier agreements with the London Clinic, the Mediterranean Hospital in Limassol, Cyprus, and University Hospital Birmingham NHS Foundation Trust (UHB).

Adapting our structure to address health, social and environmental challenges

Our long-standing aspiration of creating value for society and for our future business is more relevant than ever, given the mounting threats to people's lives and livelihoods posed by the health, social and environmental challenges dominating today's global agenda. The past two years have underscored the essential role of science in tackling these challenges, whether managing a rogue virus or transitioning into an eco-friendlier environment.

In that regard, we are committed to being a sustainable business. To achieve this ambition, we strive to do business in a financially, environmentally, and socially responsible way. We have designed a breakthrough proton system that is well-positioned to meet the increasing needs of our customers and patients who are demanding more circular and sustainable products around the world. We have a clear, science-based, disciplined and affordable path to further promote our ESG principles; which is particularly relevant as we continue to grow our capacity.

Furthermore, we are committed to strong diversity through ensuring academic qualifications are not the sole criteria for hiring, bespoke training and mentoring, flexible working policies and an inclusive culture as well as having the right competences to meet future challenges.

Financing foundations

We have been able to continue with progressing our activities as a result of the completion of equity investments since January 2021 totalling c.£58 million (before costs). Funds raised have supported the Company as it progresses towards having a fully operational LIGHT system operating at 230MeV during summer 2022.

Our financial results

The Company recorded a comprehensive loss of £30.3 million in the year ended 31 December 2021 (2020: £23.4 million), with shareholder funds as at 31 December 2021 of £61.4 million (2020: £44.1 million). Cash and cash equivalents at the year-end were £4,260,490 (2020: £2,317,451).

Outlook

Looking ahead, 2022 is a significant year for us at Advanced Oncotherapy as we move towards the delivery of our first LIGHT system operating at 230 MeV. We have made significant strides towards achieving this milestone during the period and have set the foundations to fast forward the global adoption of the LIGHT system. We remain on track with our timeline of summer 2022 to deliver a machine at 230 MeV.

In closing

The Company has emerged stronger despite the challenges it faced in 2021. We have made significant progress towards the delivery of our first LIGHT system operating at 230 MeV and have shown resilience in the face of adversity. We are convinced that this Company is taking the right steps to shape a successful future.

Such progress would not have been possible without the tremendous effort and dedication of our staff. We remain confident in our ability to deliver the first machine with a 230 MeV beam during summer 2022 and look forward to what will continue to be a significant year for the Company.

On behalf of the Board of Directors, we would like to offer our sincere thanks to all Advanced Oncotherapy employees for their dedication and contributions to the good operational and strategic progress and to the management team for their leadership. And most importantly, thank you for supporting us as shareholders, for your loyalty and for being a part of our journey.

Dr Michael Sinclair
Executive Chairman
30 June 2022

Nicolas Serandour
Chief Executive Officer
30 June 2022

PURPOSE, VALUES AND EXCELLENCE

Our Purpose

At Advanced Oncotherapy, we strive to defeat cancer and democratise proton therapy across the globe.

Our Values

Life

We collaborate across our professional disciplines, and with our suppliers and investors, to create outcomes that go beyond the sum of the parts. Putting the well-being of patients and staff at the heart of our mission, we change people's lives for the better.

Safety

We choose the right path, not the easy path. We do the right thing to ensure the safety of patients, our users, and our staff. We are rigorous in our research, our development, and our testing, never accepting short-cuts.

Quality

We focus on patient outcomes, reliability, and consistency. Our professionalism, commitment and precision deliver world-class results, meeting the most stringent medical requirements.

Innovation

We push the boundaries of what can be achieved between physics and engineering, creating something that has never been done before. Our agility and entrepreneurial spirit are changing cancer treatment for ever.

Our Areas of Excellence

- Beam dynamics
- Civil and structural engineering
- Cooling and ventilation
- Electrical engineering
- Electrical networks
- Electromagnetic compatibility & interference
- Electronics
- Health and safety
- Magnet technology
- Mechanical engineering
- Power converters
- Radiation protection
- Radiation safety
- RF technology
- Survey and alignment
- Vacuum technology

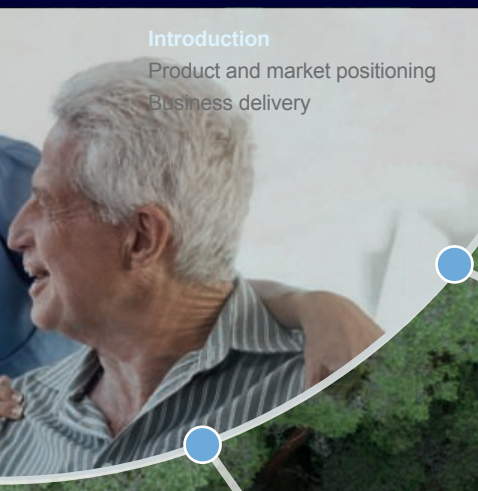
RELEVANCE AND EVOLUTION

Bringing innovative financing solutions to customers and to support the working capital needed for new machines

- 2021: Lessor financing partnership with Kineo to support financing customers' needs and working capital of the Company; £46m raised in equity
- 2020: £23m raised in equity raises and £40m credit facility with VDL and Nerano

Building an infrastructure that supports high-volume production with quality at its core

- 2021: Infrastructure in place to support assembly and testing activities
- 2019: ISO 13485 certification
- 2018: Assembly and testing site finalised with STFC
- 2016: Optimisation and industrialisation programme in partnership with Thales
- 2014/16: Suppliers selected



Bringing a differentiated technology on the market with superior medical outcomes

- 2021: LIGHT capable of delivering a proton pulse every 5 milliseconds and initial maximum intensity reached; synergistic LIGHT/ immunotherapeutic approaches; treatment room installed in Daresbury
- 2020: Manufacturing of all critical hardware completed; LIGHT treatment plan installed at the Cleveland Clinic
- 2019: Studies confirming the superiority of LIGHT and its potential for FLASH
- 2018: LIGHT capable of accelerating protons at 52 MeV
- 2017: First SCDTL integrated
- 2015: Successful RF power testing of the first CCL unit
- 2001: Successful testing of the first LINAC booster ("LIBO")
- 1993: Validation of the design

Demonstrating an agile commercial mindset with a focus on aligning interest

- 2021: Letter of Intent from Saba Partners to buy a LIGHT System
- 2020: Partnership with The London Clinic, the Mediterranean Hospital and the University Hospitals Birmingham NHS Trust
- 2019: Partnership with the Cleveland Clinic; clinical site built in Harley Street, London
- 2017: Distribution and equity partnership with Realcan

In a study dated September 2019 and published by the Harvard Medical School, it was estimated that the overall cost of development for a complex medical device was $526 million. Notably, this is more than the double the investment made into developing the LIGHT System. Furthermore, and for projects with a strong physics-content, it is estimated that 10-15 years are necessary to develop a conceptual design into an optimised design ready for industrialisation.

SUSTAINABILITY REVIEW

Our approach is holistic and integrates the three dimensions of sustainability:

- Society – how we contribute to a better tomorrow for all
- Environment – how we minimise our impact on nature
- Economy and governance – how we invest in medical advances, create jobs

Environment

- Housing a LIGHT accelerator does not involve large shielding
- The installation of LIGHT does not require expensive cranes or load handling devices
- LIGHT can be disassembled and removed from one site to another
- Our assembly site is sponsored by the UK government and with a net zero target by 2040
- We use energy saving technology and LED lights wherever possible
- We reviewed travel policies to reduce the number of journeys and trips made
- We promote the use of technology to replace travel to meetings with the use of video conferencing

Society

- Our purpose is to democratise proton therapy and offer access to people who cannot afford the treatment
- Children are a particular focus; with our partners we are committed to support their treatment at cost in the catchment area
- Our commitment to expand access to innovations will help more patients live longer, better lives
- LIGHT can be installed in densely populated areas; this means patients do not have to travel long distance; hence they can be treated at proximity to their home
- We continue to be committed to equal opportunities when it comes to recruitment, appointing and development, irrelevant of gender, race, or religion
- We emphasise employee safety, health and development while promoting diversity and inclusion, integrity, mutual respect

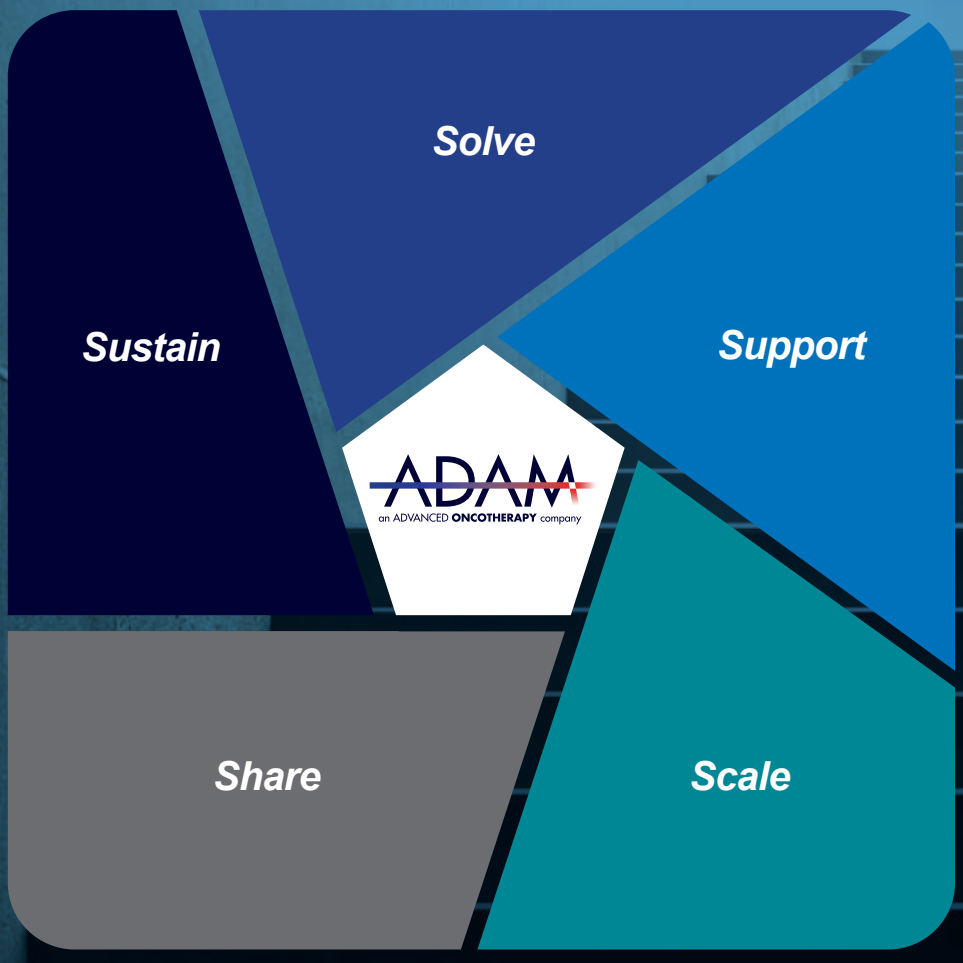
Economy and Governance

- By contributing to treat patients at a more affordable cost and reducing expensive long-term side effects of treatment, we help patients and families reallocating financial resources on other priorities
- The deployment of LIGHT is expected to be accompanied with the creation of logistic hubs in selected geographies, further expanding the skill set of people and building an important network of partners around the world
- We are committed to train physicians and engineers around the world to accelerate the deployment of LIGHT
- We follow the QCA Code on good corporate governance
- We deliver our plan in accordance with ISO-13485
- We promote flexible working for every role where this is possible

FIVE PRIORITIES IN ACTION

Our corporate strategy has five distinct focus areas. It is built on our purpose and our ambition to be a sustainable business. We aim to:

- solve customers' needs;
- support customers through long-term servicing contracts;
- scale the infrastructure to meet the demand;
- share vision with all stakeholders through long-term interest alignment;
- sustain the Company's competitive advantages.



SOLVE customers' needs

Accessing a larger segment of the radiation therapy market…
We intend to disrupt the radiation therapy market by selling to a broad range of customers that have yet to make an investment in proton therapy due to the challenges associated with conventional proton therapy.

…by providing a solution, not just a product …
We intend to be a patient-centric solutions leader. Our commitment is to solve problems through a turn-key solution. We focus on what matters for all stakeholders in our ecosystem: integrated solution including the accelerator, the imaging system, the software package; medically superior solution to existing systems; easier to install and fit; more accessible; value-enhancing for customers and the Company's shareholders.

… and enhancing awareness of the LIGHT benefits
We intend to attract new customers by educating the market about our leading and differentiated system and its unique capabilities.

SUPPORT customers through long-term servicing contracts

Providing long-term servicing contract to ensure reliability of the operations; …
We intend to support our customers – beyond the installation of a LIGHT system – by being the single-point responsibility for long-term servicing and maintenance operations. The complexity of proton therapy systems demands that they are serviced by a single source that has the knowledge and the ability to do so, so that customers can reliably operate LIGHT.

… a key strategic pillar that has many other advantages
We intend to leverage our servicing strategy; this is expected to result in future business development opportunities and generate steady income streams.

SCALE the infrastructure to meet the demand

Building the foundation for delivering a fast-growing pipeline…
We intend to scale our assembly infrastructure and deepen the relationship with our partners and suppliers to increase the number of LIGHT systems which can be installed in any given year.

… and further optimising costs and delivery times
We intend to further optimise costs and reduce lead times by implementing identified initiatives and leveraging our operational set-up.

SHARE vision with all stakeholders through long-term interest alignment

Promoting a "skin in the game" culture with key stakeholders
We intend to build partnerships through a clear long-term interest alignment. Our approach is therefore based on removing the silos arising from the conventional supplier/customer relationship. To do so, we are focused on implementing new models as exemplified by our partnership with Cosylab, a strategic supplier focused on software development and incentivised through payment in Company's shares.

Working closely with customers
We intend to expand the market opportunity through a uniquely designed business model built upon a joint risk/reward sharing policy as evidenced by the profit-sharing arrangements agreed with customers. This brings many benefits such as the opportunity to gain valuable insights about the customers' operations and generate more recurring revenue streams.

SUSTAIN the Company's competitive advantages

Leveraging our proprietary LIGHT platform
We intend to leverage our proprietary LIGHT platform by continuously enhancing our clinical capabilities with new and improved product functionalities and technologies, including the development of FLASH, the deployment of mini-beams and the synergistic combination of proton therapy with immunotherapies. The latter leverages the unique features of LIGHT, including its high precision and ultra-fast delivery, and offers the opportunity to treat cancer types which can not be treated today. Further routes for innovation relate to beam delivery, patient imaging, positioning and motion management and streamlined clinical workflow.

Investing in talent
We intend to attract and retain top talent as the industry remains characterised by scarcity and competition for skills and capabilities. This is key to sustain our competitive edge and nurture our culture.

Making a positive impact on society and environment
We intend to integrate sustainability in a systematic way throughout the entire value chain and decision-making process to truly influence the Company directions and build resilience.

CANCER, SET TO BECOME THE NUMBER-ONE CAUSE OF DEATH IN MOST SOCIETIES

Cancer, the abnormal proliferation of cells which is capable of both invading surrounding normal tissue and spreading throughout the body

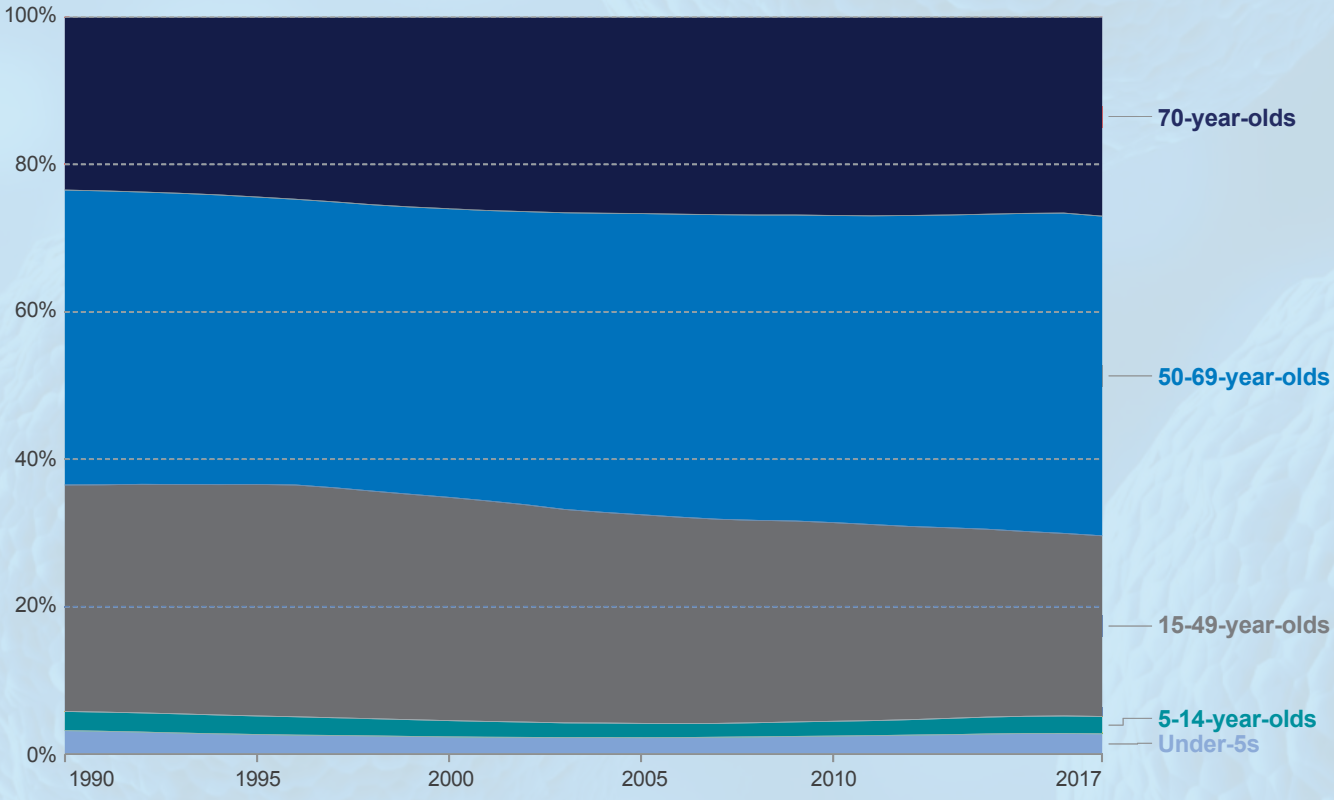
Cancer is a broad term often used to describe a large group of diseases defined by uncontrolled cell growth and division. These cancer cells do not die. They invade normal tissues and organs, and eventually spread throughout the body. Their generalised loss of growth control is the net result of accumulated abnormalities in multiple cell regulatory systems and is reflected in several aspects of cell behaviour that distinguish cancer cells from their normal counterparts:

- **Cancer cells do not stop growing and dividing.** Unlike normal cells, cancer cells do not stop growing and dividing when there are enough of them. So, the cells keep doubling, forming a lump (tumour) that grows. A tumour forms, made up of billions of copies of the original cancerous cell. Cancers of blood cells (leukaemia) do not form tumours, but they make many abnormal blood cells that build up in the blood;
- **Cancer cells have abnormal differentiation.** They do not mature normally; therefore, they are not able to carry out their functions;
- **Cancer cells ignore signals from other cells.** Cells send chemical signals to each other all the time. Normal cells obey signals that tell them when they have reached their limit and will cause damage if they grow any further. But something in cancer cells stops the normal signalling system from working;
- **Cancer cells invade nearby tissues.** Normal cells respond to signals from other cells which tell them they have reached a boundary. Cancer cells do not respond to these signals and extend into nearby tissues often with finger-like projections. This is one reason why it is difficult at times to surgically remove a tumour. The word cancer, in fact, is derived from the Greek word carcinos for crab, referring to these claw-like extensions into neighbouring tissues;
- **Cancer cells can spread to other regions of the body via the circulatory or lymphatic systems (metastasis).** Unlike normal cells which make substances called adhesion molecules that cause them to stick to nearby cells, cancer cells can break free and float to other regions of the body. Only malignant tumours are properly referred to as cancers, and it is their ability to invade and metastasise that makes cancer so dangerous. Whereas benign tumours – which remain confined to their original location, neither invading surrounding normal tissue nor spreading to distant body sites – can usually be removed surgically, the spread of malignant tumours to distant body sites frequently makes them resistant to such localised treatment;
- **Cancer cells do not repair themselves or die.** Normal cells can repair themselves if their genes become damaged. This is known as DNA repair. Cells self-destruct if the damage is too bad in a process called apoptosis. In cancer cells, the molecules that decide whether a cell should repair itself are faulty;
- **Cancer cells have specific tumour markers.** They can express proteins, called antigens, on the cell surface, which makes them different from normal, healthy cells.

Cancer is a devastating disease that takes an enormous emotional toll. Not only on the patient, but on the patient's loved ones, as well. It is a battle that humans have been fighting for centuries. And while we have made some advancements, we still have not beaten it. Two out of five people in the US will develop cancer in their lifetime. Of those, 90 percent will succumb to the disease due to metastases.

Every time cells divide; they make a copy of the genetic code contained within them. This copying process is not always perfect and occasionally results in typos, or errors in the DNA, which are called mutations. Cells have ways to detect and fix these mistakes, but they do not always work. If a cell develops a mutation, it may start to act differently to a normal cell.

Prevalence of cancer by age, World, 1990 to 2017



Source: IHME, Global Burden of Disease

Cancer can affect people of any age but occurs more often in older people, most likely from cumulative exposure to carcinogens, agents that are known to increase cancer risk. Cancer comes from our own cells; however, our chances of being affected by the disease can be linked to factors that come from both within and outside of our bodies.

CANCER, SET TO BECOME THE NUMBER-ONE CAUSE OF DEATH IN MOST SOCIETIES_Continued

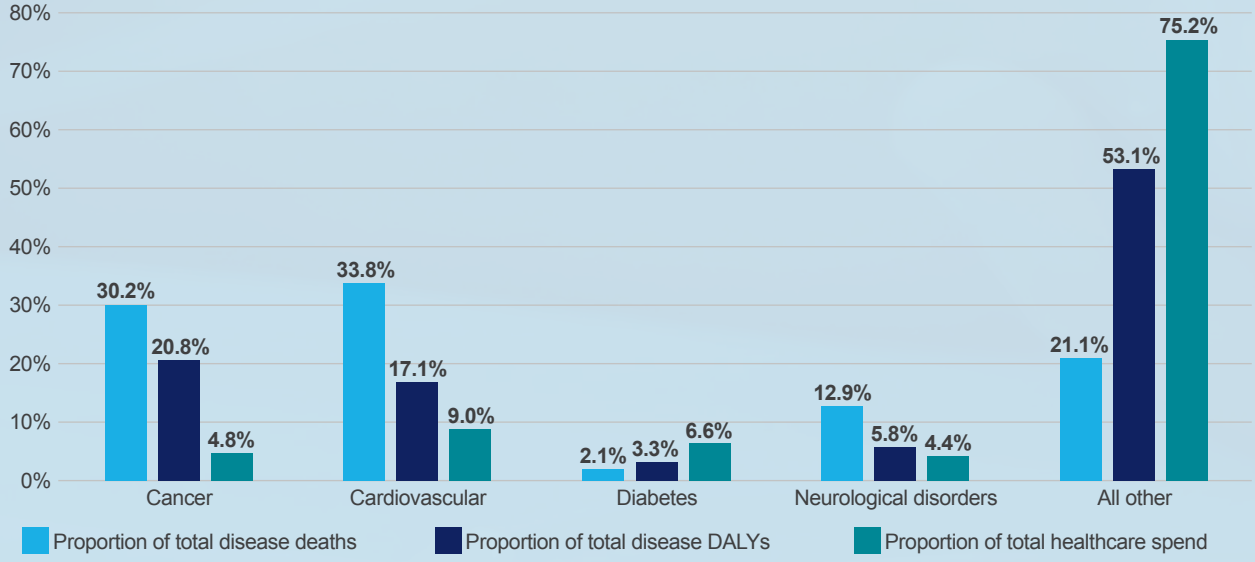
Despite advances, the number of cancer patients is set to climb over the coming decades

Cancer is not always a death sentence. In many countries more people are surviving cancer than ever before. In fact, there are now 28 million people living with or beyond cancer worldwide, a number that has increased nearly five-fold since the 70's. Cancer's death rate has been reduced by 27 percent over the past 25 years, giving cancer patients increased hope for survival. This is largely due to the emergence of new treatments and technologies as well as earlier detection.

Yet, this should not obscure three important challenges.

- GLOBOCAN 2020 made a staggering prediction: with an aging population, it expects the number of new cancer cases to rise markedly, reaching an astounding 28 million cases annually by 2040, a 47 percent rise from 2020. The U.S. Cancer Society estimates that almost 40 percent of men and women will be diagnosed with cancer during their lifetime;
- Despite the upward trajectory of cancer survival rates, it remains chillingly apparent that there is still a huge, unmet need in the fight against cancer. Several forms of cancer are almost completely unresponsive to treatments that have been developed over the last 40 years: for example, the five-year survival rate from pancreatic cancer remains barely above five percent at five years after diagnosis. Brain tumours probably cause more "years of life lost" than any other sub-type of disease, and the most aggressive forms of this disorder offer some of the greatest challenges within medicine. Despite the disease burden, the level of investment and healthcare expenditures in cancer remains below major chronic diseases.
- For patients and their families, the costs associated with direct cancer care are staggering. In the UK, young people (under 35) and people approaching pension age (55-64) are most likely to see a decline in their financial health because of cancer, at 67 and 60 percent respectively. Drawing on this, the total economic cost of cancer to the UK economy in terms of lost wages and benefits is estimated at approximately £1.4 billion a year or £7.6 billion a year when considering mortality.

Average proportion of mortality, DALYs and healthcare expenditure, by disease (2015)



Note: DALY = Disability Adjusted Life Years; this represents the number of years lost due to ill-health, disability or early death

Schlueter M, Chan K, Lasry R, Price M (2020) The cost of cancer – A comparative analysis of the direct medical costs of cancer and other major chronic diseases in Europe. PLOS ONE 15(11): e0241354. https://doi.org/10.1371/journal.pone.0241354 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0241354

Compared to cardiovascular diseases, neurological/mental disorders and diabetes, cancer is associated with the highest disease burden (20.8% of DALYs across all diseases) but the second-lowest healthcare expenditure levels (4.8% of total healthcare expenditure) among the studied major chronic diseases.

CANCER, SET TO BECOME THE NUMBER-ONE CAUSE OF DEATH IN MOST SOCIETIES_Continued

Cancer is complex, so approaches to its treatment must match that complexity

Once a cancer has formed, the cells do not remain the same, but rather continued mutations may occur. This, in fact, is why resistance develops to chemotherapy and targeted therapy drugs in time. The cancer cell develops a mutation that allows it to bypass the damaging effects of these treatments. That cancer cells change is very important in treatment. For example, a breast cancer that is oestrogen-receptor positive may be oestrogen-receptor negative when it recurs or spreads. It also helps explain why cancer cells in different parts of a tumour may be different. This is referred to as "heterogenicity" and is important in diagnosis and treatment as well.

Consequently, clinicians must have an array of treatment options for their cancer patients.

- Surgery is aimed at removing tissue from the body. It remains a mainstay in the cure and control of most solid cancers; it is often the first treatment offered to patients. Surgery can have different purposes: cure; prevent; diagnose; uncover the extent of cancer (staging surgery); remove a portion, though not all, of a cancerous tumour (debulking surgery), relieve discomfort and pain, etc. Surgery is not used for some types of cancer of the blood system (leukaemia), or lymphatic system (lymphoma), because cancer cells might spread throughout the body. Surgery may also not be possible because of its location near delicate tissues or blood vessels.

- Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cells. Chemotherapeutic agents are cytotoxic that harm malignant as well as healthy cells in cancer patients. There are different drug types of chemotherapy drugs available which includes alkylating agents, plant alkaloids, antitumour antibiotics, antimetabolites and topoisomerase inhibitors. To improve patients' quality of life, chemotherapy is often used as an adjuvant to other therapeutic modalities such as radiation therapy and surgery.

- Targeted therapy is a cancer treatment that uses drugs to target specific genes and proteins that are involved in the growth and survival of cancer cells. Targeted therapy can affect the tissue environment that helps cancer grow and survive or it can target cells related to cancer growth, like blood vessel cells.

- Immunotherapy is a type of cancer treatment that helps the immune system fight cancer. The immune system helps fight infections and other diseases. It is made up of white blood cells and organs and tissues of the lymph system. There are different categories of immunotherapy which includes immune checkpoint inhibitors, T-cell transfer therapy and monoclonal antibodies. Immunotherapy is one of the most recent advancements in cancer therapy that has improved the effectiveness of overall cancer therapy. This treatment option is based on a commonly accepted hypothesis that the immune system is an effective tool for combating various diseases. Researchers have developed certain approaches for the use of immunotherapeutics in cancer treatment that include stimulating the immune system externally so that it would act forcefully or destroy the tumours with tumour specific proteins. Immunotherapy, most often, is used in combination with surgery, radiation, or chemotherapy to augment the therapeutic effectiveness of the cancer treatment.

- Hormonal therapy is a treatment that adds, blocks or removes hormones to slow or stop the growth of cancer cells that need hormones to grow.

- Radiation therapy is an important technique for shrinking and killing tumours. High energy waves are targeted at the cancerous cells. The waves stop certain internal functions of the cell that are involved in cell division, so the cells eventually die.

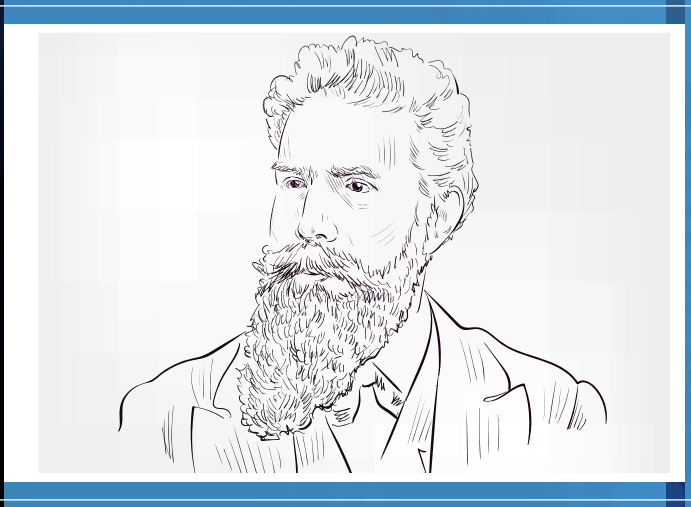
Over the past decade, we have witnessed the evolution from evidence-based medicine to precision medicine, making it clear that 'one-size-fits-all' treatment protocols are not the way to conquer cancer.

RADIATION, THE CHEAPEST AND MOST WIDELY USED CANCER MODALITY

Radiotherapy, a well-proven technology with a longstanding history of treating cancer patients

Today, radiotherapy is provided to up to two-thirds of cancer patients, either on its own or alongside other forms of therapy. It has won a place as a mainstay of modern cancer treatment, coming a long way since Wilhelm Conrad Roentgen, a German physics professor, presented in 1896 a lecture entitled “Concerning a New Kind of Ray.” Roentgen called it the “X-rays”, with “x” being the algebraic symbol for an unknown quantity; he received the first Nobel Prize awarded in physics in 1901. Three years after Roentgen’s breakthrough, the physicist Marie Curie discovered the chemical element radium, another source of radiation. Scientists in the US and Europe then began studying the use of radium and X-rays to treat cancer. They also discovered that daily doses of radiation over several weeks greatly improved the patient’s chance for a cure. Soon, it became clear that radiation was a highly effective tool against cancer, but it was also harmful for patients and clinicians. Early radiologists developed leukaemia after testing their machines on their own arms: they were estimating the daily fraction of radiation by looking for a dose that would produce on their skins a pink reaction (erythema) which looked like sunburn.

Further advances were made in the first half of the 20th century following the work of the English physicist Hal Gray – after whom the radiation unit of measurement (the Gray) is named – on how cells respond to radiation. High-energy X-rays were also introduced, providing improved treatment of deep-seated tumours. In the 1990s, the advent of computers, CT scanners and the use of CT for radiation planning were dramatic breakthroughs in radiation treatment because they allowed the ability to design radiation beams to directly target the tumour and for the first time accurately calculate doses received by nearby healthy organs. Conformal Radiation Therapy ("CRT") – which uses CT images and special computers to map the location of a cancer very precisely in three dimensions – was deployed in hospitals. Although 3D-CRT was a significant improvement over conventional 2D planning, it had limitations: 3D-CRT beams deposit a uniform strength of radiation (intensity) across specific field(s), thus they cannot conform to concave structures. Concave conformality requires the ability to modulate radiation beam intensity across a field. With the development of Intensity-Modulated Radiation Therapy ("IMRT"), it became possible to adjust the intensity, giving more control in decreasing the radiation reaching normal tissue while delivering a high dose to the cancer.



X-rays were discovered by accident. Roentgen had been doing experiments with cathode rays—streams of electrons in vacuum tubes. He had prepared a glass cathode ray tube completely covered with black cardboard, and noticed that even though the cardboard completely covered the tube, a glow still appeared on a fluorescent screen several feet away. After Roentgen prepared one of the earliest X-ray images of the bones in the hand of his wife, she remarked: “Now I have seen my death!”

Since then, new techniques have been introduced such as stereotactic radiosurgery and stereotactic radiation therapy which are used to deliver a large, precise radiation dose to a small tumour. The term surgery may be confusing because no cutting is done. The most common site treated with this radiation technique is the brain. A significant attention is also currently placed on the development of chemical modifiers or radiosensitisers which are substances that make cancer more sensitive to radiation. The goal of research is to develop agents that will make the tumour more sensitive without affecting normal tissues. Researchers are also looking for substances that may help protect normal cells from radiation.

However, there is a general consensus that the development of X-rays techniques has now reached a limit, which is due to the physics of photons.

RADIATION, THE CHEAPEST AND MOST WIDELY USED CANCER MODALITY_Continued

X-rays, using the basic unit of all light (photons) to damage cancer cells

Approximately 98% of radiation is currently delivered through X-rays. X-rays are packets of electromagnetic energy – also called photons – that originate from the electron cloud of an atom. X-rays photons are created through an energy change in electrons, which are excited, causing the excess energy to be released. This change of energy is generated in a vacuum-sealed X-ray tube, using a high voltage potential to accelerate electrons from a cathode to a spinning anode, often comprised of tungsten.

Radiation therapy works by exposing clusters of cancer cells to a dose of high energy radiation sufficient to damage their genetic information, the DNA which contains the information used to control cell growth and division. When cancer cells are exposed to radiation, they cannot divide successfully and die.

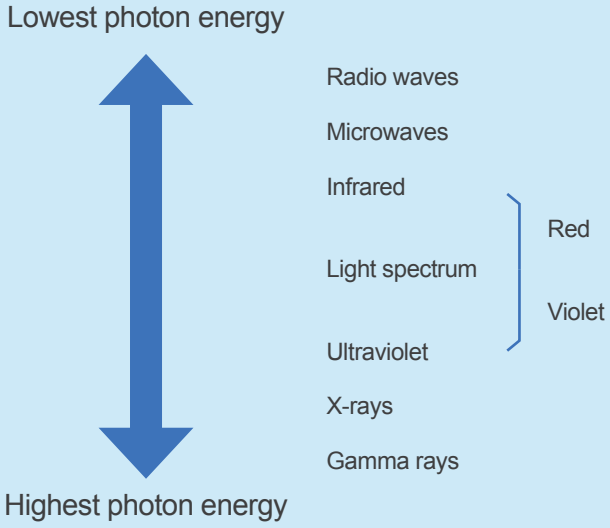
Radiation therapy damages both healthy cells and cancer cells in the treatment area. Therefore, the clinician's goal is to target radiation delivery to the tumour as precisely as possible to maximise the radiation dose delivered to cancerous tissue and minimise the exposure of healthy tissue. Still, radiation affects cancer cells more than normal cells. Cancer cells reproduce faster than normal cells and lack the controls found in normal cells. Because of this, it is harder for cancer cells to repair the damage done by radiation. So, cancer cells are more easily destroyed by radiation, while healthy cells are better able to repair themselves and survive the treatment.

Radiation can be used alone or in addition with other treatments to cure or stabilise cancer. Like other therapies, the choice to use radiation to treat a particular cancer depends on a wide range of factors. These include, but are not limited to, the type of cancer, the physical state of the patient, the stage of the cancer, and the location of the tumour.

Photons are subatomic particles which are always in motion, travelling at the speed of light in empty space. The energy of a photon depends on radiation frequency; there are photons of all energies from high-energy gamma- and X-rays, through visible light, to low-energy infrared and radio waves. Photons have no electric charge and zero mass

Types of electromagnetic radiation

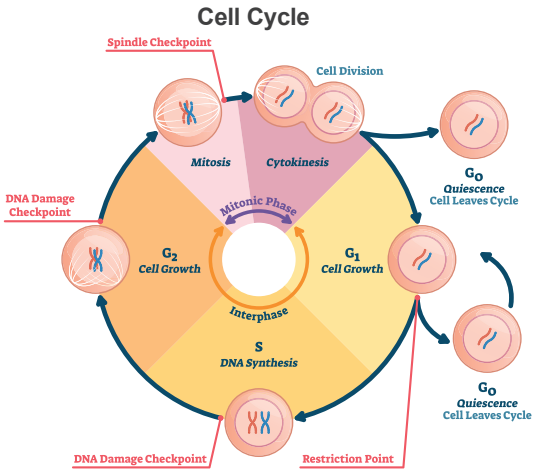
Einstein proved that light is a flow of photons, the energy of the light being directly related to the wavelength. Shorter wavelengths are higher energy. Therefore, X-rays and ultraviolet can be harmful, unlike radio wave and infrared light. In the case of an X-rays, its wavelength is 0.01 to 10 nanometres. As a comparison, fingernails grow about one nanometer per second. Photons possess enough energy (100 eV to 100 keV) to disrupt molecular bonds and ionise atoms making it, by definition, ionising radiation.



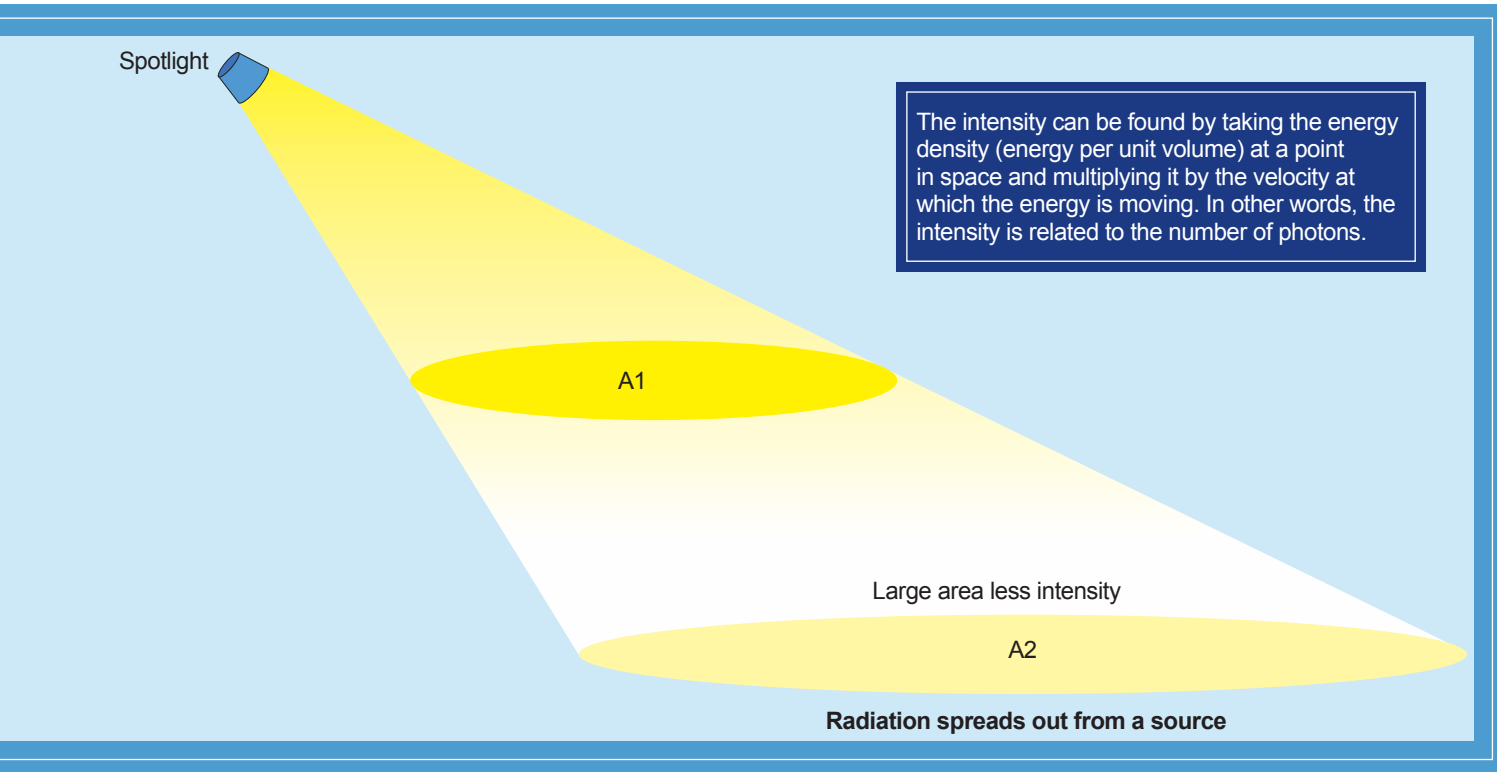
Allowing healthy cells to recover between treatments through fractionation

Radiation therapy is delivered in small doses called fractions, which are measured in centigray or cGy. These fractions are given each day, most often Monday to Friday, for a period of five to seven weeks. This fractionation seeks to maximise the destruction of malignant cells while minimising damage to healthy tissues: splitting the total radiation dose allows healthy cells an opportunity to repair this sublethal damage between fractions. Meanwhile, malignant with impaired DNA repair pathways are less able to recover from radiation damage to their DNA. The effect of fractionation is further supported by two fundamental cellular mechanisms:

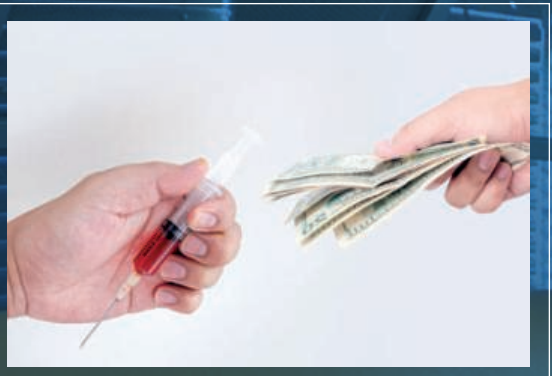
- The radiosensitivity of cells depends on their stage in the cell cycle. Cells are most sensitive to radiation in the M and late G2 phase of their cycle and most resistant in the late S phase. Since a group of malignant cells are at various points in their cell cycle, delivering the entire dose of radiation in a single fraction is ineffective against a proportion of the tumour cells. Dividing the total dose of radiation into multiple fractions maximises the probability of irradiating cells when they are in the most radiosensitive period of their cell cycle; and
- The concentration of oxygen in the body ranges from 14% in the alveoli to 5% in peripheral tissues, a proportion that may be significantly lower in tumours. Cancer cells with a low oxygen concentration are less susceptible to the effect of radiation. Therefore, fractionation allows cells which are closer to sources of oxygen to be killed first whilst the other malignant cells will become more sensitive to subsequent doses of radiation once they receive a greater oxygen supply.



	Conventional fractionation	Hypofractionation
Dose	From 180cGy to 200cGy	Higher doses per fraction
Typical treatment	Once a day, 5 days a week, over 6-7 weeks	Shorter schedule, usually 3 to 4 weeks; treatment sometimes not given every day
Cancer types	Most common type of fractionation; used in many types of cancer	Not appropriate for all cancer types



PROTON THERAPY, THE MOST ADVANCED RADIATION TECHNIQUE



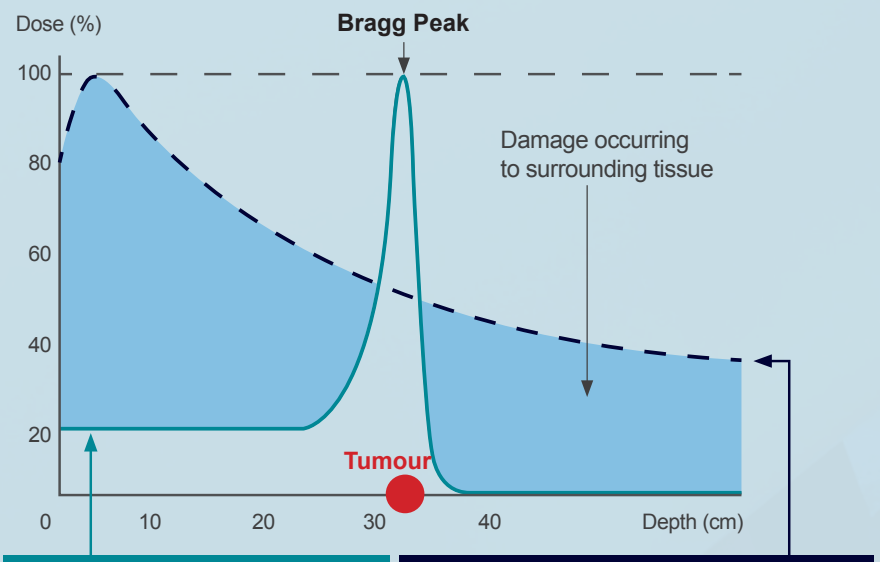
Protons are positively charged and therefore attract negative charges. When a proton – as a positively charged particle – is launched near a molecule such as DNA, negatively charged regions of the molecule will be attracted to the proton, thus interfering with that molecule's normal orientation and function. The result of this process is ultimately the death of cancer cells.

Fundamental facts around protons and their relevance in a medical setting

The physical property of protons, the key for a superior medical outcome in cancer treatment

Protons are particles with a positive electric charge which are, along with neutrons, in the nucleus of an atom. The rest of the atom consists of electrons with a negative electric charge that orbit the nucleus. Therefore, the atoms of elements are neutral, all the positive charges cancelling out all the negative charges. Atoms differ from one another in the number of protons, neutrons and electrons they contain. Atoms of hydrogen have a single proton in their center and a single electron whilst helium atoms, on the other hand, have two protons and two electrons. Protons used in proton therapy are typically extracted from hydrogen through electrolysis, a process aimed at separating the proton and the electron.

When protons are accelerated in a particle accelerator, they acquire an energy: the more they get accelerated, the more energy they acquire, the higher their speed and the deepest in the body they stop. Once protons are accelerated and hence, they are "energised", then they lose their gained energy based on the Bragg peak curve: the amount of energy lost by protons is inversely proportional to the square of their velocity; this explains why protons release their maximum energy – which damages the DNA of cancer cells – just before they come to a complete stop. This point corresponds to the Bragg peak; this is the spot where the maximum damage is made to a tumour. Therefore, and due to this physical property, proton beam radiation can deliver more radiation to the cancer while reducing damage to nearby normal tissues. This is in stark contrast with X-rays photons which gradually lose their energy, hence damaging the tumour but also the healthy tissues before and after the target. This is further compounded by the fact that protons are significantly heavier than photons, hence the rays of proton therapy scatter less easily than photons X-rays, thereby preventing radiation risk to healthy tissues beyond the cancerous cells.



Protons
The proton dose increases with depth, resulting in a Bragg curve with a peak at the required depth level. This results in significant extra dose in the tumour.

X-rays (Photons)
Photon dose distributions as a function of depth show a maximum dose close to the entrance after a short build-up and then an exponentially decreasing energy deposition with increasing depth in tissue.

Proton therapy's greatest advantage over conventional radiation therapy is its accuracy and its ability to powerfully treat cancerous tissues while avoiding healthy ones.

Conventional X-rays are made of photons that pass through the body and deposit considerable energy before and after the tumour. Proton therapy offers great promise in the treatment of a wide variety of cancers owing to the sharp drop-off in radiation dose at a defined point, known as the Bragg peak, beyond which there is no appreciable dose. Therefore, it deposits less energy on its way to the tumour and does not affect tissues beyond it. This confines the radiation dose to the tumour and decreases the risk of injury to surrounding healthy tissues.

Steve Myers
Executive Chairman of ADAM

Putting things in perspective: The energy of a particle is measured in electronvolts. One electronvolt is the energy gained by an electron that accelerates through a one-volt electrical across a distance of 1 metre. As they race around the Large Hadron Collider ("LHC"), the protons acquire an energy of 6.5 million million electronvolts, known as 6.5 tera-electronvolts or TeV. It is the highest energy reached by an accelerator, but in everyday terms, this is a ridiculously tiny energy; roughly the energy of a safety pin dropped from a height of just two centimetres. But an accelerator concentrates that energy at the infinitesimal scale – protons have radius of under a millionth of a billionth of a metre – to obtain very high concentrations of energy close to those that existed just after the Big Bang.

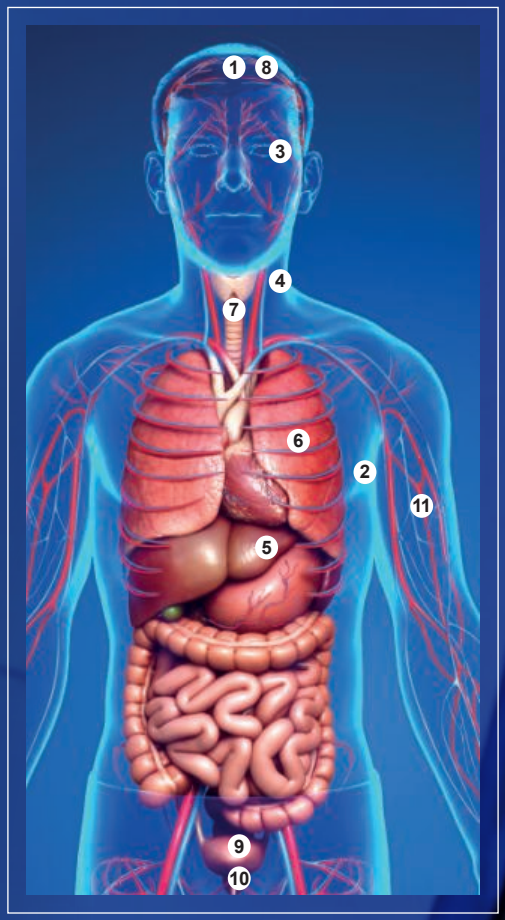
Advanced Oncotherapy's LIGHT accelerator is designed to accelerate protons to 230 million electronvolts or 230 Mega electronvolts ("MeV"); this is equivalent to 0.004% of the energy of protons accelerated in the LHC.

PROTON THERAPY, THE MOST ADVANCED RADIATION TECHNIQUE_Continued

The advantages of proton therapy over conventional X-rays

With a success rate of up to 96%, proton therapy is unique in its accuracy and in its heightened ability to avoid damage to healthy cells or tissues during treatment. This results in a wide range of benefits for patients. More specifically:

- Proton therapy is ideally suited for treating hard-to-treat tumours such as tumours located near critical organs (e.g., brain, head, and neck, etc.) as well as children and young adults who are more susceptible to injury from standard X-rays radiation because their tissues and organs are growing more rapidly. This is due to the higher precision of proton therapy and the reduced scattering effect of protons. It is estimated that on average proton therapy will damage 60% less healthy tissues when compared to conventional radiation therapy;
- Proton therapy is a highly preferred radiation treatment option for the elderly and weakened people due to its attractive safety and tolerability profile;
- By targeting the tumour precisely, side effects can be reduced. Patients experience fewer side effects with proton therapy because damage to healthy tissue and surrounding organs can be limited. Studies have shown that proton therapy can significantly decrease the estimated risk of developing secondary malignancies;
- Radiation oncologists have more flexibility in the way they can treat patients. Due to fewer complications and side effects, physicians can deliver higher curative doses of radiation to the tumour. They can also more safely escalate the level of radiation to the tumour, if needed;
- Proton therapy may be used for early cancers that in theory should be operable, but are deemed inoperable due to their location near vital structures or when a patient is not a good candidate for surgery;
- Generally, proton therapy does not require hospitalisation and allows for daily treatment on an outpatient basis. Depending on the specific treatment plan, patients typically receive daily treatments for several weeks. Treatments vary according to tumour type, location, size, and the patient's overall health and diagnosis;
- Because proton therapy is a more accurate method for delivering radiation to the site of a tumour, it is the only radiation treatment available that can treat recurrent tumours that have previously been treated with radiation. Lung cancer dominates this group of patients, although the same logic applies to other groups;
- Proton therapy can be used in conjunction with other cancer treatment modalities;
- Proton therapy is well-proven and has been used around the world for decades. It was pioneered in the United States more than 50 years ago. By 2020, it had been used to treat more than 250,000 patients. Over the last few years, proton therapy has emerged as the most effective treatment method for a variety of cancers. This is supported by a growing body of clinical evidence showing that proton therapy is effective while reducing side- effects for many cancers.



Key indications targeted by proton therapy

Proton therapy is being used to treat tumours in these areas of the body:

1. Brain;
2. Breast;
3. Eye melanomas;
4. Head and neck;
5. Liver;
6. Lung;
7. Oesophagus;
8. Paediatric brain tumours;
9. Prostate;
10. Rectum;
11. Skull base sarcomas.

Protocols are being developed to explore the use of protons in other parts of the body.

Essentially, proton therapy is minimally invasive, provides a better quality of life for cancer survivors, and therefore is the most economic and efficient cancer treatment available today, sparing the cancer survivor repeated post-treatment complications that are common with more traditional options.

Cancers treated with proton therapy

Currently over 120 clinical trials open across a wide variety of disease sites.

120 clinical trials

2	*Melanoma of the eye*	*Brain tumours*	*7*
20	*Base-of-skull tumours*	*Head and neck tumours*	*30*
35	*Lung cancer*	*Breast cancer*	*20*
58	*GI cancer*	*Tumours near the spine*	*12*
40	*Prostate cancer*	*Paediatric cancers*	*15*
4	*GU cancer*	*Sarcoma*	*23*

Most studies are comparative as opposed to randomised studies due to the fact that patient acceptance[1] and insurance coverage are needed. Most studies are coming out of academic centres rather than from free standing community-based proton centres.

[1] i.e. patient willingness to be randomised can be challenging to obtain, given the advantages of protons over photons

Growing body of clinical evidence supporting the effectiveness of proton therapy

Retrospective and prospective studies have shown promising outcomes with proton therapy for children and young adults with cancers, and for sites such as tumours near skull base and spine, CNS tumours, head and neck, oesophageal, hepatocellular, and thoracic cancers.

The past few years have seen a noticeable spurt in prospective and randomised studies, including trials for several sites such as breast, prostate, lung, head and neck, hepatocellular, oesophageal and brain cancers. This is expected to result in a wider scope of clinical application and acceptance amongst clinicians.

PERSPECTIVES OF KEY STAKEHOLDERS ON PROTON THERAPY

Experiencing proton therapy, from the patient's point of view

Proton therapy is delivered in brief outpatient sessions which last on average between 15 to 30 minutes, although the delivery of the proton beam only takes a few minutes. Most of the time spent relates to the patient positioning and adjustments to the equipment settings. During each visit, the patient receives a "fraction" of the entire radiation dose that must be delivered over the entire treatment cycle. Typically, a patient receives 30 fractions over a period of 45 days. Proton therapy treatment is painless. Children under 6-year-old might need to get general anaesthesia to keep them completely still during the treatment.

Several preparation steps are needed before the patient begins proton therapy. The first step is a procedure referred to as "simulation," in which the patient is fitted into a specialised immobilisation device to ensure the person maintains the same exact position for every visit. Sometimes, placing a metallic marker – a fiducial marker – in or around the tumour is needed to help guide the treatment. If necessary, these procedures are usually performed a few days before the simulation. Images of the tumour are also taken, using various techniques such as CT, MRI, PET-CT, or 4D-CT. These images are often "fused" together to give physicians more detailed information about the extent of a tumour and the surrounding organs. The purpose of this simulation is to create a virtual 3-D reconstruction model of the tumour and normal tissues around it as well as determine its exact shape and location. Data gathered by radiation oncologists and physicists are then used to assess the most effective treatment plan.

Following this simulation phase and for each visit, the patient is fitted with the same personal immobilisation device that has been constructed during this first stage. The patient is positioned with the aid of laser lights to within a few millimetres of the needed position to ensure the tumour is properly aligned with the proton beam. In some cases, a CT system will be used to image the target before each treatment. During that process, temporary ink on the patient's body can also be used to help position the patient. This special alignment and imaging process is repeated before each treatment to assure the highest precision.

Once positioning and treatment parameters are verified, the medical team leaves the treatment room to avoid radiation and steps out into the control room; the treatment starts, and the patient is monitored to ensure his/her safety and comfort. Once the prescribed radiation dose has been delivered, the computer shuts off the proton beam and the technologists re-enter the room to assist the patient in removing the immobilisation device.

Post-treatment, the patient is escorted out of the room and returns home until the next daily fraction where the treatment process is repeated until the total planned dose is reached.

Experiencing proton therapy, from the hospital's point of view

Hospitals and cancer centres are facing several urgent imperatives: to strengthen clinical quality; increase the delivery of personalised, patient-centred care; improve the patient experience; and enhance their efficiency and productivity. Consequently, they must introduce innovations in care delivery, often to achieve multiple aims. These innovations include purchasing new technologies to deliver better-quality care, adopting lean and standardised processes to improve quality and optimise productivity, increasing the use of automation to change how the clinical workforce is deployed, and harnessing patient-generated data to personalise treatments.

In response to these strategic imperatives, medical technology providers must adapt themselves and offer the right product offering. This is particularly relevant for the proton therapy industry.

Strategic imperative	What proton therapy brings
Strengthen clinical quality	• Proton therapy offers unique medical advantages; it is the latest advancement in radiation oncology; • Having proton therapy in the service offering is a magnet for hospitals when attracting key talents and patients.
Deliver a more personalised treatment	• Proton therapy is the most targeted radiation-based technique; the opportunity to deliver minibeams and provide a fast rate of deposition of protons onto the target is essential in sculpting radiation doses based on the irregular shape of the tumour and treating moving targets; • Preliminary scientific data suggests a strong synergistic potential for combining proton therapy and developing approaches, such as immunotherapy, making personalised treatment a more tangible and effective reality. This combination – which leverages the unique features of LIGHT, including its high precision and ultra-fast delivery – offers the opportunity to treat cancer types which can not be treated today.
Improve the patient experience	• Proton therapy is painless; • Reducing the number of patients' visits through hypofractionation and installing proton therapy systems at proximity to patients represent a breakthrough in terms of patient experience and comfort.
Enhance efficiency and productivity in a cost-effective way	• Setting up a proton therapy facility is complex and time-consuming; reducing this complexity is essential to limit disruption of the management teams of hospitals as well as accelerate the returns on investment; • Ensuring a smooth integration between the proton therapy department and the other existing functions helps generating synergies and efficiency; • Proton therapy systems must include the latest software developments, including the optimisation of the patient workflow and facility management; • The proton therapy equipment must be affordable, both in terms of upfront and running costs.

PERSPECTIVES OF KEY STAKEHOLDERS ON PROTON THERAPY_Continued

Experiencing proton therapy, from the payer's point of view

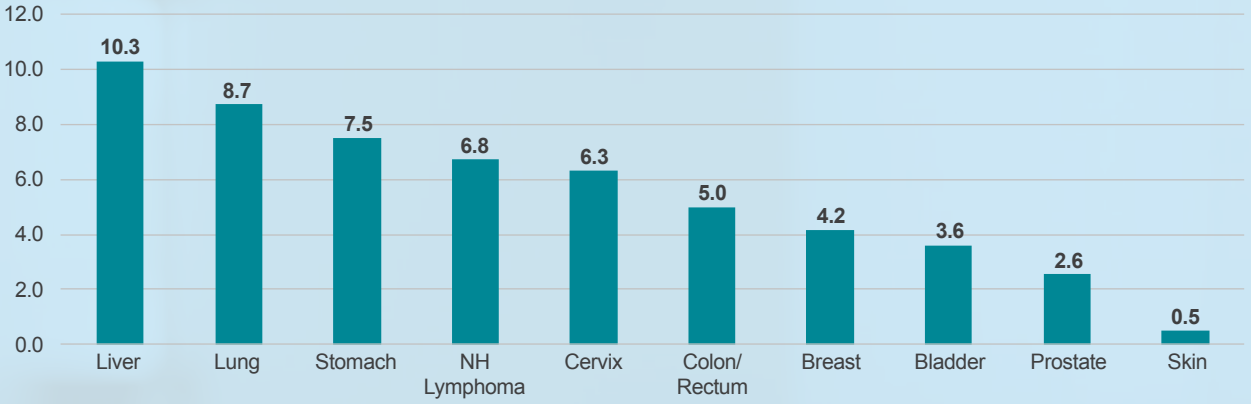
It is widely accepted that proton therapy is more effective than conventional radiation for treating certain cancers, such as paediatric, spine, and head and neck tumours. Proton therapy is more likely to cause less damage to surrounding healthy tissue and organs and its precise delivery can mean fewer complications for patients, especially in the long term; that precision also means protons can be delivered in higher doses requiring fewer treatments than conventional radiation therapy. Therefore, proton therapy is widely reimbursed for the above cancer types across the world.

Yet, particularly in today's healthcare landscape, the cost of any care is a large and growing focus for physicians, hospitals, patients, insurers, and governments. Proton therapy is no exception. It is generally viewed as an expensive radiation technique – around two to three times the cost of Intensity Modulated Radiation Therapy ("IMRT"), the latest technological advancement in delivering X-rays. Building and operating a proton therapy centre with a legacy system is a costly proposition. Against that background, the questions around pricing and payers' acceptance for new indications must be taken in a broad context:

- Radiation therapy remains the most established cancer modality, with up to two-thirds of cancer patients in the US receiving radiation. It is also the most economical cancer therapy. A study published in October 2021 by a team of Penn State College of Medicine researchers showed that drug costs represent the most expensive category for treating cancer patients, about twice as much as surgery or radiation. As an illustration, recent developed agents, such as CAR T-cell therapy, may cost up to almost $500,000 per year per patient and many new immunotherapies have price tags in excess of £100,000 per patient per year;
- Given the benefits of proton therapy, many patients self-refer;
- With high treatment costs and limited capacity, decisions on which adult patients to treat with proton therapy must be based on the relative value compared to the current standard of care. Cost-benefits analyses are the gold-standard method for doing this. Benefits of proton therapy are evident when considering that both proton and standard photon radiation achieve the same goal of damaging tumour cell DNA, but the former is associated with significantly fewer side effects. From a cost perspective, one must consider the treatment tariff, but also the cost for managing the side effects and the financial impact associated with a lower quality of life post-treatment. Significant research activity is ongoing with a growing body of evidence supporting the use of proton therapy and its clear financial benefits when addressing side effects and quality of life. Preliminary data bodes well for the expansion of the reimbursement schedule to new cancer types;
- Briefer courses – with the emergence of hypofractionation (refer to pages 47 and 50-51) – have resulted in greater acceptance and wider reimbursement schemes. Radiation oncologists have embraced this trend, which is expected to continue and further contribute to the increasing value of proton therapy to health systems and payers, particularly as the cost per treatment – and not the cost per fraction – is set to decrease.

Proton therapy as a highly targeted cancer modality is key to reduce side-effects for patients as well as the number of Disability-Adjusted Life-Years and their associated costs

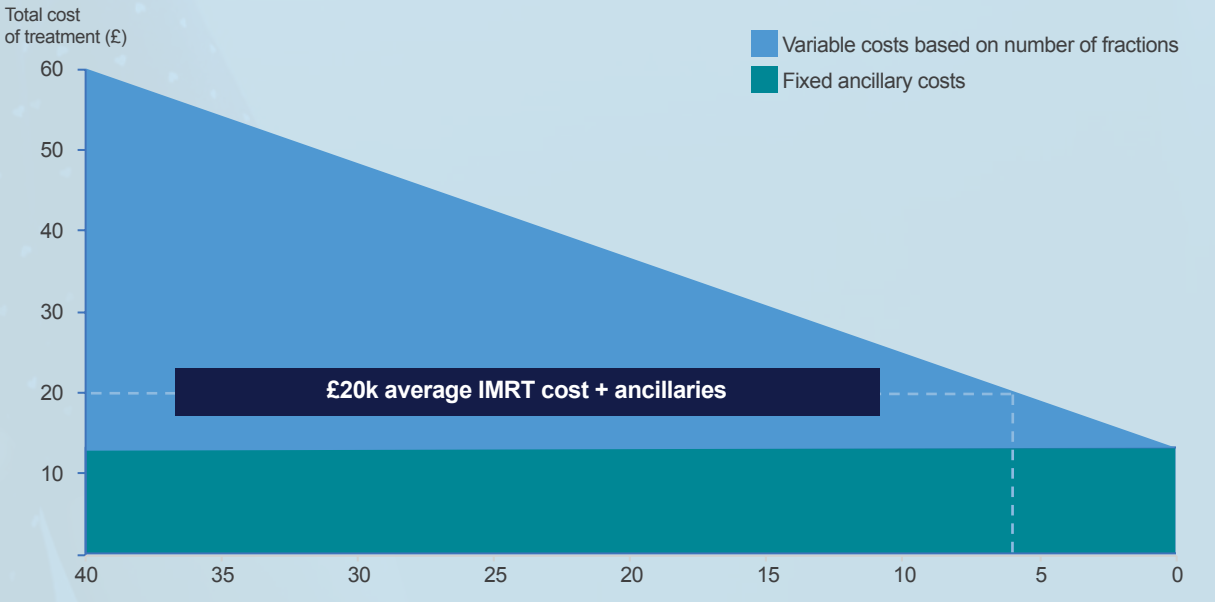
Number of Disability-Adjusted Life-Years ("DALYs") lost per cancer patient in countries with a high Socio-Demographic Index



Source: JAMA Oncology

It costs about $70,000 to avoid one DALY in very high Socio-Demographic Index countries

Changes in treatment protocols like hypofractionation will reduce the cost of proton therapy



Source: Company

As prices to complete proton therapy treatment (at lower fractionation) approach conventional radiation therapy rates, reimbursement policies are expected to become more favourable towards proton therapy

PROTON THERAPY LOWERS RISK OF SIDE EFFECTS

The body of clinical evidence is rapidly growing, also caused by the increasing number of facilities and therefore greater capacity to perform clinical studies.

JAMA Network

Comparative Effectiveness of Proton vs Photon Therapy as Part of Concurrent Chemoradiotherapy for Locally Advanced Cancer

In this comparative effectiveness study of 1483 adults with nonmetastatic cancer and treated with curative intent, proton therapy was associated with a two-thirds reduction in adverse events associated with unplanned hospitalizations, with no difference in disease-free or overall survival.

ELSEVIER

Oral Oncology

Volume 110,
November 2020, 104879

Past, present and future of proton therapy for head and neck cancer

Proton therapy in head and neck cancer has a unique advantage given the complex anatomy and proximity of targets to vital organs.

Cancer Medicine

Volume11, Issue6
March 2022 Pages 1502-1510

The comparison of acute toxicities associated with craniospinal irradiation between photon beam therapy and proton beam therapy in children with brain tumors

(…) In conclusion, in the present study, although the P-CSI group received higher CSI doses than the X-CSI group, the incidence rates of more than grade 2 nausea and vomiting in the P-CSI group were lower than in the X-CSI group. The present study suggests that P-CSI reduces the incidence of acute gastrointestinal toxicities associated with irradiation.

cancers MDPI

March 2022 Cancers
14(7):1653

Acute Hematological Toxicity during Cranio-Spinal Proton Therapy in Pediatric Brain Embryonal Tumors

(…) In our study, we demonstrated that the proton technique was proven to be safe in CSI, even in brain cancer patients with significant baseline hematologic toxicity due to previous chemotherapy. Moreover, patients did not require supportive therapy with transfusions or HGFs, and there were no delays in treatment. Finally, it saves patients additional therapies and time spent as inpatients, which can also be very important in improving the patient's quality of life during medical care.

ELSEVIER

Medical Dosimetry

Available online
21 December 2021

Intensity Modulated Proton Therapy Better Spares Non-Adjacent Organs and Reduces the Risk of Secondary Malignant Neoplasms in the Treatment of Sinonasal Cancers

(…) For the treatment of SC, IMPT spares OARs that are not immediately adjacent to the treatment volume and reduces the risk of SMNs when compared to VMAT (…)

ScienceDaily

December 26, 2019
University of Pennsylvania School of Medicine

Proton therapy lowers risk of side effects in cancer compared to traditional radiation

Study found protons led to two-thirds reduction in unplanned hospitalizations

Proton therapy leads to significantly lower risk of side effects severe enough to lead to unplanned hospitalizations for cancer patients when compared with traditional radiation

Medscape

Nick Mulcahy
July 28, 2020

In a First, Proton Therapy Bests Radiotherapy in an RCT

Less Toxicity in Esophageal Cancer

In a first, proton beam therapy has demonstrated significantly reduced toxicity when compared with conventional radiotherapy in a randomized controlled trial (RCT) in patients with esophageal cancer.

ELSEVIER

International Journal of Radiation Oncology*Biology*Physics

Volume 111, Issue 3, Supplement, 1 November 2021, Pages e170-e171

Second Cancer Risk in Childhood Cancer Survivors Treated with Intensity-Modulated Radiation Therapy (IMRT): An Updated Analysis of More Than 10 Years of Follow-Up

With a median follow-up of 11 years, there was an increased Cumulative Incidence of solid second malignant neoplasms (SMNs) after IMRT in childhood cancer survivors. SMNs developed both in and out of the high dose region. These data serve as a foundation for comparison with other modalities of radiation treatment, namely proton therapy.

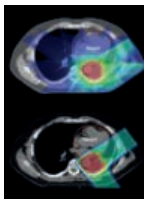
International Journal of Particle Therapy

Issues
Volume 8, Issue 2
Fall 2021

Consensus Statement on Proton Therapy for Prostate Cancer

Several prospective and retrospective studies have been published documenting the safety and efficacy of proton therapy in the management of prostate cancer and some long-term follow-up data are available and are accumulating. Consequently, proton therapy should not be considered experimental in the management of prostate cancer.

Washington University School of Medicine in St. Louis



Proton therapy for cancer lowers risk of side effects

Proton therapy was associated with a substantial reduction in the rates of severe acute side effects — those that cause unplanned hospitalizations or trips to the emergency room — compared with conventional photon, or X-ray, radiation for patients treated with concurrent radiation and chemotherapy […] While there have been other studies suggesting that proton therapy may have fewer side effects, we were somewhat surprised by the large magnitude of the benefit.

zaobao 质子束疗法 使癌症放疗更安全

Proton beam therapy makes cancer radiotherapy safer

(…) Dr. Li Jinxiang said: "Children's tumors can benefit from proton beam therapy because it can significantly reduce acute and long-term side effects, such as abnormal growth, neurological complications, lower IQ, heart, lung and intestinal side effects, and second malignant tumors." In addition, it also includes central nervous system tumors, sinus tumors, skull base and sacral chordomas (sacral chordomas) and so on. Re-treatment of tumors that have undergone radiotherapy can also benefit from proton beam therapy. Dr. Li pointed out that clinical research and trials on tumors in the head and neck, esophagus, lungs, breasts, liver, pancreas, and prostate are still ongoing. The current challenge is how to obtain mature data to make objective comparisons between proton beam therapy and modern advanced radiotherapy techniques, such as intensity-modulated radiation therapy.

ELSEVIER

International Journal of Radiation Oncology*Biology*Physics

Volume 111, Issue 3, Supplement, 1 November 2021, Pages e371-e372

Acute Toxicity in Patients Treated With Proton vs. Photon Chemoradiotherapy for Locally Advanced Head and Neck Cancer

(…) Concurrent chemoradiotherapy with proton therapy for head and neck cancers was associated with lower dose to nontarget structures and significantly reduced acute grade ≥3 toxicity and acute grade 2 oral cavity toxicity compared to photon therapy (…)

OUR COMMITMENT TO CHILDREN

Cancer in children and young people is thankfully much rarer than cancer in adults.

Survival is higher too: more than eight in ten children and young people in the UK, aged 0 to 24, survive their cancer for ten years or more, compared to one in two adults in England and Wales aged 15+.

However, cancer remains the principal cause of death by disease in children beyond the age of one. Without additional investment in childhood cancer care, over 11 million children aged 0 to 14 are expected to die from cancer over the next 30 years worldwide. The vast majority of those – more than 9 million deaths (84%) – will be in low-income and lower-middle-income countries. In 2020, over 15,500 children and adolescents in the European Union were diagnosed with cancer, with over 2,000 young patients losing their lives to it.

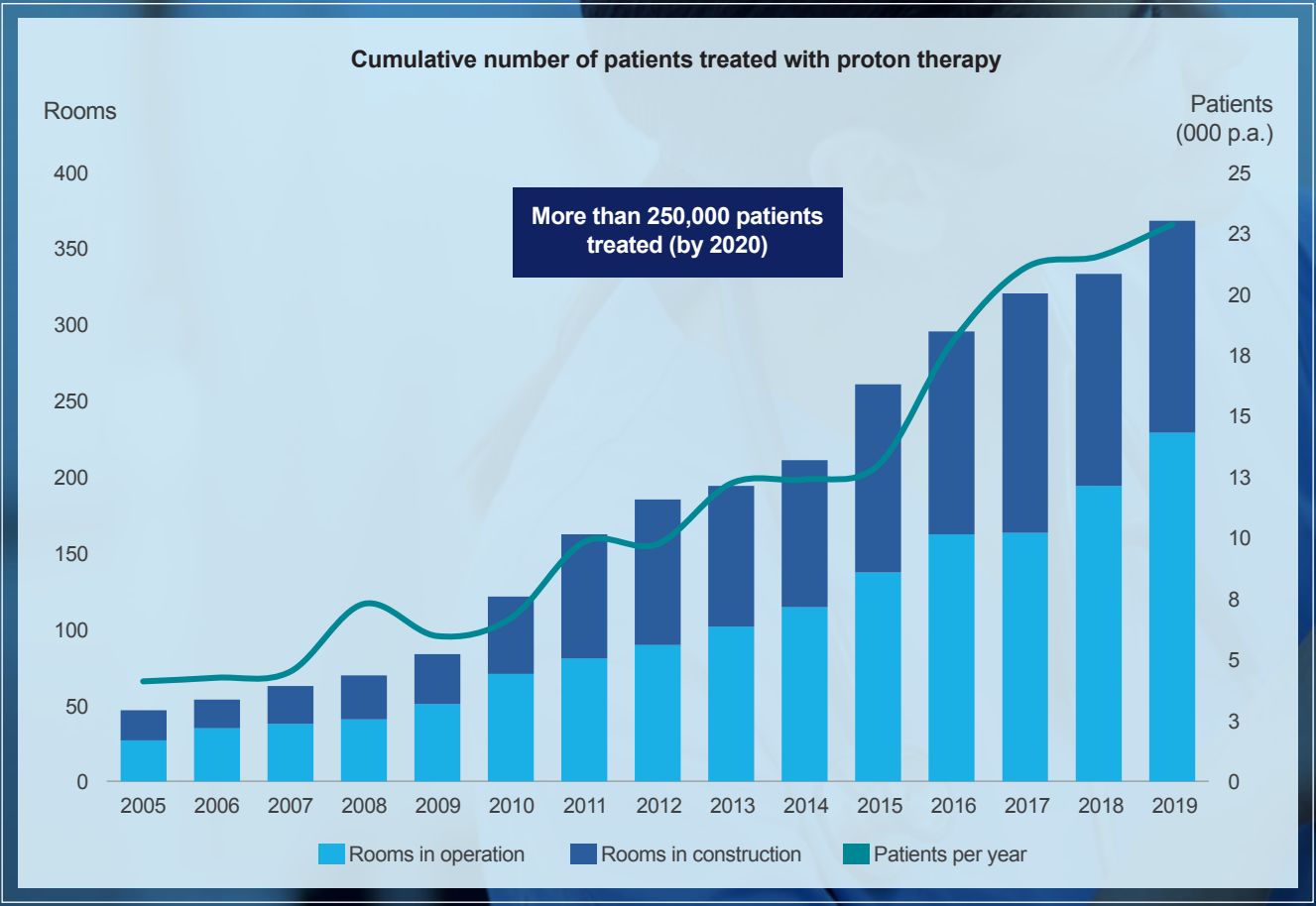
Important differences exist between childhood and adult cancers in terms of the type of cancer, how far it spreads, and how it is treated. For example, by the time they are diagnosed, 80% of paediatric cancers have already spread to other parts of the body, compared to about 20% of adult cancers.

Up to 30% of children who survive experience serious, long-term side effects from their treatment. Proton therapy is ideally suited for paediatric cancers.

At Advanced Oncotherapy, we feel it is our responsibility to support children. We are committed to do so by democratising access to proton therapy.

THE MARKET UPTAKE AND THE NEED

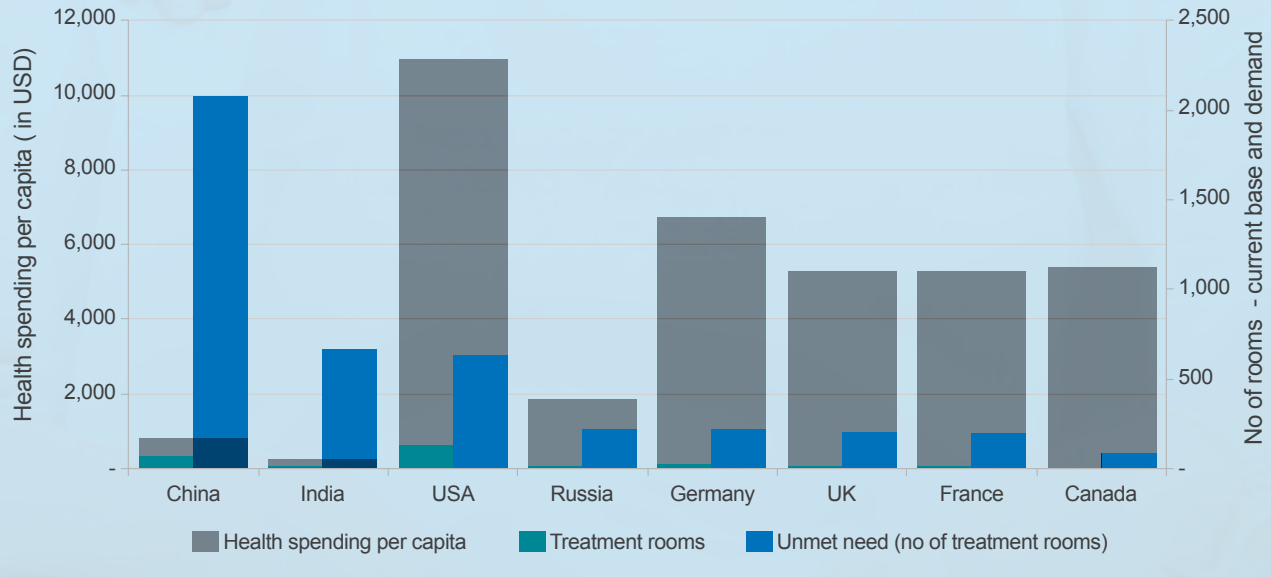
Originally, most patient treatments with high energy protons have been carried out at large-scale research facilities such as the Harvard Cyclotron Lab or Paul Scherrer Institute, by installing an extra treatment room besides several experimental target stations used for fundamental research in nuclear physics. In the 1990s, first stand-alone centres have been built and dedicated to treat cancer patients with proton therapy. One of the first was the cancer centre in Loma Linda in the US, a centre set-up by Optivus with the installation and servicing activities led by Ed Lee, the COO of Advanced Oncotherapy.



The availability of and the demand for proton therapy is growing exponentially. However, in absolute terms, the availability is still very low. There are currently only 114 operational proton therapy facilities in the world, addressing less than 5% of clinical demand. Only less than 1% of all radiation therapy patients receive proton therapy, even though between 15% and 50% would benefit from it. The reason for this discrepancy is the high cost and the large size of the equipment, which does not fit in conventional treatment spaces. The primary factor contributing to this is the use of legacy circular proton accelerators which bring significant challenges and constraints in terms of cost and size.

Since then and with an increasing number of companies offering turn-key solutions for proton therapy systems, the number of proton therapy centres has increased rapidly since the beginning of the 21st century, but much more remains to be done.

Indicative estimate of proton therapy treatment rooms needed to treat 20% of radio-sensitive tumours



Source: https://www.livepopulation.com/, DIRAC, PTCOG

OUR LIGHT SYSTEM

We have developed the LIGHT system to address the key limitations of conventional and circular proton therapy machines; it has been designed to deliver superior medical outcome whilst providing a proton treatment environment at a fraction of the cost, footprint, and operational complexity of legacy systems. We believe this enables the deployment of proton therapy into a broader variety of cancer care facilities, creating greater access for more patients.

The LIGHT system has been designed to enable delivering most of the treatments in a comfortable seated patient position. The comfortable patient position ensures better patient immobilisation, the critical factor in delivering radiation treatments both safely and effectively. It also allows treating patients with impaired breathing who cannot lie down due to asthmatic attacks. In addition to ergonomic benefits, patient's accommodation before treatment in a seated position stabilises the motion of internal organs. The seated positioning minimises the motion magnitude by a factor of 4 and shifts the heart toward the diaphragm. Such anatomical and physiological characteristics ensure effective and safe irradiation of lung, breast, chest wall, and upper gastrointestinal tissues sparing the damage of the critical healthy organs like heart. The treatment setup also guarantees better treatment outcomes in treating tumours in liver, pancreas, kidney, as well as head and neck and brain.

The heart of our LIGHT system is our proprietary linear proton accelerator that integrates with an in-room sliding Computerised Tomography (CT) scanner, a robotic positioning system, and the patient support system, real time X-rays modules, the room control system, and a full suite of medical software.

The LIGHT accelerator

The LIGHT accelerator accelerates protons to a high speed by subjecting them to a series of oscillating electric potentials along the linear beam line. What makes LIGHT as a linear proton accelerator preferable to circular accelerators is that the energies of the accelerated protons can be adjusted rapidly, i.e., in milliseconds, and without loss of beam intensity. The beam energy determines how deeply the protons penetrate tissue, so this ultra-fast tunability is useful for adjusting the beam position within the body as the patient breathes or to precisely hit different spots on a tumour.

The in-room sliding CT scanner

The LIGHT system includes a big Bore CT scanner that is integrated into a uniquely designed sliding platform. The setup enables scanning a patient in the treatment position while keeping the patient stationary. The scanner has 85 cm opening size suitable for scanning, and then treating, oncology patients. The scanner is installed with the special software capabilities for low dose scanning. The mode enables generation of high-quality images while exposing the patients to only 20% of the standard radiation level. The scanning supports both helical and axial modes with fast image acquisition. The images can be used for treatment planning, for positioning, and for adaptive therapy. Other key features include 4D CT capabilities; low dose image acquisition; up to 204 kg patient load; and additional pendant operating panel.

Treatment planning at a correct phase of the breathing cycle is crucial for delivering the treatment dose accurately. Having the 4D CT integrated in the treatment room allows verifying the breathing cycle pattern prior to each treatment event, particularly for treatment of breast, lung, and upper gastrointestinal tumours. The 4D capability is possible with helical and axial scanning modes. To accurately "position" the beam on the target, the belt-based approach is used. Synchronisation between the belt motion and multiple CT dataset enables acquisition of ten separate scans defining the most appropriate target for treatment.

The robotic positioning system and the patient support system

The robotic arm is the robotic patient positioning system, with 6 degrees of freedom. The base of the robot is placed on the floor. The reach of the distal arm enables the positioning of the patient in both seated and laying

positions at imaging setup, and at treatment isocentre.

The real time X-rays module

In order to visualise the patient anatomy in real time, the set of orthogonal X-rays sources and detectors are integrated into the system. The system is static and enables to image the patient at treatment isocentre during the actual treatment. The system can image the patient in both seated and laying positions. The imaging information serves for precise patient positioning with 0.5 mm accuracy. The imaging is based on registration of digitally reconstructed radiographs generated from treatment planning CT and actual X-ray images received prior to or during the treatment.

The room control system

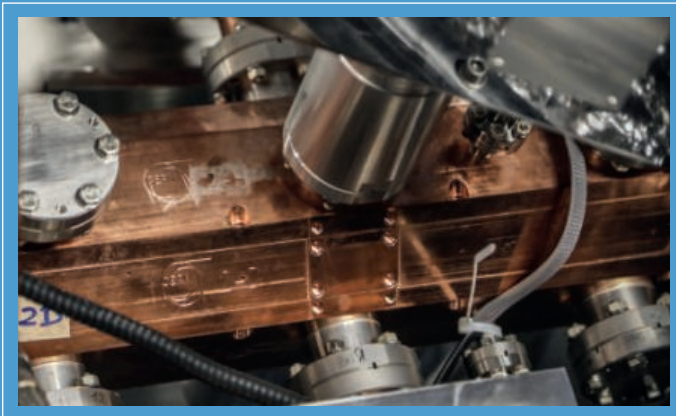
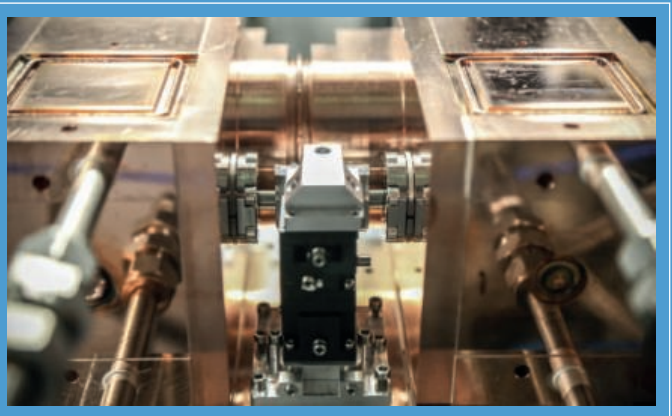
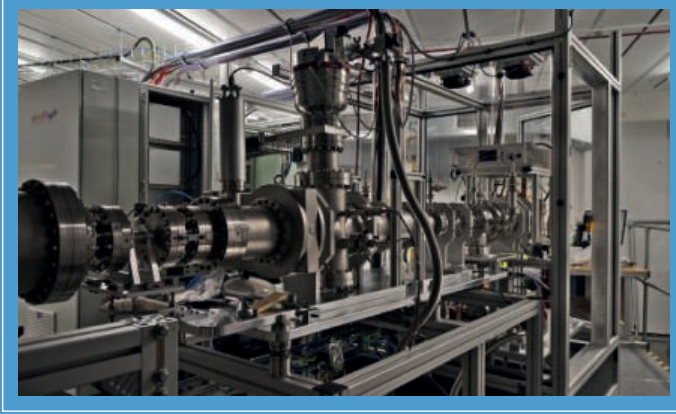
The room control system is responsible for delivery and monitoring of the LIGHT particle beam: The LIGHT Room Control System is the system that controls and monitors the delivery of proton irradiation to the tumour, and provides a user interface for the radiographer to start, stop, or interrupt the beam delivery. It consists of sub-systems, including the LIGHT Enhanced Nozzle System, traditionally referred to as the nozzle, that controls and monitors irradiation; and the Light Redundant Charge Recorder, which provides the direct hardware interface to the radiographer.

The computing medical software suite

Proton therapy systems include a wide range of software, ranging from the preparation of the full treatment plan, daily proton delivery to patient workflow and recording of patient data. To respond to one of the key challenges currently faced by end users – namely the lack of an integrated control software suite – we have worked with Raysearch and successfully tested a seamless software suite customised for LIGHT. This provides users with a single interface for patient preparation, treatment and follow-up processes, whilst limiting potential risks and facilitating a better end user experience for clinicians and healthcare workers.

The major components of the medical software package include:

- Treatment session manager (TSM). The TSM software developed by Raysearch, acts as the control system to connect and manage various sub-systems of the LIGHT system. It allows the management of the daily proton treatment for patient delivery.
- Treatment planning system (TPS). The TPS software provides superior functionality for treatment planning, encompassing patient positioning through to treatment solutions. The software is well established and familiar to oncologists.
- Oncology information system (OIS). The OIS is the software, developed in partnership with Raysearch, which integrates with the TPS to offer managed workflows and to enable patient treatment to be modified daily.


OUR LIGHT SYSTEM_Continued

The Medical Treatment Room (MTR) required for the clinical treatment of patients with the LIGHT system has been completed at the Company's Daresbury integration site. Subsequently, the necessary permissions have been received to use the MTR with ionising radiation.

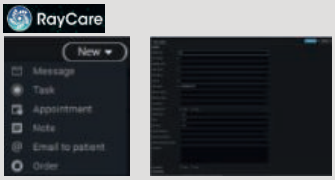
Proton therapy requires high accuracy placement (positioning) of the patient, typically with 1 mm tolerance or less. As such, the Company has developed and installed in the MTR a bespoke LIGHT Patient Positioning System (PPS) to provide the required accuracy in a compact and efficient system. The PPS comprises of a robotic patient positioner for aligning patients in the upright position in a treatment chair, a CT imaging subsystem, an X-Ray imaging subsystem, and computing software and hardware which are important components as proton therapy requires highly accurate placement, imaging, and image processing of patients.

LIGHT Medical Technical System

The LIGHT Proton Therapy System (PTS) is a comprehensive package including all hardware and software needed for delivering proton beam treatment to patients. The LIGHT PTS is a "Product Family," incorporating medical devices collaboratively developed by AVO-ADAM and its main suppliers. LIGHT's unique proton therapy solution comprises a compact, modular Beam Production System (BPS) for proton acceleration up to 230 MeV; the Medical Technical System (MTS), encompassing all the clinical components to facilitate treatment of seated patients, without need for a large, costly gantry; and the Computing Infrastructure, which coordinates all components of the PTS.

1) Patient Intake

- Administrative details (including patient ID and demographics, insurance, etc) are collected and recorded in RayCare, the **LIGHT Oncology Information System** (OIS)
- Appointment with Radiation Oncologist scheduled using the OIS



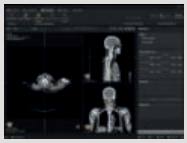
2) Medical Appointment

- Clinical details discussed and recorded in the OIS
- Imaging appointment scheduled using the OIS
- Treatment prescription defined and recorded in the OIS

3) Imaging Appointment

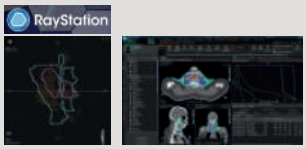
RayCommand

- Coordinated by RayCommand, the **LIGHT Treatment Control System** (TCS)
- Patient immobilised in seated position on the **LIGHT Patient Positioning System** (PPS)
- Patient moved to imaging position
- CT images acquired
- Data sent to and stored in the OIS



4) Treatment Planning

- Planning CT images analysed in RayStation, the **LIGHT Treatment Planning System** (TPS)
- Target volumes and organs at risk delineated
- Treatment geometry designed
- Dose distribution optimised
- Plan approved for treatment

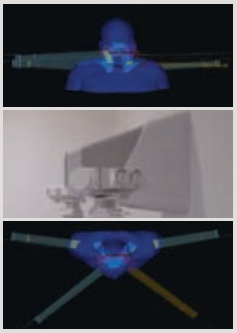


5) Patient-specific QA

- Treatment plan verified using **LIGHT System of Dosimetry** (SD) equipment and/or using mathematical simulation
- Results analysed and treatment sessions approved in the OIS

6) Treatment Delivery

- Patient immobilised in same position on PPS as defined in planning CT imaging session
- Image guidance steps for accurate patient positioning using PPS and TCS
- Proton beam delivered via the **LIGHT Enhanced Nozzle System** (ENS)
- The **LIGHT Patient Observation & Communication System** (POC) provides a level of safety and comfort during treatment
- The **LIGHT Medical Interlock Device** (MID) ensures safe and accurate beam delivery



The LIGHT Clinical Workflow starts with patient admission, intake appointments, and creating images for treatment planning. The treatment plan is verified, approved, and delivered to the patient, typically over multiple sessions. The MTS is responsible for planning, execution, and recording of the patient treatments with the LIGHT System. It also serves as a patient database and appointment scheduler.

OUR LIGHT SYSTEM_Continued

LIGHT Patient Positioning System

ADVANCED ONCOTHERAPY

The LIGHT Patient Positioning System (PPS) is a medical device used for volumetric imaging in the upright position for treatment planning, and the safe and accurate positioning of the patient during treatment delivery. Components of the PPS include the CT and X-ray imaging systems, as well as a Patient Positioning Device (PPD), comprised of a chair mounted on a robotic arm. These components are controlled by software, which communicates with the Treatment Control System (TCS). Use of the LIGHT PPS, along with a fixed-beam delivery system, is both space and cost-effective, facilitating instalment with less infrastructure than conventional proton therapy systems.

Fixed-beam treatment room, showing components of the LIGHT PPS.

The high cost for gantry installations is a major limitation to the expansion of proton therapy facilities. An alternative technical option is provided by fixed-beam treatment rooms (see Figure 1), where the patient is rotated and translated in space by a robotic arm to enable beam incidence from various angles.

Lasers in the Treatment Room are used for initial patient setup.

The LIGHT Patient Positioning System (PPS) includes a chair mounted on a robotic arm, and a CT scanner mounted on a vertical sliding platform (Figure 2a), which allow for imaging in the upright position (acquiring the CT for treatment planning or for image guidance during treatment delivery).

The robotic arm can then move the patient to the treatment position, where orthogonal images of the patient can be acquired by the X-ray system (Figure 2b) for comparison with images digitally generated from the treatment planning CT image, allowing for position adjustments to be made (if required) prior to treatment delivery.

A

B

Imaging components of the PPS
A) Vertically mounted CT scanner
B) Orthogonal X-ray system; robotic-arm/chair in position

Clinical Capabilities of the PPS:

- Set up patient
- Move to imaging position
- Acquire images
- Image registration
- Move to treatment position
- Move to beam position
- Verify and correct position
- Treatment delivery
- Unload patient
- Imaging for treatment planning
- Clinical QA
- Clinical system commissioning

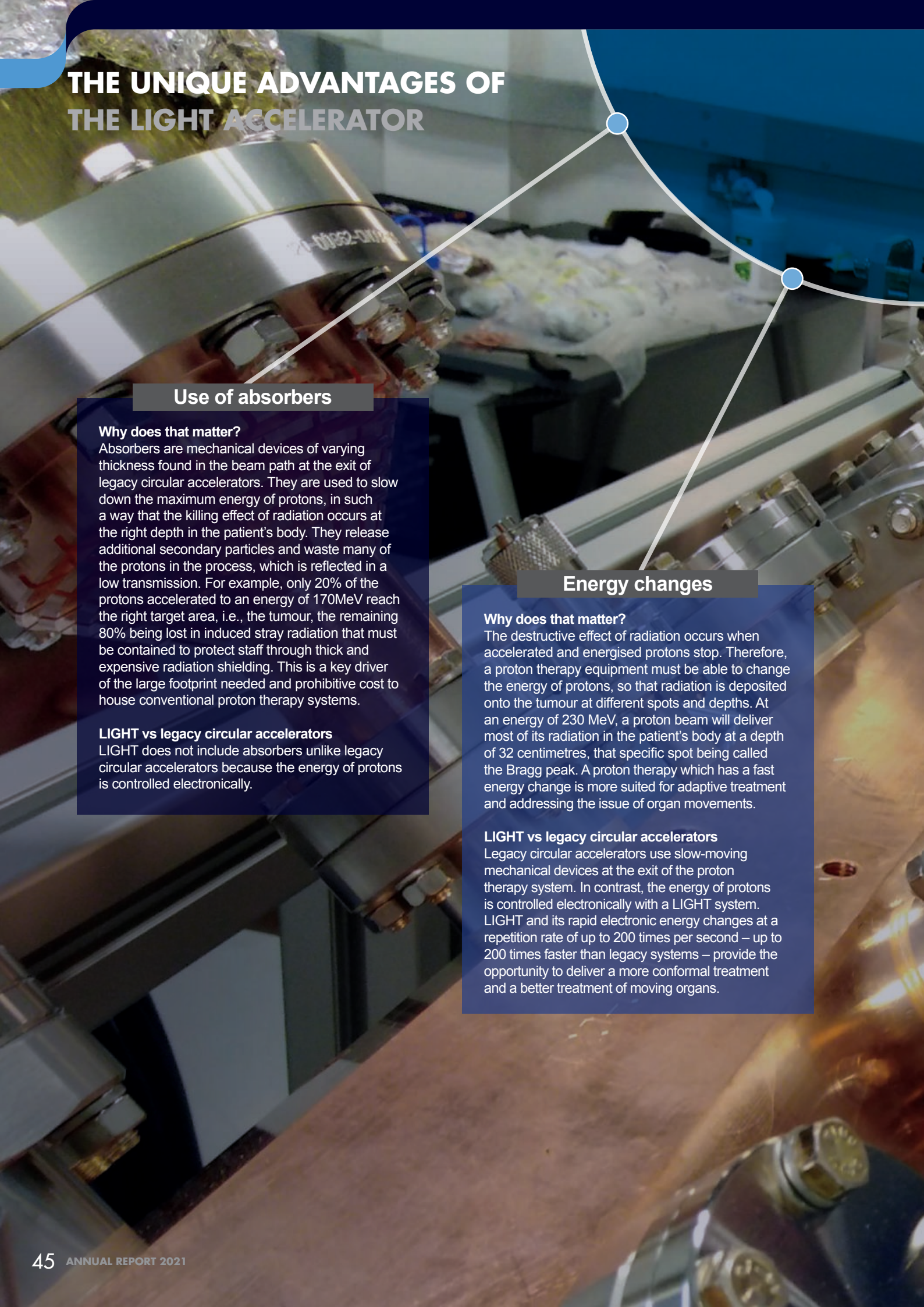
Patient imaging in the upright position.

Roles of the PPS:

- Patient Positioning Device (PPD)
  - moves patient to required positions
- Patient Positioning Acquisition System (PPAS)
  - acquires data on patient position prior to beam delivery
- Patient Position Registration System (PPRS)
  - registers acquired data, (i.e., actual patient position) against reference data containing information about the intended patient position, prior to beam delivery
- Patient Position Definition System (PPDS)
  - determines the correction needed (if any) to reach the intended treatment position

The LIGHT PPS allows patient imaging and treatment in the upright position (Figure 3) within a fixed-beam treatment room. Accuracy and reproducibility of the PPS devices are very important in their design and development. The compact nature of the LIGHT PPS reduces cost and space requirements for new Proton Therapy Facilities.

THE UNIQUE ADVANTAGES OF THE LIGHT ACCELERATOR



Use of absorbers

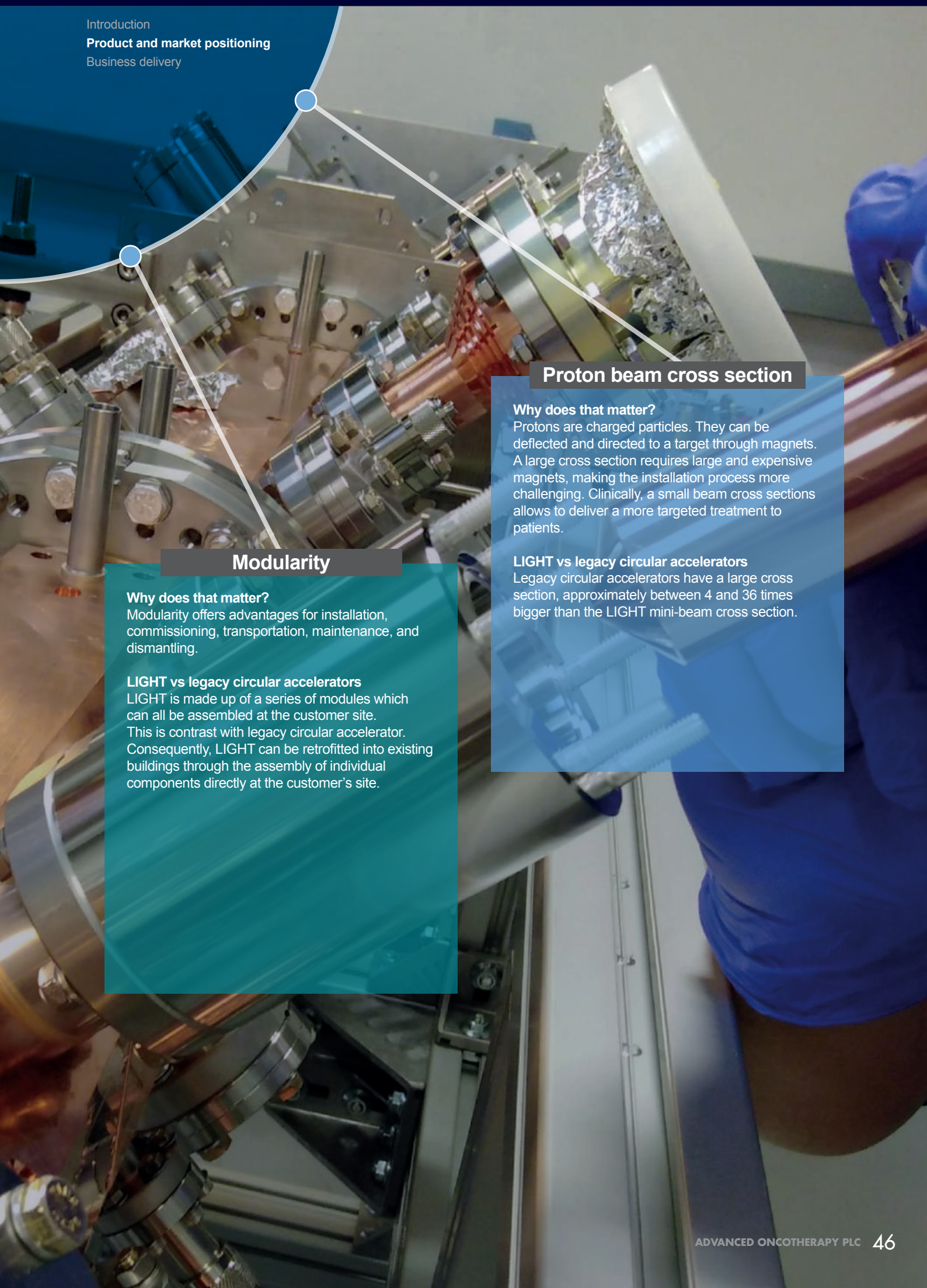
Why does that matter?
Absorbers are mechanical devices of varying thickness found in the beam path at the exit of legacy circular accelerators. They are used to slow down the maximum energy of protons, in such a way that the killing effect of radiation occurs at the right depth in the patient's body. They release additional secondary particles and waste many of the protons in the process, which is reflected in a low transmission. For example, only 20% of the protons accelerated to an energy of 170MeV reach the right target area, i.e., the tumour, the remaining 80% being lost in induced stray radiation that must be contained to protect staff through thick and expensive radiation shielding. This is a key driver of the large footprint needed and prohibitive cost to house conventional proton therapy systems.

LIGHT vs legacy circular accelerators
LIGHT does not include absorbers unlike legacy circular accelerators because the energy of protons is controlled electronically.

Energy changes

Why does that matter?
The destructive effect of radiation occurs when accelerated and energised protons stop. Therefore, a proton therapy equipment must be able to change the energy of protons, so that radiation is deposited onto the tumour at different spots and depths. At an energy of 230 MeV, a proton beam will deliver most of its radiation in the patient's body at a depth of 32 centimetres, that specific spot being called the Bragg peak. A proton therapy which has a fast energy change is more suited for adaptive treatment and addressing the issue of organ movements.

LIGHT vs legacy circular accelerators
Legacy circular accelerators use slow-moving mechanical devices at the exit of the proton therapy system. In contrast, the energy of protons is controlled electronically with a LIGHT system. LIGHT and its rapid electronic energy changes at a repetition rate of up to 200 times per second – up to 200 times faster than legacy systems – provide the opportunity to deliver a more conformal treatment and a better treatment of moving organs.



Modularity

Why does that matter?
Modularity offers advantages for installation, commissioning, transportation, maintenance, and dismantling.

LIGHT vs legacy circular accelerators
LIGHT is made up of a series of modules which can all be assembled at the customer site.
This is contrast with legacy circular accelerator. Consequently, LIGHT can be retrofitted into existing buildings through the assembly of individual components directly at the customer's site.

Proton beam cross section

Why does that matter?
Protons are charged particles. They can be deflected and directed to a target through magnets. A large cross section requires large and expensive magnets, making the installation process more challenging. Clinically, a small beam cross sections allows to deliver a more targeted treatment to patients.

LIGHT vs legacy circular accelerators
Legacy circular accelerators have a large cross section, approximately between 4 and 36 times bigger than the LIGHT mini-beam cross section.

THE UNIQUE MEDICAL ADVANTAGES OF THE LIGHT SYSTEM

The medical advantages of the LIGHT System: from a uniquely designed accelerator to a state-of-the-art treatment

THE ONLY SYSTEM INTEGRATED WITH AN IMAGING SYSTEM

The LIGHT system is fully integrated with a diagnostic grade, fan beam, wide-bore CT scanner in the treatment room. The seamless integration between the treatment planning, treatment control, and CT scanner provides unparalleled versatility for on the fly adaptive proton therapy, the next step in personalised medicine.

THE CHANGE OF ENERGY

Due to fast energy changes, LIGHT rescans much quicker than any other proton therapy system. This rapid energy change means LIGHT is ideally suited for volumetric repainting of tumours, conformity of the radiation dose, and tracking moving tumours.

THE SIZE OF THE BEAM

The LIGHT system can have a significantly smaller proton beam than legacy systems. Fundamentally, IMPT (intensity-modulated proton beam therapy) systems depend on conformity's spot size (emittance). Having the smallest beam size, minibeams provides the utmost conformity, expected to improve outcomes for many indications.

THE CONSTANT SPOT SIZE

The LIGHT system features a constant, small spot size from 150-230 MeV. The spot size increases with decreasing energy for all other systems. The LIGHT constant spot size has been shown to improve treatment plan quality (conformity) in comparison to legacy systems.

THE OPPORTUNITY TO DELIVER FLASH TREATMENT

LIGHT is the ideal system to deliver FLASH because the LIGHT system proton output does not vary with energy. Hence, instead of "shooting thru" the patient as with legacy FLASH deliveries, the FLASH LIGHT treatments resemble current proton therapy treatments, except they go much faster. Unlike other proton systems, this allows both conformal and FLASH in the same treatment with the LIGHT system.

UPRIGHT TREATMENTS

LIGHT's capacity for upright seated treatment can improve cost, quality, and patient comfort. Lung volume is greater (averaging 27%) in the upright position, resulting in less tissue density within the radiation field and potentially less irradiated normal tissue mass. Upright positioning can be more reproducible for breast patients and pelvic patients. It is also expected to be more comfortable for head and neck patients, many of whom have difficulty swallowing. The accumulation of saliva can make breathing difficult in the supine position. Because of gravity, upright positioning is more comfortable for the head and neck patient.

OUR INNOVATION ROADMAP

Creating innovative concepts to meet the needs of patients is a prerequisite to strengthening our market position and a premise to sustaining our competitive advantages whilst leveraging our CERN roots. We therefore remain highly committed to maintaining a full and innovative pipeline of new ideas, bringing new groundbreaking LIGHT technologies to life, and investing into sustainable enablers. True to the vision of creative collaboration, our innovation approach is widely based on our unique mindset.

Meeting the needs and expectations of patients and customers

The modern innovation landscape extends beyond product development and increasingly requires innovation teams to consider the development of experiences and services, as well as the provision of greater levels of transparency and direct integration of our current and prospective customers through co-creation.

In partnership with our commercial, medical and engineering teams, trends, insights and foresight are shared on an ongoing basis through our innovation panel. This provides the starting point to build concepts of relevance.

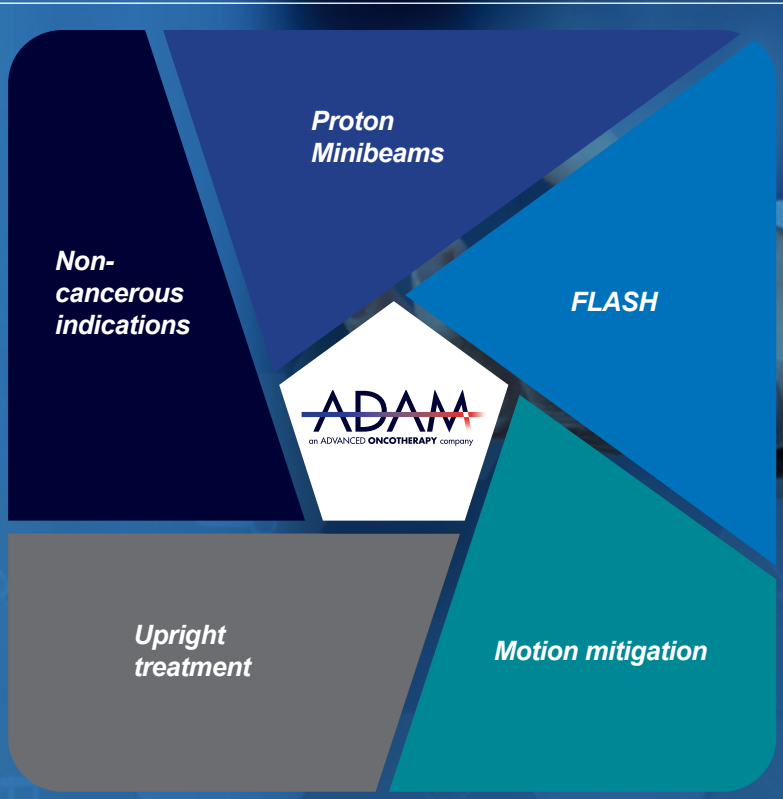
At Advanced Oncotherapy, we have set-up a dedicated team tasked to develop a strong portfolio of innovation capabilities and provide a platform for meaningful patient-centric concept development. Projects are incubated within our Company and aligned to the strategic imperative of creating long-term value, ensuring a robust and impactful innovation pipeline.

Innovation approach based on a unique mindset

Our approach to innovation reflects our mindset, where we seek to build value together with our partners as well as national and international governments and research organisations. In addition to opening up our doors to valuable feedback, we also get inspired by the input from knowledgeable partners, including our suppliers and customers.

Commercialisation of innovations

We believe developing industry-leading technologies is only one aspect of being an innovation leader. Equally important is the successful commercialisation of those innovative concepts.



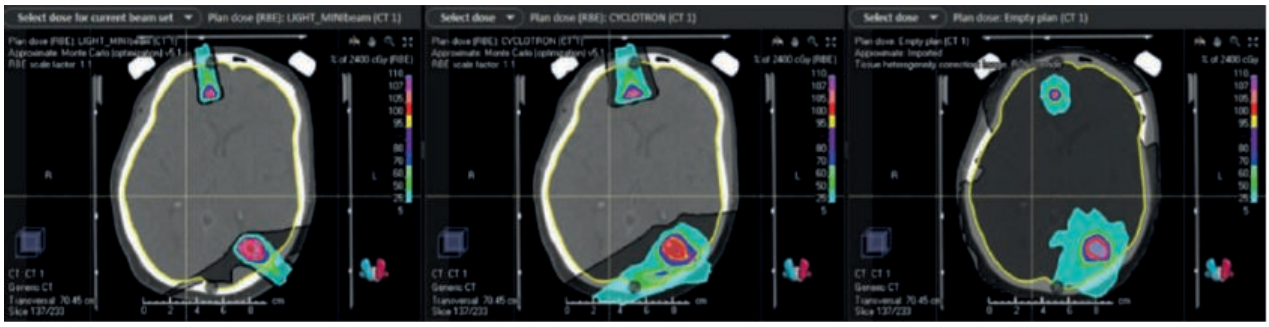
The democratisation of proton therapy is a way to accelerate the acceptance of proton therapy towards new cancer types.

Further development has progressed this year with applications of the LIGHT system. Our LIGHT application developments are primarily based on the disruptive LIGHT system generated proton beam properties: beam size and 3D spot position delivery speed. Secondarily, our developments focus on revolutionary imaging and treatment in the upright (seated) position. We are also exploring new applications for the LIGHT system in a non-cancerous medical treatment context.

Proton Minibeams

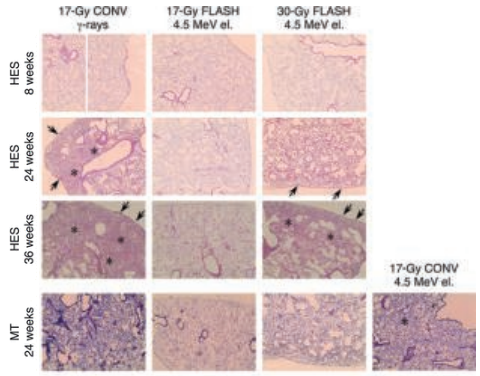
The LIGHT system produces a class-leading proton beam quality designed to deliver spot sizes less than one mm Gaussian sigma, called proton minibeams ("MB"), which are much smaller than beam sizes produced by legacy circular accelerators. This year, together with our research partner, the Cleveland Clinic, we investigated the potential clinical advantages of proton minibeams compared to photon and cyclotron beams ("CB"). We have reached more than 60 patients with brain, head and neck, and lung cancers. The results are presented at scientific conferences such as the American Society for Radiation Oncology ("ASTRO") and the American Association of Physicists in Medicine ("AAPM"). Below is a resulting comparison from our work "Can proton linear accelerator beams and minibeams achieve superior plan quality over cyclotron generated proton beams and photons in treating multiple brain metastases?"

LIGHT MB **Cyclotron** **GammaKnife**



Comparison of LIGHT minibeams, cyclotron beam, and photon GammaKnife treatment quality for patients with multiple brain metastases. The colour wash represents the desired radiation dose to the target and the undesirable amount to normal brain tissue.

Compared to photons and CB, the LIGHT MB provides the greatest conformity to the target whilst maximally sparging normal brain tissue.



Source: Favaudon et al. 2014
Note: From the pioneering work, it was demonstrated that high dose rate doses (17-Gy FLASH 4.5 MeV) may have a strong tissue sparing effect, compare the 17-Gy FLASH 4.5MeV column with the unirradiated Control, they appear the same. This may also permit dose escalation, improving the therapeutic index (Figure 1). Compare the FLASH dose of 30-Gy, at about 2x with the 17-Gy non-FLASH (CONVentional) column, the FLASH irradiation still looks less damaging.

FLASH

Recent in vivo studies in mice[1] demonstrated that electrons delivered to cancerous tissues at high dose rates within 0.5 second (FLASH), inhibit tumour growth equally as in conventional therapy, but with significantly more sparing of surrounding healthy tissues. Normal tissue sparing with FLASH enables a dose increase without additional complications, widening the therapeutic window and virtually reducing the number of fractions to one single fraction/visit.

Hence, FLASH radiotherapy, where the entire patient treatment is administered in less than 0.5 second, shows great promise in sparing patients from the toxicity burden of radiation therapy.

Proton FLASH, compared to other types, should have no exit dose. Proton FLASH has been investigated using cyclotrons. These machines can produce FLASH at their extraction (maximum) energy. However, at shallow and medium depths, the dose rate is significantly reduced due to degraders and range shifters. Moreover, these passive scattering methods to irradiate the target generate a higher number of neutrons and unwanted scattering, which could hinder FLASH's advantages. FLASH may not be possible with synchrotrons or synchro-cyclotrons.

[1]*Favaudon, V., et al. 2014. Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. Science Translational Medicine. 6 (245):245ra93. https://www.science.org/doi/10.1126/scitranslmed.3008973*

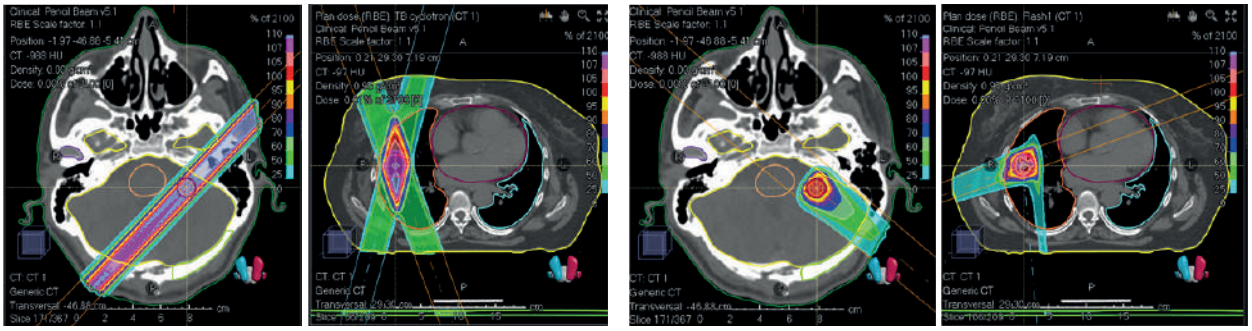
OUR INNOVATION ROADMAP_Continued

Two aspects of the LIGHT system performance are uniquely suited to FLASH. Unlike legacy systems, the proton beam intensity (current) does not vary on the energy, and energy changes are ultra-fast. These advantages support LIGHT in delivering FLASH conformally to any site in the body.

This year, we pioneered further developments in "scanned conformal FLASH" (SCF). In comparison to legacy technology, SCF presents a major advantage with the LIGHT system. This is because, due to the associated thick energy absorbers, cyclotrons can only produce FLASH at a single, maximum energy, making their FLASH treatment like X-rays, i.e. their proton beam must penetrate the entire patient and exit outside of the patient. This “shoot-through” technique is called Transmission Beam (TB). TB is “not how protons are meant to work,” i.e. it looses the advantage of the proton beam stopping the Bragg peak in the tumour. Cyclotron systems seek to avoid this by using further custom patient absorbers, but this approach is also inferior. Superiorly, only LIGHT, due to its ultra-fast energy changes and high beam output, can deliver SCF, retaining the advantage of proton therapy conformity, with the proton beam stopping in the tumour (Stopping Beam SB), and adding FLASH on top.

Cyclotron
Transmission Beam (TB)

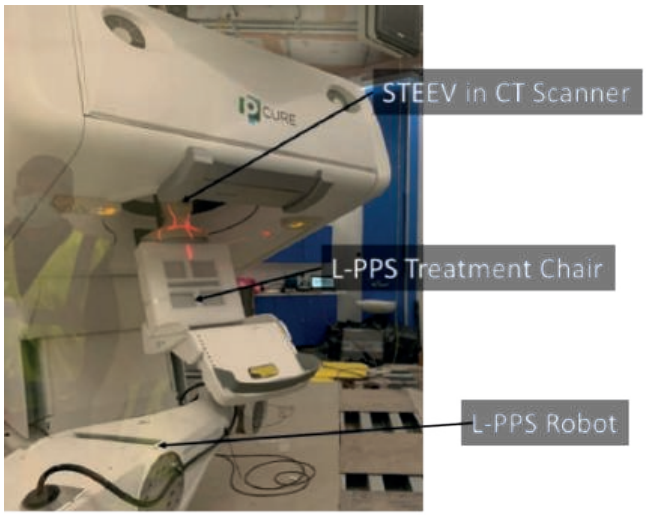
LIGHT
Stopping Beam (SB)



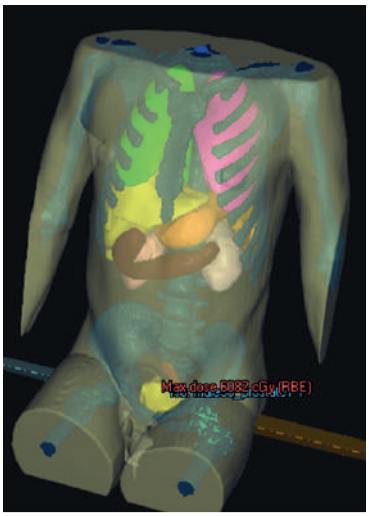
Transmission of FLASH beams from cyclotrons cause excess dose (in the colour wash) to healthy tissues compared to Stopping FLASH beams from LIGHT.

Upright treatment

The LIGHT system features upright (seated) treatments. Most current radiotherapy is performed with the patient laying on a treatment “bed”, called the supine position. Because upright is different from supine positioning, we have investigated the possible benefits of upright vs supine patient positioning. Our upright positioning investigations have progressed. This year, the LIGHT Patient Positioning System (L-PPS) was installed at the Daresbury Integration Site. We are preparing to scan the first human patients in the upright position with the L-PPS. The below shows the L-PPS installed with an artificial human mannequin prepared for CT imaging in the upright position.



The LIGHT PPS under test for the upright position in Daresbury.



Modified upright human figure.

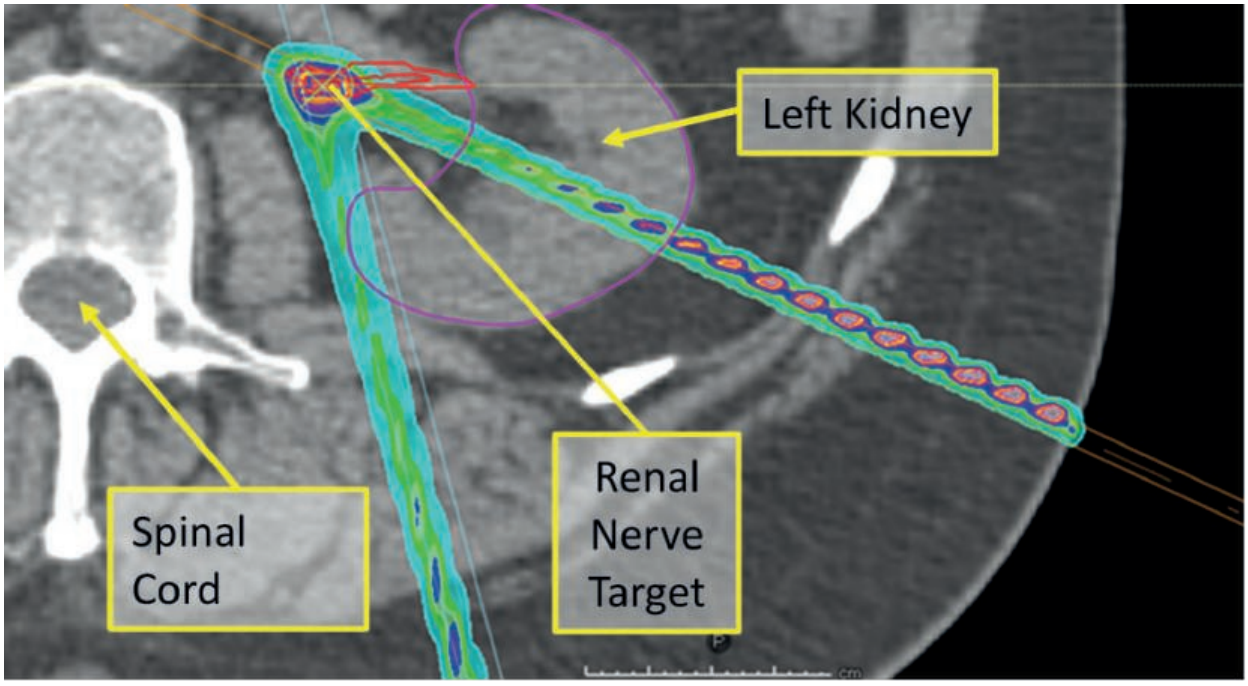
Last year, we partnered with the UK National Physical Laboratory (NPL) to assess the accuracy of our L-PPS "cubic phantom," used for the calibration of our system. The study results indicated excellent L-PPS cubic phantom accuracy. According to the NPL, "the standard deviation of the centre-to-centre distance of spheres was less than 20 µm".

The LIGHT potential beyond cancer

A promising topic is a consideration of using LIGHT to treat non-cancerous diseases. The indications we are exploring include the treatment of cardiac arrhythmias, hypertension, epilepsy, age-related macular degeneration (ARMD), and addictive behaviours, naming a few non-cancer areas we intend to study. For example, cardiac arrhythmias are a significant contributor to sudden cardiac death and are commonly treated by catheter ablation. However, the success rates of catheter ablation in these diseases are limited, and catheter ablation is linked to several complications. By employing LIGHT proton minibeams and split-second beam energy changes, Advanced Oncotherapy intends to develop a non-invasive treatment.

Similarly, the LIGHT System has the potential to be used for non-invasive ablation of arteriovenous malformations associated with epilepsy and renal nerve ablation to help regulate blood pressure in unregulatable patients. The below demonstrates how the LIGHT mini beams will be used to target the renal nerve nexus. The LIGHT mini beams are minimally invasive, avoiding the spinal cord, and such treatment may free patients from pharmaceutical dependence for hypertension.

Another opportunity for future growth is the use of LIGHT to reduce or eliminate the frequency of anti-VEGF treatments for ARMD patients. Furthermore, pre-clinical activity is expected to establish the feasibility of using LIGHT mini-beams to modulate dopamine transmission from the nucleus accumbens to treat opiate addiction.



LIGHT Minibeam plan for renal nerve ablation

INTERVIEW WITH OUR CHIEF CLINICAL OFFICER

Jonathan Farr,
Chief Clinical Officer

What made you join Advanced Oncotherapy?
I came to radiotherapy wanting to make a difference to improve patient outcomes. Early in my 20+ year career, I learned that I had the aptitude to develop and improve advanced radiotherapy systems, specifically particle therapy systems, thereby benefiting many patients. Joining Advanced Oncotherapy and assisting in developing the first proton therapy linear accelerator system is the ultimate expression of this goal. And the first day I met the Advanced Oncotherapy team, I knew it was where I wanted to be. Collaborating with my colleagues, all world-class experts in their respective fields, we deliver the future of radiotherapy and make it more accessible than ever before.

As a medical physicist, what do you find particularly exciting about LIGHT?
As the new platform for proton therapy, LIGHT is poised to realise the true promise of proton therapy. I say this because two aspects holding us back from that ideal today are uncertainties with target motion management in proton therapy and the need to improve the high dose conformity for some clinical indications. The LIGHT system is uniquely capable of ultra-fast energy changes, and the smallest beam size is called proton minibeams; it is designed to address the two challenges directly.

What is motion management and how important is it?
Motion management is more vital in proton therapy than with the more common X-ray therapy. This is because proton therapy is more accurate than X-ray therapy. Consequently, the "fuzzy" X-ray beams are not as strongly affected for moving targets if a tumour briefly moves away from the ideal treatment location, whereas a proton beam might completely miss it. Hence, motion management is obligatory for proton therapy. There are different types of motion management; the most basic enlarges the treatment region, thereby assuring coverage, but this is not ideal for patients, as it irradiates more healthy tissue than necessary, potentially limiting the efficacy of the treatment or causing later treatment-related complications. The LIGHT system is designed to provide improved motion management by tracking the tumour during treatment and staying "locked on" to it like a smart bomb. We expect this could result in improved clinical outcomes for some indications.

What about size of the beam?
The size of a proton beam spot is a critical treatment quality parameter. The most advanced type of proton therapy, pencil beam scanning, actively moves the beam across the tumour during treatment. And the regular beam diameter in proton therapy is about the width of a pencil, hence the name. But if you made a drawing with such a dull pencil, it would look very blurry, which is directly analogous to what happens inside the patient. Instead, if you had a very sharp pencil, say a 0.5 mm mechanical pencil, for example, the drawing would be razor-sharp. Incidentally, 0.5 mm is about the size of the LIGHT proton beam as it exits the linear accelerator, a unique aspect of LIGHT.

Using this sharp beam size, called minibeams, our calculations indicate a potential patient benefit for many indications. We are currently exploring this advantage together with the Cleveland Clinic, evaluating the potential for many of their patients.

For which cancer types do you expect these clinical aspects will be most appropriate?
The LIGHT system is designed to treat all clinical indications suitable for proton therapy. But the unique aspects of LIGHT, such as motion management and minibeams, are ideal for specific uses. Specifically, LIGHT minibeams may provide the most significant benefit where the ultimate normal tissue sparing is needed, such as with brain tumours abutting the brainstem or optic nerves. But LIGHT minibeams also show great promise for radiosurgery in the lung. The LIGHT motion management features are naturally associated with tumours that have motion during treatment; these are found in the thoracic cavity near the diaphragm, such as the lungs and liver organs. We see the most significant potential to expand the treatment of thoracic tumours with the LIGHT system and expect it is only a question of time before the adoption grows.

How do you see the journey towards commercialisation as the physicians tend to be conservative when new technologies hit the market?
Advanced Oncotherapy's LIGHT system offering has advantages in two broad areas, commercial and clinical. The greatest hindrances to the broader global penetration of proton therapy are its cost and complexity: not only complexity in terms of its use but also complexity in terms of a proton therapy endeavour realisation. To lower the entry bar, our Company has developed an appealing solution from the ground up. Examples of our solution are that no individual LIGHT component is larger than a "Class C" shipping container. Each of the modular linear accelerator components can fit on a tabletop. This dramatically simplifies shipping and installation. Hospitals are designed to accommodate the installation of CT scanners and MRI units; the installation of LIGHT is more akin to those than legacy proton equipment which requires road closures and giant overhead cranes.

In terms of LIGHT system usability, this is another area we have developed to ease the transition to proton therapy for centres. The LIGHT system use is "workflow-driven," hence the new user is not wondering what the next step is. The management software directs and supports their work.

Also, we tend to focus on the technical innovations at Advanced Oncotherapy, but our financial and commercial developments are equally as innovative. In addition to offering Turn-key proton therapy facilities, together with our partners, we have sophisticated financial solutions we can offer our customers. This key Advanced Oncotherapy solution can make the difference between realising a new proton therapy centre or not.

I have already touched on some of LIGHT's differentiating clinical design aspects, focused on additional healthy tissue preservation and reducing the toxicity burden sometimes associated with radiation therapy. Every clinician is keen to improve the care of their patients. Even if it requires change, physicians are convinced by the opportunity to change practise for patient benefit. The LIGHT system keenly appeals to this desire. In summary, I am confident that the unique combination of best-in-class treatment and our commercial advantages, Advanced Oncotherapy and LIGHT, are bringing life-sparing proton therapy to more people in need.

What are you and your team currently working on in the clinical space?
Together with my team, my role is roughly split into bringing our first LIGHT system into clinical use and exploring and developing applications of the LIGHT system.

Naturally, our top priority is beginning patient treatments at our Daresbury integration site, in the UK, something I personally pushed very hard for. We were delighted to receive the approval of the UK Science and Technology Facilities Council to use the facility at Daresbury for patients. There is much to prepare, roughly divided into hardware and software. We are engaged in realising the Medical Treatment Room ("MTR") and Area. The MTR has been constructed, and we are actively completing its fit-out and testing with the necessary LIGHT sub-components such as the CT scanner, robotic treatment chair, and X-ray positioning systems. We are also preparing for the required proton beam measurements before first use. There is a great deal of software control systems to complete and integrate. This is typically the Achilles' heel of new proton therapy systems, as the effort can be underestimated compared to the hardware. With this awareness, Advanced Oncotherapy started our LIGHT software development early on. We rely on a treatment planning system, a patient database system, and a therapy control system. All three systems have been running on our servers since 2020. Indeed, there remains more work to do, but we are on the straight path to success with these systems. The final step is bringing all sub-systems together in a coordinated way, resulting in a system ready for patient treatment. I have done it before a few times and greatly look forward to this result for our company, staff, and primarily for the patients that will benefit.

I am also engaged with our current clinical partners, such as the University Hospital Birmingham and The London Clinic, UK. Together, we are preparing the needed clinical treatment protocols for our first patients. Also, we perform extensive planning for staffing, training, insurance billing, and operations. The Cleveland Clinic, USA, is our close research partner. We work together directly to determine how the LIGHT system could benefit their patients.

Exploring LIGHT developments is some of the exciting work we are engaged in. It is so rewarding because the LIGHT system has boundless potential that responds to our ideas in the most positive manner. We are pushing into unchartered waters, and that is keenly exciting. An example is with our FLASH-LIGHT development. The type of treatment called

INTERVIEW WITH OUR CHIEF CLINICAL OFFICER_Continued

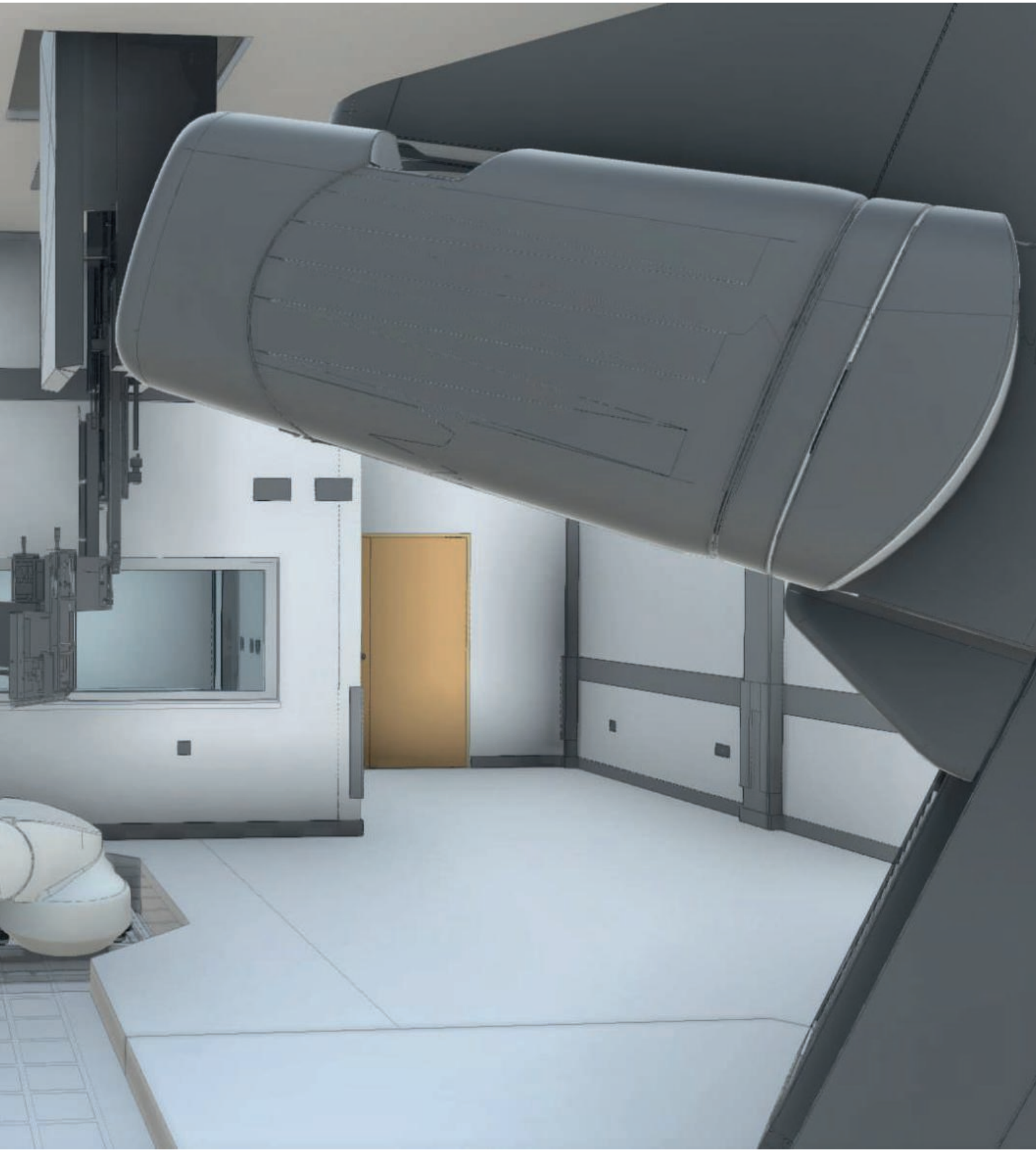
FLASH is a biological effect where a differential response is observed between normal and tumour tissue when exposed to ultra-high dose rates. This means that if the entire radiation treatment can be given incredibly fast, in less than half of a second, the tumour cells are killed, but the healthy tissue is almost completely spared from damage. The underlying science is still being worked out, but FLASH is the most exciting development in radiation therapy in decades. The LIGHT system was largely designed when I first became aware of FLASH a few years ago. I immediately wondered what FLASH might be like with the LIGHT system. I was astounded to learn from my colleagues that the proton output of our machine does not depend on energy. As we say in physics, it is "invariant." As we discovered, the invariant output of LIGHT is fundamental to enabling what we call scanned, conformal, FLASH, radiotherapy, something no other system can perform. There are many other similar examples, some we have mentioned, of how the LIGHT system "rises to the challenge" of what we ask it. One is left with the impression that it was meant to be.

You mentioned FLASH. How do you define the opportunity?

FLASH is both a clinical and commercial opportunity. Clinically, the reduction of healthy tissue damage can be used to "open the therapeutic window." This can be realised in either of two ways: either patients can be treated to higher tumour doses than are currently possible, or lower side effects can be realised from existing dose treatments. As different examples, certain lung tumours might benefit from higher doses than are presently used. In contrast, other tumours such as the prostate are well controlled with current doses, and there, the goal is less toxicity to the surrounding tissues, such as the rectum. In all cases, the goal is to have fewer treatment sessions, ideally just one, compared to the multiple weeks of radiotherapy typical of treatments today. The patients prefer fewer treatments, leading to a win-win commercial opportunity. Treating more patients annually produces more revenue, as usually, patient treatment is compensated on a per capita basis. Proton treatment centres are costly to build and operate. Here, FLASH may further make the endeavour attainable by more minor concerns, improving community access.

In conclusion, what is driving you?

My personal wish is to have more time in the week. Our patients are waiting, depending on the LIGHT system's completion and readiness. Whenever the obstacles seem high, I think of the patients waiting to be cured with our LIGHT machine, patients who live in areas not accessible to proton therapy today. The faster we can complete LIGHT, the more lives that can be saved. Our company is working at the maximum rate. If we could bend time, we could get to the goal sooner. We are approaching the end goal now. Again, the greatest wish must be for the suffering cancer patients without access to proton therapy. So, my motivation and my pride are to help these people. This is very much in the DNA and culture of our Company, and this is why I get up every day with full energy, racing to the goal.

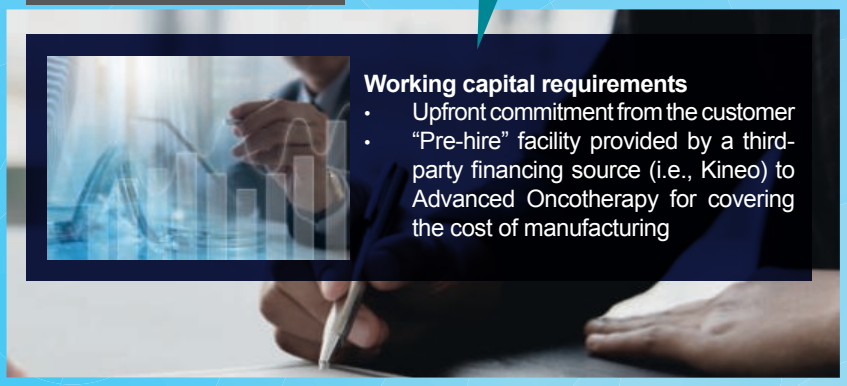


OUR DELIVERY PLAN

The relevance
- Limits cash requirements of Advanced Oncotherapy
- Accelerates the delivery of the commercial pipeline

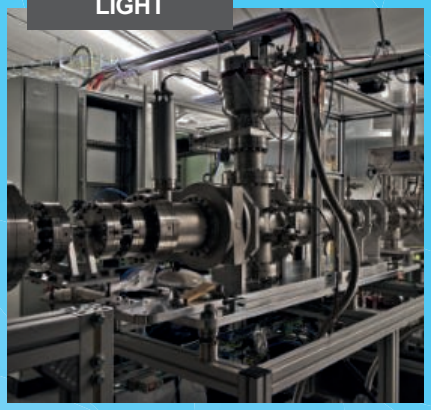
Financing

Contract signing



Working capital requirements
- Upfront commitment from the customer
- "Pre-hire" facility provided by a third-party financing source (i.e., Kineo) to Advanced Oncotherapy for covering the cost of manufacturing

LIGHT



Outsourced production launched

- Lead times to reduce to 6/12 months
- Significant cost savings expected on the first machines
- Suppliers incentivised to reduce costs and times

Customer / Centre

Preparation phase: Planning, training, marketing, budgeting, etc.

Patient

The relevance
- Limits cash requirements of the customer
- Allows Advanced Oncotherapy to receive a share of the profit of the centre; aligned interests

Roll-over of the "pre-hire" facility

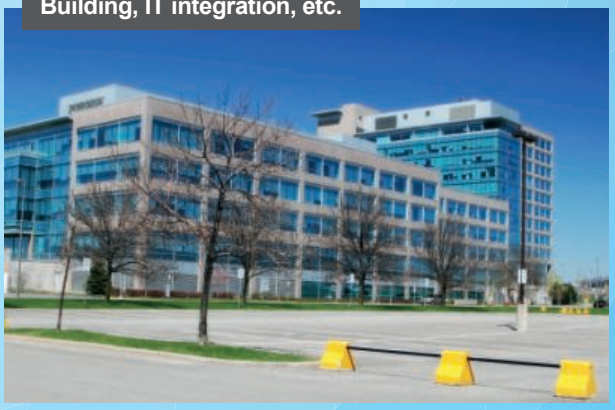
- Financial obligations transferred from Advanced Oncotherapy to the customers; repayment through a leasing model
- Terms subject to the credit quality of the customers

Delivery

LIGHT Installation

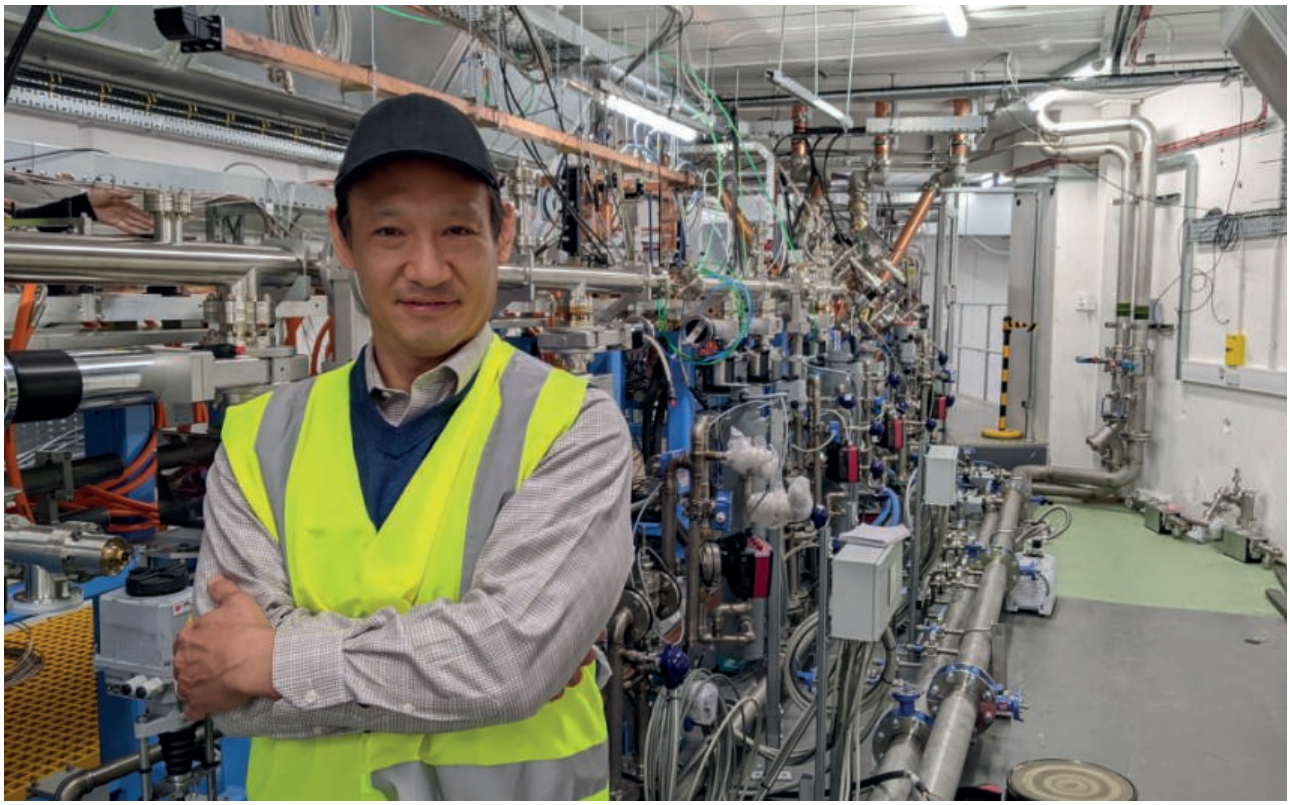
Operation, maintenance and upgrades

Building, IT integration, etc.



Operational centre

INTERVIEW WITH OUR CHIEF OPERATING OFFICER



Ed Lee,
Chief Operating Officer

You worked at the proton therapy center in Loma Linda in California before joining Advanced Oncotherapy in Geneva. Why did you move?
The first hospital-based proton treatment centre was offered by Loma Linda University Medical Center which is in Loma Linda, California. The proton therapy centre has treated over 17,500 patients and has been in operation for over 25 years. I learned a lot about cancer treatment and got to see in person what patients and their family experience during their journey of beating cancer: tragedy, hope, as well as the tangible benefits and effectiveness of proton therapy. After seeing many patients come through the Loma Linda Proton Center, I am convinced that proton therapy is the best radiation treatment option readily available to patients. The challenge is to lower treatment cost whereby the oncologist can confidently prescribe proton therapy without any pushback from insurance firms due to cost factors. LIGHT has the potential to do this.

I decided to join Advanced Oncotherapy because of a few reasons. The first was the next-generation technology in proton therapy. Advanced Oncotherapy's LIGHT System provides the capability to control the radiation dose delivered at each single "point" of the tumour. This has the potential to dramatically lessen collateral damage of healthy tissues, lower the number of treatment sessions and hence reduce the treatment cost to patients and clinics, increase treatment capacity from a patient throughput perspective with upside of increasing treatment center revenue to name a few key factors. The second reason was the modularity of the design. The LIGHT design simplifies the installation by segmenting the system to manageable "modules". For the most part, we only need a conventional forklift or equivalent lifting capability to install our heaviest module – it can even be manually moved by four strong men. The modularity also offers repetition during installation. Repetition is a key enabling factor in high-volume production. With repetition, we can then focus on efficiency and reduction of cost and time. The third reason is to participate in a technology that has never been done before. Of course, we had our own challenges but this is also what motivates me when getting up every morning with driven ambition toward helping cancer patients realise the best radiation therapy possible.

What are the biggest challenges you are facing?
Our challenge can be summarised into one phrase: we are producing, for the first time, a very complex and cutting-edge proton accelerator-based treatment system which will be certified and cleared for patient treatment by governing authorities such as the FDA. The technology has been proven since the data and result of the prototype announcement in 2018. Hence, the technology is not a concern based on the data from the technical team. The remaining challenges are

related to implementation (learning curve of doing something for the first time) and cultural evolution. Doing something for the first time includes complex design documentation with full traceability and technical rationale, documented evidence of a business process which is certified per ISO 13485, our supply chain partners, and the rigours of installation, validation, and verification. We, collectively, have implemented many lessons learned toward continuous improvement of quality, delivery, and cost during our first system deployment journey. There is no one single issue but a collection of many low-level technical or logistical issues which were overcome through excellent collaboration and teamwork. During installation, milestones which first took weeks are down to days. These improvements have not been easy but with resolve, commitment, and grit, the team have proven to be effective, and we are continually accelerating our progress. The topical areas include personnel skill and knowledge base improvement, continually improving installation documentation and processes, early identification of faulty components coupled with effective and efficient countermeasures, applying pre-assembled kits and assemblies to minimise critical path activities, and applying rigours test and inspection processes to name a few.

The organisational culture evolution is transitioning from a pure R&D organisation towards a commercial organisation while still maintaining our roots in R&D and with our affiliation with CERN and STFC. Our staff are responding well as time progresses. Since I joined five years ago, we are continually shaping our organisation to have the right balance between commercial and R&D mindset. The second challenge is the "nuts & bolts" of the business which is the technical file. The technical file provides the full detailed documentation package which traces from requirements (clinical and business-case) all the way down to the specifications of wires, nuts, and bolts. The documentation package includes design selection rationale, conceptual design related data, detailed design documentations, risk assessments at all levels, all aspects related to supply chain and logistics management, manufacturing, installation, test, and inspection data. This rigour is applied to the LIGHT system, sub-systems, sub-sub-systems, assemblies, sub-assemblies, and components related to the LIGHT system. The similar discipline is also equally applied to the building and infrastructure at our first system deployment site in STFC-Daresbury Laboratory whereby we have received patient treatment approval. In a nutshell, doing "this" for the first time, there is no published manual we can refer; we are creating the manual and we will be the experts. I am very proud of our team's progress.

Is that the reason why the Company has decided to outsource the manufacturing process and focus on the assembly processes?

As a key business strategy to minimise financial costs, we outsource all manufacturing activities but perform the necessary assemblies. We can leverage the immense supply chain network, their capital equipment, and component and assembly know-how to produce the components while we focus on the assembly and integration of the system. This is also possible because we have ample knowledge and expertise in the manufacturing realm. Without our manufacturing expertise, we would not be able to outsource the manufacturing of our key components. Further to this point, we rely on our relationship-building capability to transform a traditional customer-supplier relationship to a partnership. The key enabler is doing what we say and saying what we do, which relies upon integrity and transparency. The announcements with VDL and CosyLab are evidence of our transformation from a supplier-customer relationship to a supply chain partnership. Our aim is to advance our existing partners toward a higher tiered platform, for example by advancing from a component provider to a sub-system provider. There is much work to be done to realise this strategy; however, we believe this is key toward meeting the future pent-up demand of our LIGHT system. Coupling supply chain partnerships with strategic tiered platforms will provide capacity expansion as well as adapting to the everchanging geopolitical and environmental variations. We will maintain our manufacturing and integration know-how while partnering with our suppliers to foster and maintain a win-win relationship.

How do you manage your supply chain?

We apply the robust supply chain management based on the experiences of our staff who come from radiation therapy medical device, automotive, aerospace, defence, nuclear, high-energy physics, utilities, and construction to name a few. This starts with a clear scope of work, detailed and clear requirement and specifications, progressive Q&A review session to ensure input information are clearly understood by our supply chain partners, rigorous contract negotiation to ensure the interests of the Company are at the centre of all negotiations while maintaining our partnership spirit, robust audits related to quality and business systems, identification and management of deliverable milestones, strategic supplier visits to "kick the tires" and verifying milestones in progress as well as certificate of conformance, factory acceptance testing and inspection, site acceptance test and inspection, and compliance review of our suppliers' traceable documentation packet.

We also have implemented and plan to bolster the supply chain management practice of commodity assignments, supply chain project engineering practices which include expertise in specific areas to complement our supply chain partners, performance measurements coupled with routine feedback and reviews, standardised quality and regulatory compliance agreements, and recurring supplier audits to name several key initiatives.

Which initiatives do you foresee for future machines?

We aim to launch several key initiatives to reduce cost, lead time, and further improve quality. Our partnership model will extend to recurring cost reduction initiatives with measurable goals. We have, even now, realised cost savings of our first treatment system compared to the first prototype which include but are not limited to value engineering; we will continue this practice. The aim of cost reductions is not only to increase profitability but, most importantly, improve the affordability of the LIGHT system and lower the treatment cost to cancer patients. We

INTERVIEW WITH OUR CHIEF OPERATING OFFICER_Continued

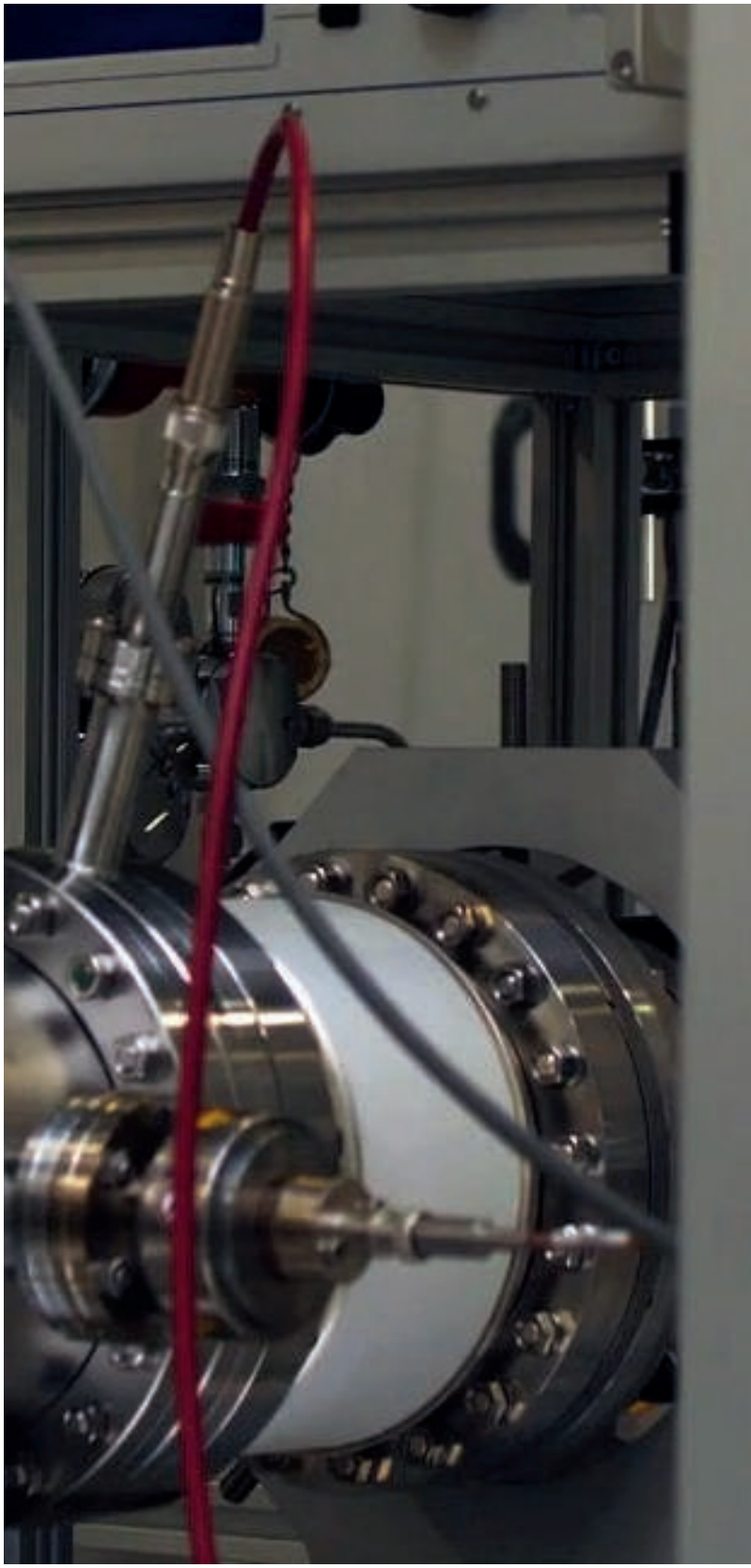
earnestly look forward to leveraging material purchases, utilising alternate materials which are less expensive but meet performance requirements, manufacturing cycle time reduction resulting in reduced labour cost and lead time, and improving first-pass yield through thorough data analysis and process improvements. A key enabling foundation to act on cost, quality and lead times is through implementing lean manufacturing coupled with six sigma and statistical process control, which involves reducing waste, eliminating variations, and maximising the ratio of value-added activities versus non-value-added activities.

We are also addressing the need to increase capacity. We have already identified the maximum capacity per our key supply chain partners based on various market demand scenarios. Further to a very positive market demand, we have strategically established various deployment scenarios at various geographic locations. This strategy also includes leveraging our existing staff's expertise with local clinical site personnel. We look forward to our next challenge once we complete the first system deployment to help improve lives through democratising cancer treatment with a much more affordable LIGHT system.

How are you working with your suppliers to deal with Covid-19, Brexit and other challenges?

Brexit has certainly been a logistical challenge. With no clear advanced prescriptions from EU and UK, we incurred unexpected or unnecessary shipping delays at the UK border as well as additional costs related to custom duties. As time progressed, more shipping lead times were added to the overall delivery contract and program management processes. We have also had to contract custom brokers as necessary to ensure reliable custom clearance and transportation of our goods. Combination of these two categorical actions have now virtually negated shipping delays.

COVID-19, during the last two years, have compounded the complexity of our endeavour. Nevertheless, I am proud of the achievements made by our staff and our supply chain partners. Though the temporary shutdown due to COVID-19 caused start-up delays, the team have quickly demonstrated immense improvements as momentum progressed. To ensure continual operation once the very strict shutdown was lifted, we implemented COVID-19 protocol policy and procedures to ensure the utmost safety of our staff. We applied recommended Personnel Protective Equipment coupled with sanitisers and tests on a daily basis to ensure zero infection at our workplace. Nevertheless, we had to deal with the residual impacts of the shutdown at our supply chain partners. They too experienced raw material shortages, personnel shortages, production capacity significantly below pre-COVID which led to delayed receipt of vital components. Nonetheless, we creatively assessed how to minimally impact the program critical path.

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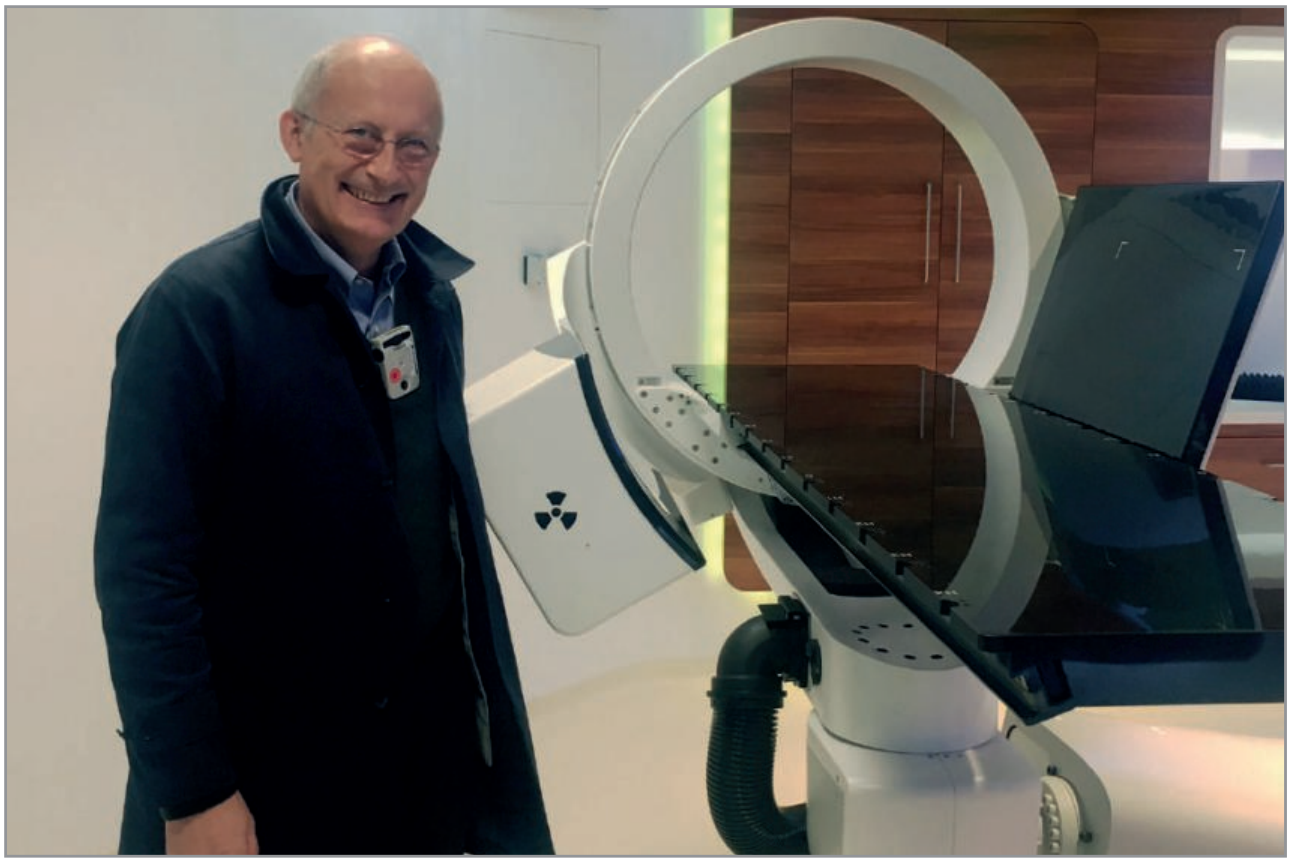
INTERVIEW WITH OUR DIRECTOR OF REGULATORY AFFAIRS



Michel Baelen,
Director Regulatory Affairs, Quality & HSE of Advanced Oncotherapy

What is needed for market authorisation?
Our LIGHT medical device is subject to extensive regulation by numerous agencies, such as the FDA in the US or the MHRA in the UK. To varying degrees, each of the agencies requires us to comply with laws and regulations governing the development, testing, manufacturing, labelling, approval, marketing, reporting, record keeping, tracking, etc. Our regulatory strategy is also shaped by environmental health and safety laws and regulations worldwide.

To be distributed in the US, our LIGHT product must receive a 510(k) clearance from the FDA. 510(k) is a process that requires us to demonstrate that our system is substantially equivalent to a legally marketed medical device in the field we operate. In the EU, LIGHT must carry a Conformité Européenne ("CE") mark indicating that it conforms to the European Medical Device Regulation as well as the associated enforced EU guidelines and essential conformity standards. Upon its CE marking, it can be marketed in any EU member state.

Thankfully, the approval of medical devices such as our LIGHT system in both the EU and the US share many similarities. To obtain certification, our product must meet minimum standards of performance, safety and quality as well as comply with one or more of a selection of conformity assessment routes, which depends on the classification of our product.

What is the classification of your LIGHT product and how relevant is this?
In the EU, the LIGHT system – as a radiotherapy equipment – is a class IIb medical device. It is positioned in the proton therapy market that has a long history of treating patients. The level of evidence required for approval is largely focused on demonstrating that LIGHT is safe and performs as expected. We must also demonstrate the effectiveness of LIGHT by making our system available for the entire treatment course over more or less 25 consecutive irradiation days and by ensuring the necessary up-time requirements.

In EU and UK, we must perform a Clinical Investigation Plan to receive our conformity approval, the CE in EU and the UK-CA in UK. This comes from the fact that our Class IIb medical device differs from the existing Proton therapy systems

in the way the energy of the protons used for treatment is electronically modified without the need to use degraders for energy changes between 70 MeV and 230 MeV.

In the US, our LIGHT System is also a class II device. In China it is a class III device as any other proton therapy equipment. While clinical trials are necessary in China – as for any other proton therapy equipment – this is not the case in the US since we follow the similar equivalence route.

Which evidence do you have to provide?
Following the new Medical Device Regulations ("MDR"), we must meet two requirements: the submission of our technical file and the demonstration that we can operate to a high standard of quality through a Quality Management System. The latter is evidenced through our ISO 13485 certification, which is regularly audited and re-validated. The former must contain sufficient effectiveness, safety, and quality data, in particular the verification and validation test results, along with traceability back to clinical user needs, product requirements, and design specifications.

Verification, validation, traceability, requirements, specifications, etc. Tell us more…
Verification and validation – also called V&V – are critical activities that confirm that LIGHT as the "contracted for" product provides the required operational capability. The validation is the process by which we prove that our product works for the end-user as intended. Therefore, the user needs must be broken down into product requirements and design specifications to design and build the right product. Validation testing is needed to prove that our product, as built, operates according to the users' expectations under the conditions where they intend to use it. Verification, on the other hand, is the process aimed at confirming that the specified requirements have been fulfilled. Put it simply, we must demonstrate that the product we built is the product we said we would build.

In that context, traceability is important because it is the link between user needs and test cases. A trace matrix provides part of the V&V evidence that the certification agencies require.

Is this a difficult process?
No, it is not. Personally, I have been through 13 certification processes with the US-FDA, 13 certification processes with the European Notified Body, two certification processes with the Chinese Food and Drug Administration ("NMPA") and other processes in other geographic areas. Therefore, my confidence comes from the fact that the process of getting the conformity approval of LIGHT is not that different, whilst we must remember that regulators can always ask for additional data.

A critical success in our regulatory strategy is to ensure we do not leave any stone unturned. Our regulatory plan follows a very thorough process that requires the right tool and the right mindset across the whole organisation. It is a time-consuming activity because each of the subcomponents and components that make up the LIGHT product must be verified, integrated, and tested. This operational testing is the venue that gathers data to validate that the ultimate product satisfies the required operational capabilities.

If you consider the validation activities as an example, we must undertake various activities ranging from the comparison of LIGHT against the equivalent equipment performing for similar purposes, the simulation of functionalities through mathematical modelling, the testing of the final design to prove the system operates as defined in the user needs, the preparation, implementation and reporting of test plan, test cases, test execution records which must be documented and maintained as a part of design records. So, validation, in its entirety, is not the result of a single activity, but the collection of results from all validation activities.

You are talking about having the "right mindset". Can you explain this further?
The product certification is an important milestone in the journey of a company, but this is not the end of the road. On the contrary, this is rather the beginning… To go far and have a long product life cycle, quality – one of our key corporate values – must be embedded in everything we do. This is based on the premise that no single tool, test, or person can guarantee quality. For quality to be a solid part of our culture, everyone needs to support and contribute to it – from management and sales teams to developers, architects, and product managers. At Advanced Oncotherapy, we have this mindset, a pre-requisite for a sustainable success.

Who are your points of contact to ensure your regulatory strategy does not result in surprises and delays?
In Europe, our approval application must be reviewed by a Notified Body which is authorised by the health agency. Its role is to assess and assure conformity with requirements of the relevant EU directive. Notified Bodies are accredited private companies that contract with manufacturers such as ourselves to supply product certifications for a fee.

At the highest level of the European Commission Medical device regulatory organisation, the Medical Device Coordination Group ("MDCG") is the instancy delivering the accreditation to the Notified Bodies and it is also the authority defining special enforced guidelines. The Proton Therapy medical equipment is classified as class IIb for which a mechanism for scrutiny of conformity assessments is in place. This is applied for certain class III and class IIb devices.

Because of this applicable mechanism for scrutiny of conformity assessments, once our Notified Body agrees that our product meets requirements for conformity, it must submit its report to the EU-MDCG for approval and only after this it can issue a certificate of approval for conformity requirements of the Medical Device Regulation. Once we get this certificate, we are then authorised to issue a

INTERVIEW WITH OUR DIRECTOR OF REGULATORY AFFAIRS_Continued

CE mark conformity certificate, and LIGHT can then be marketed in the EU member states and delivered to our clinical customers for clinical use.

In the US, the counterpart is the FDA. As part of our pre-submission process – called Q-Sub process – the FDA has and continues to provide constructive comments on our filing strategy. This Q-Sub process applies because LIGHT is considered as an innovative proton therapy system. The FDA favours an interactive dialogue through the development process which aims to facilitate the approval once our dossier is submitted.

What is driving you?

I am very proud to be part of this journey. Playing a role in offering physicians the opportunity to treat tumours in organs that cannot be immobilised during treatment and improve patient access to proton therapy treatments is extremely rewarding.

The LIGHT system is a world first for the advanced treatment of cancers integrating imaging equipment combined with a pulsed proton beam that will be able to modulate the energy and the protons current of the beam in real time. After the introduction of the cyclotron-based proton therapy systems in the 50s, the new generation of proton therapy systems is almost there now!

Throughout my career, I have seen the enormous challenges of using and getting approved cyclotrons. Their proton beams must be degraded with poorly efficient transmission absorbers, which is generating a significant number of neutrons in the bunker, further impacting the equipment and the building as well as creating decommissioning problems. I am a believer that we all have a duty to protect our planet. So, introducing LIGHT to the market is a major step forward in this commitment. I also find the opportunity to manufacture LIGHT in a high-volume production setting particularly compelling, thanks to its design that largely relies on very pure copper units. I see this as a fundamental difference against cyclotrons which require a large amount of steel and necessitate magnetic field mapping and correction of steel defects during each production cycle.

Put it simply, what is keeping my passion intact after all these years dedicated to get cyclotrons and synchrotrons on the market is the opportunity to solve many of the limitations of current proton therapy systems.

OUR BUSINESS MODEL

Enablers

Clinical, engineering and scientific excellence

- Technology originated from CERN, the world-leading centre of physics and engineering excellence that develops and operates some of the world's largest and most complex scientific instruments
- Significant barriers to entry
- Know-how and patent protection

Commercial agility

- Intimate knowledge of the customers' mindset and the key success factors relevant to radiation- and proton-based technologies
- Lean organisation built upon outsourcing the manufacturing activity and assembling in-house the LIGHT components
- Strong results driven culture and teamwork

The team

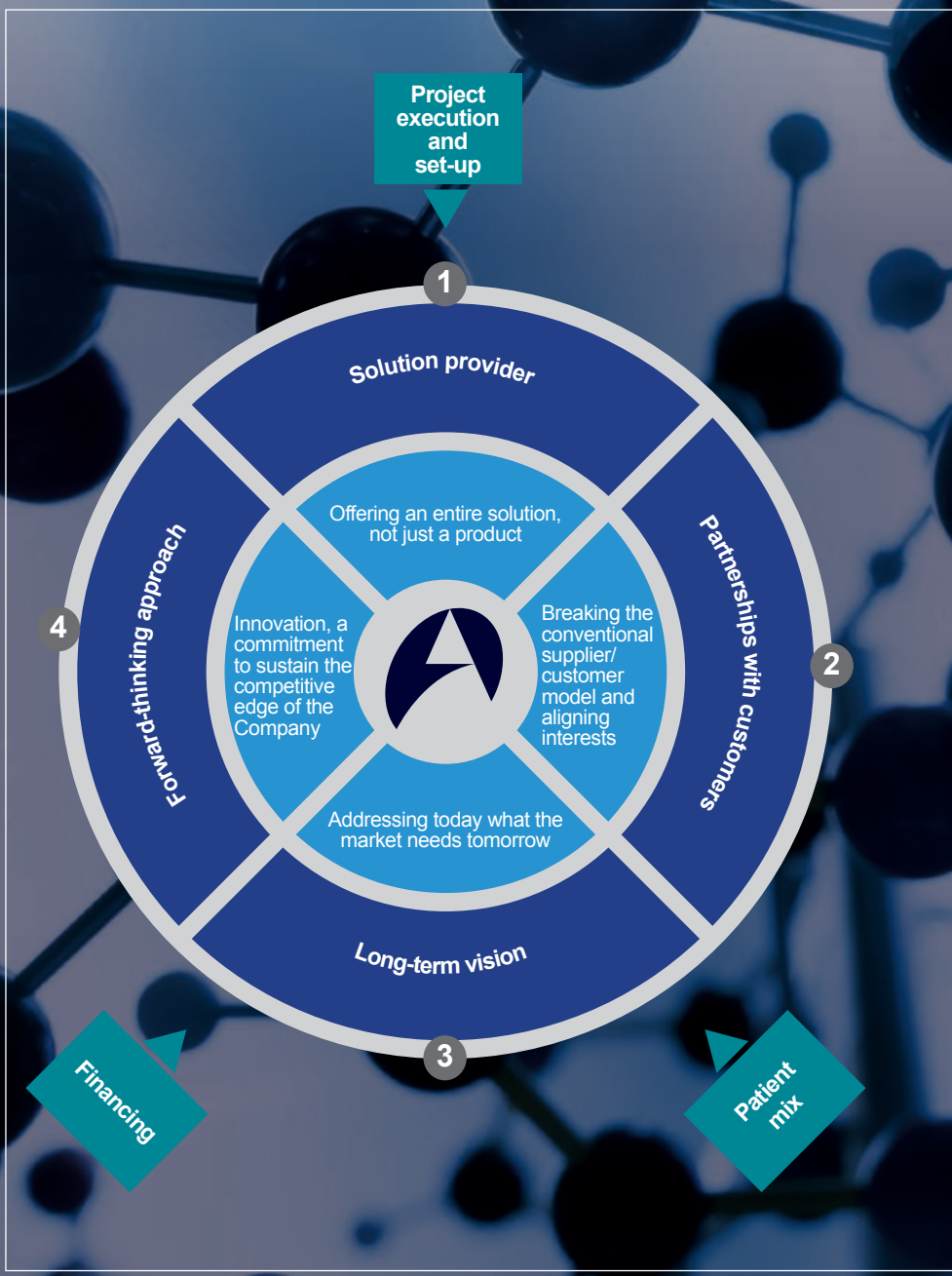
- Highly experienced and motivated team focused on innovative solutions
- Team with a successful track-record in launching new products, in particular in the medical equipment industry
- Project endorsed by key opinion leaders and eminent scientists whose reputation is unquestionable

Partnerships with key stakeholders across the entire value chain

- Suppliers incentivised as business partners for excellent delivery
- Financing partnership in place to support working capital requirements and customers
- Commercial customer-centric partnerships

How we create value

We have laid out the key foundations of our business model. This is to ensure LIGHT has the market reach and penetration, giving cancer patients and physicians the tool to defeat cancer and providing returns to our shareholders. Through strategic long-term customer-centric and innovative partnerships, we believe we have a balanced and robust business model to address customer's needs, drive our commercial growth and democratise proton therapy.



What is in the mindset of customers when contemplating a proton therapy project

1. The LIGHT system is the only solution that integrates the delivery of protons with a state-of-the-art imaging system directly in the treatment room; it offers significant advantages over legacy systems, including smaller footprint, modular design, ease of installation, fast electronic control of the proton beam and energy, significant cost saving for customers. Given the modularity of LIGHT, a unique feature in proton therapy, the package provided to customers is also complemented with tailor-made financing solutions. This is the basis of the partnership between Kineo and the Company, a major source of differentiation and a key stepping-stone in accelerating the market adoption.

2. Commercial partnerships are built upon a participation of the Company to the operations of the clinical centre through a risk-reward strategy. This aligns interest, provides Advanced Oncotherapy with unique insights in terms of future engineering and clinical developments, increases responsiveness, and provides a long-term source of revenues for the Company. Further details can be found on pages 69 and 70.

3. Given the investment needed for building proton therapy centres, long-term servicing contracts (typically 20 years +) are the norm. This must be accompanied with a clear understanding of the market dynamics and the cancer centres aspirations. This must consider the long-term need to integrate and optimise the proton therapy operations with the other cancer services of the operators as they seek to continually differentiate their product offering.

4. Staying at the forefront of innovation is predicated on the Company's ability to leverage the versatility of the LIGHT platform and deploy the series of future technical upgrades which have already been identified, such as FLASH LIGHT. This is done through scientific partnerships as well as clear internal processes with well-defined KPIs. This forward-thinking approach is essential when planning and installing new LIGHT systems, so that customers always benefit from the latest technological advancements.

Creating value for our key stakeholders

- **Patients**
- **Regulators**
- **Commercial partners**
- **Supply chain**
- **Investors**

Please refer to Section 172 for further information

OUR PARTNERSHIP FINANCING MODEL

In January 2021, Advanced Oncotherapy announced a partnership with medtech financing specialists, Kineo[1]

kineo finance

Background

- Leasing company specialising in MedTech
- Founded by ex-CEO of Siemens Healthcare
- Based in Basel, Switzerland
- Funded by large family offices and institutional investors

Objectives:

- Provides leasing arrangements to customers
- Provides working capital for the manufacturing of LIGHT

In Practice:

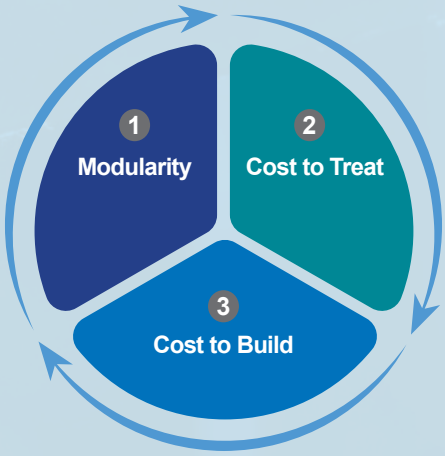
- Funding partner to cover 50/100% of the cost of LIGHT
- Finished machine transferred to Funding Partner balance sheet and leased to customer
- Customer guarantees a minimum throughput of patients, equal to the value of the lease obligations
- Customer enters into operating services agreement whereby Advanced Oncotherapy provides maintenance services
- Advanced Oncotherapy receives % of profits from the project in perpetuity

Outcomes:

- Sustainable revenues, increased returns over time, and strong commercial alignment with customers

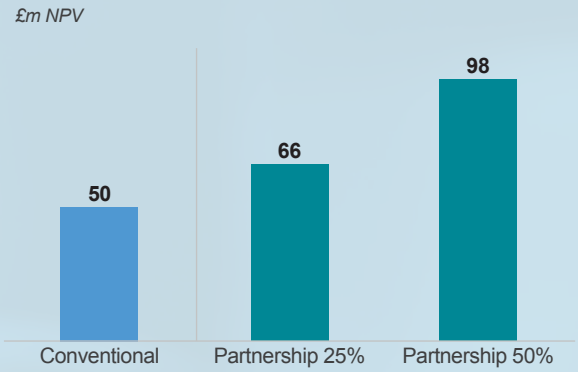
[1] *Formally DiaMedCare*

Why this opportunity is unique to Advanced Oncotherapy?



1. Modularity and movability of devices makes LIGHT system securable under financing package
2. Lower treatment cost enables customer to service lease obligations
3. Lower machine cost brings project risk in line with financing partners appetite

Indicative Value of One Commercial Order[2]



Conventional Business Model

- 100% of 45m selling price paid on day of installation at 40% gross margin
- Maintenance of £4m paid per year

Partnership Business Model

- Advanced Oncotherapy receives portion of the centre's £15m p.a profit (25% and 50% cases considered)
- Profit calculated after lease payments, which cover upfront cost of machine
- Maintenance of £4m paid per year

[2] Indicative 3 room system. NPV calculated using a discount rate of 10% over a period of 20 years (no terminal value)
Figures are for illustrative purposes only and do not intend to reflect the real economics of a project

SECTION 172 STATEMENT

Effective engagement with our key stakeholders and managing our impact on stakeholder interests

Effective engagement with our stakeholders is critical to the business. It helps us to appreciate the impact our decisions have on stakeholder interests and better understand their needs and concerns. It strengthens our relationship with them, is an ongoing part of the operational management and governance of the Company and is key for long-term sustainable growth.

As required by Section 172 of the Companies Act 2006, the Directors must act in the way they consider, in good faith, would most likely promote the success of the Company for the benefit of its shareholders. In so doing, the Directors must have regards, amongst other matters, to the:

- Likely consequences of any decision in the long-term;
- Interests of the Company's employees;
- Need to foster the Company's business relationships with suppliers, customers and others;
- Impact of the Company's actions on the community and environment;
- Desirability of the Company maintaining a reputation for high standards of business conduct;
- Need to act fairly between members of the Company.

Our Stakeholders

Patients

Our purpose is clear: help patients afford access to the latest technology in the cancer treatment and proton therapy. Through the LIGHT system and services, the Group is looking to provide large and small health practices with the flexibility to equip themselves with what the Company thinks is the best technology, and at the same time decreases the cost of a proton therapy treatment. Because patients are at the heart of everything we do and because their needs are fundamental to our success, we consult with Key Opinion Leaders regularly and conduct market research to help us with patient insights.

Employees

We are a people-centric, equal opportunity business driven by our values and – as of December 2021 – employ 174 people, aiming to develop them to the best of their abilities whilst maintaining their safety and well-being. The Board, and especially the Remuneration Committee, have also had particular regards to employees as they reviewed and revised the long-term incentive arrangements as part of its strategy to attract, retain and motivate employees in order to deliver value for shareholders. These actions were consistent with the Board's commitment to investing in and responsibly rewarding employees as they deliver the Company's strategy.

Regulators

Safety and quality are two of our four key values. We are committed to do the right thing to ensure the safety of patients, our users, and our staff. We focus on patient outcomes, reliability and consistency. To do so, we engage with competent authorities and our Notified Body; this ensures we operate within the appropriate regulatory and legal framework, further accelerating our plan for the certification of the LIGHT system in the targeted markets.

Safety is also linked to data protection; our cyber strategy is constantly evolving to anticipate and respond to the advances being made in the technologies we use and the threats we face.

Commercial partners

The Board places great emphasis on selecting the most suitable commercial partners who share the Company's vision and do not accept proton therapy is reserved to a minority of patients. The Board keeps itself aware of changes in the industry by fostering existing relationships and through extensive networking. Furthermore, the Company has appointed specialist advisers – in support to its commercial team – to identify and target the right potential partners and facilitate discussions and negotiations.

Supply chain

Centred on an outsourced manufacturing model, the Company relies on circa 150 third-party suppliers. The support of the Group's supply chain is vital in becoming a sustainable business. Our expanded relationship with VDL and Cosylab exemplifies the strength of the bond that we build with our partners. For enhanced transparency and mutual protection in the management of our third-party relationships, the Company uses automated purchasing and approvals processes, coupled with robust service level agreements.

Investors

Effective communication with shareholders on strategy and governance is critical. The Board naturally considers its shareholders to be key stakeholders of the Company and is focused upon delivering long-term value for their benefit. The Company engages with its shareholders and potential investors on a regular basis with meetings throughout the year. External strategic communications advisors provide further support to manage the relationship with investors and analysts and assist with market interactions and announcements. The results of this investor engagement are reported to the Board to help inform our strategy and communications.

Engagement and achievements

PATIENTS

- Worked closely with Key Opinion Leaders and attended industry events to enable us to keep informed on any trends or changes that will affect how proton therapy is delivered to cancer patients
- Gained real world knowledge on the mindset of both patients and customers
- Consolidated views on future opportunities and positioning of LIGHT

EMPLOYEES

- Focused on providing a Covid-19 safe workplace
- Enhanced environment, health, and safety
- Increased the focus on making a positive impact on the environment
- Employee portal to achieve closer engagement with employees and allow regular access to HR
- Communication with employees through intranet, industry newsletters, staff meetings
- Updated training and information for employees regarding Covid-19; implemented ways of supporting employees, including home working
- Undertook a talent review and business process mapping to nurture future talents and ensure an effective succession plan across the whole organisation
- Of eligible employees, 80 employees participated in the SAYE Option Plan at the end of the year.

REGULATORS

- Committed to being open and transparent with regulators and to work closely with them
- Continued to work with our Notified Body to get LIGHT approval; worked in partnership with our Notified Body to ensure we understand the latest regulatory developments and that our LIGHT system is approved as quickly as possible
- Ongoing dialogue with the MHRA and the FDA – through the Q-submission – to garner feedback and accelerate certification process
- Gained increased understanding of regulatory requirements during the extended MDR transition period
- Significantly increased resources available to support the Verification and Validation activities
- New controls and procedures were defined to ensure sufficient data backup and decreased cyber risk. This resulted in new control definitions and guidance for cloud security to support secure growth across the businesses

COMMERCIAL PARTNERS

- Reviewed the care pathways with health insurance companies
- Engaged with existing commercial partners on supporting activities, including marketing activities, integration of IT systems, patient referral strategies, etc.
- Attended trade and research conferences

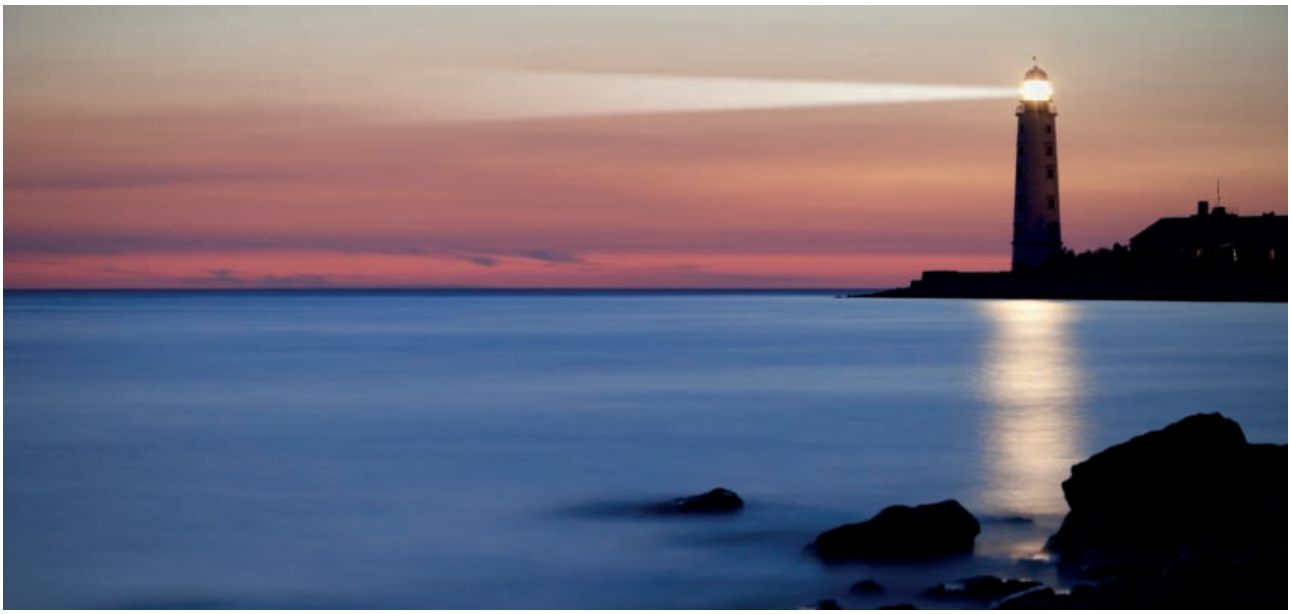
SUPPLY CHAIN

- Met with key suppliers and sub-contractors to ensure we receive the level of service expected, contracting on favourable commercial terms
- Held update calls and meetings to ensure critical suppliers are aware of our plans
- Reviewed mitigation and continuity plans
- Robust supplier audit schedule to enhance regulatory compliance

INVESTORS

- Regular investor meetings covering areas such as technology, market developments, business model, etc.
- Consulted with major shareholders
- Timely market updates, financial results and AIM compliant website kept shareholders informed regularly on performance
- The use of social media by the Company is an opportunity to reach a broader network of investors and stakeholders
- The resolutions for 2021 were passed based on acceptance levels of more than 97%

PRINCIPAL RISKS AND RISK MANAGEMENT

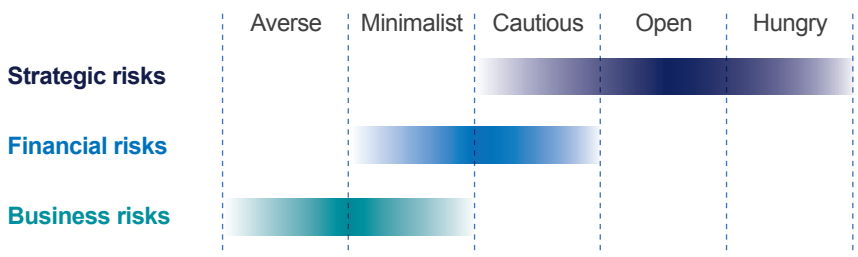


At Advanced Oncotherapy, we adopt a sensible risk-taking approach, which cannot be defined by one figure or formula. We set our risk boundaries to align with our strategy, values, policies and corporate directives. Our approach depends on the type of risks, as follows:

- **Strategic risks:** Strategic risks are risks that can significantly impact the execution of our business strategies and our ability to achieve our objectives. We include external and emerging risks in this risk area, such as industry shifts and technological shifts. These risks can all impact our business negatively long term but often also create business opportunities if managed well. Our approach to managing these risks differs from other categories as it includes evaluation of which strategic risks to take and improving the business ability to manage them by establishing risk tolerance, predicting the impact of possible risks and monitoring key risk indicators.
- **Financial risks:** The Company is exposed to multiple financial risks such as macroeconomic risks and execution risks associated with the Company's financing plan. The Board of Directors establishes the principles for the Group's financial risk management, which comprises guidelines, objectives, and limits for financial management as well as the management of financial risks within the Group.
- **Business risks:** In this risk area we include operational and commercial risks. These types of risks can often impact the financial performance of the business negatively or can have a negative reputational impact on Company. Examples are sustainability risks, such as compliance risks, and operational risks, such as IT failures as well as talent attraction and retention. The approach to managing these risks is through active prevention and by designing and implementing mitigation actions and controls.

We have implemented a risk management cycle whereby all key risks are identified, discussed, assessed and monitored. In 2021, we identified approximately 136 risks. They were classified and consolidated using a quantification method to weigh potential impacts and likelihoods of the various risks.

AVO's risk appetite



Strategic risks and mitigation strategies

The cancer market and proton therapy industry are subject to rapid changes and the light technology could be replicated

Description: The industry is characterised by rapid technological changes, new product introductions and enhancements and evolving industry standards, all of which could impact the commercial success of the LIGHT System. New alternative cancer treatment modalities could also be introduced, which would hinder the commercial prospects of the Company. A competitor could attempt to replicate a linear proton accelerator technology for medical use.

Mitigation: The Company understands that future success will depend on its ability to keep pace with the evolving needs of its customers and the medical profession on a timely and cost-effective basis and to pursue new market opportunities that develop as a result of technological and scientific advances. To keep pace with evolving standards of care, the Company has identified new opportunities and established an innovation roadmap, which is expected to enhance the product technology offering and develop new product features. An increasing number of innovations could be used in combination with radiation, such as immunotherapy. Such innovations are therefore perceived as an opportunity rather than a threat.
The development and introduction of a linear-based turn-key system requires a combination of technology and specialised skills which is hard to replicate. The Group's patent portfolio, the know-how and the diversity of the required skills which are complex to develop constitute a further barrier for new entrants.

The market for proton therapy equipment is characterised by intense competition

Description: The Company faces competition from numerous companies, many of whom have large resources, which may make it more difficult for LIGHT to achieve significant market penetration. Competitors may be better positioned to spend more aggressively on marketing, sales, intellectual property and other product initiatives and research and development activities.

Mitigation: The Company strives to be a trusted partner to customers. To do so, it relies on a business model uniquely designed to leverage the features of LIGHT and focused on aligning interests with customers. The Company has established the key foundations of a new financing approach with Kineo; this plays a crucial role in removing the upfront costs of acquiring and installing LIGHT by converting CapEx to OpEx; in addition, this reduces the reliance on the Company's balance sheet, hence further unlocking significant additional upside and accelerating

Financial risks and mitigation strategies

The successful execution of the financing strategy of the Company depends on a variety of factors and risks

Description: The financial risks faced by the Company include the ability to cover working capital needs, raise sufficient funds to support the Company through to profitability and failure to secure further contracts. The financing requirements of the Group also depend on numerous factors, including the rate of market acceptance of the LIGHT System and the ability to attract and retain customers. This means the Company often faces uncertainties in its cash flow till the installed base is large enough.

Mitigation: The Company has successfully advanced the LIGHT technology for several years, including securing research collaborations and sale contracts. The Group employs tight cost controls across the business and has raised £146 million between December 2017 and December 2021. It continually monitors opportunities which provide financing flexibility to deliver on its strategic priorities. The Company also prepares short term and medium cash flows to ensure that the business has adequate funding to execute its business strategy.

Exposure to international markets and risks

Description: The Company's strategy is focused on marketing LIGHT in various countries. Its international operations are therefore subject to a variety of risks, including difficulties in staffing and managing foreign and geographically dispersed operations, differing regulatory requirements for obtaining clearances or approvals to market LIGHT; fluctuations in foreign currency exchange rates; imposition of limitations on production, sale or export of proton therapy systems in foreign countries, etc.

Mitigation: The Company's structure across the UK, Europe and the US creates a diversified base and a natural "hedge". Furthermore, and in the context of exchange rates fluctuations, the Group does not issue or use financial instruments of a speculative nature and the Group's treasury function does not act as a profit centre. The Company has a strong commitment to anti-corruption, anti-bribery and ethical behaviours, as reflected in its current policies. All policies are regularly reviewed, and compliance training is given. Each employee is required to sign an agreement to confirm that they understand and will comply with the policies.

Macro-economic or business instability

Description: Geopolitical issues and continuing concerns over Covid-19 have contributed to volatility for the global economy. If the economic climate does not improve, the operations of the Company, its customers and suppliers could be adversely affected. Additionally, the instability has resulted in diminished liquidity and high market volatility, which could impair the ability of the Company to access capital if required. In the event of further economic slowdown, investment in medical device companies may also experience a corresponding slowdown.

Mitigation: The Company mitigates this risk by having an increasingly broad offering, service, and geographical range, limiting the impact of events in any single territory. The Group also considers political risk when assessing new contracts or product acquisitions. The Group will continue to monitor the Brexit and Covid-19 situations and assess the impact on the Group's ability to access capital in the UK.

PRINCIPAL RISKS AND RISK MANAGEMENT_Continued

Business risks and mitigation strategies

The launch of light and its market acceptance are subject to risks

Description: LIGHT is subject to market clearance and there is no certainty that it may receive market acceptance from regulators. If there is any delays to obtain market clearance, the Company may require further working capital. This means that it faces uncertainties in its cash flow until the installed base is large enough.

Mitigation: The research and development team – whose outputs rely on a validated technology (LIBO) – has identified the main technological risks and performed focused studies to ensure the underlying concepts remain viable with improved clinical outcomes. The Company's technology strategy is also regularly reviewed to ensure that the systems it operates across the Company support its strategic direction. The Directors shall seek to minimise the risk of delays by careful management of projects by working with accredited experts, suppliers and building companies.

The Company operates in an industry characterised by strict legal, regulatory and compliance requirements

Description: Changes to regulation as a result of Brexit, evolving political landscapes and more stringent norms in the medical industry could have an impact on the approval process of the LIGHT System and the Company's ability to sell and install future machines. Failure to proactively identify and comply with industry laws and medical regulatory aspects could result in fines, penalties, business disruption, reduced revenue, and/or potential exclusion from tender processes.

Mitigation: The Company proactively monitors changes in regulation and legislation and ensures that all obligations are complied with, and forthcoming legislation is appropriately planned for. It ensures that employees understand legal risks and how to comply via anti-bribery and corruption policies, reinforced by the Company's Code of Conduct. Furthermore, targeted audit reviews are undertaken to ensure policies and training are embedded. When required, external advice is also taken, particularly for situation where capabilities are not available in-house.

The commercial prospects of the Company may fluctuate

Description: The Company relies solely on the commercialisation of its LIGHT System to generate revenue. Any factor materially adversely affecting the Company's ability to market and sell its LIGHT System, its pricing and demand would have a material adverse effect on our financial condition and results of operations. Demand may not increase as quickly as planned. Sales cycles in proton therapy tend to be long, which may contribute to substantial fluctuations in the operating and financial results.

Mitigation: The Company is dedicated to understanding the requirements of customers and pre-empting their needs. As a result, it is seeking feedback from existing and prospective customers, which is key to accelerate their decision process and ensuring customers' satisfaction. The initiatives to provide vendor financing and leasing arrangements to customers as well as developing new product features such as FLASH and minibeams are consistent with the Company's commitment of building a flexible customer-centric model.

The Company has a limited history of assembling light systems in commercial quantities

Description: The Company has only a limited history of assembling and installing the LIGHT System and, as a result, it may have difficulty delivering LIGHT in sufficient quantities in a timely manner or may not have enough data to accurately predict future component demand. Following market disruptions post Brexit and Covid-19, the Company experienced delays in obtaining components from suppliers, which may delay its ability to assemble future systems. Accordingly, the Company may encounter difficulties in scaling up production, including problems with quality control and assurance, component supply shortages, increased costs, and shortages of qualified personnel.

Mitigation: The Company outsources production to trusted manufacturing and global partners which the Group assesses regularly. The Group also has industry-leading quality management systems and audits supply partners where appropriate. The Group also intends to maintain appropriate stock levels of its key parts of LIGHT, with a focus on long-lead items, allowing to better serve clients' needs.

Hiring and retaining talents is a necessity but is not without risks

Description: The Company's success depends on the skills, experience and performance of key members of the senior management team. The individual and collective efforts of these employees are important as the Company continues to develop its LIGHT System, and as it expands its commercial activities. The loss or incapacity of existing members of the executive management team could adversely affect the Company's operations if the Company experiences difficulties in hiring qualified successors. Success also depends on the Company's ability to attract and retain highly skilled engineers, scientists, and technicians. The Company may not be able to attract or retain qualified managers, engineers, scientists, and technicians in the future due to the competition for qualified personnel among medical device businesses,

Mitigation: The Company seeks to attract and retain high quality personnel by providing employees with a rewarding package of salary and benefits which include share option scheme, private medical insurance, and flexible working. Maintaining a high level of employee satisfaction and engagement is also key. This is done through an investment in appropriate quality resources and infrastructure to support the staff and efficient working practices. This includes focus on providing learning and development opportunities, training, and career paths to enable people to fulfil their potential.

Reliance on information technology systems and infrastructure is impacting how the Company operates

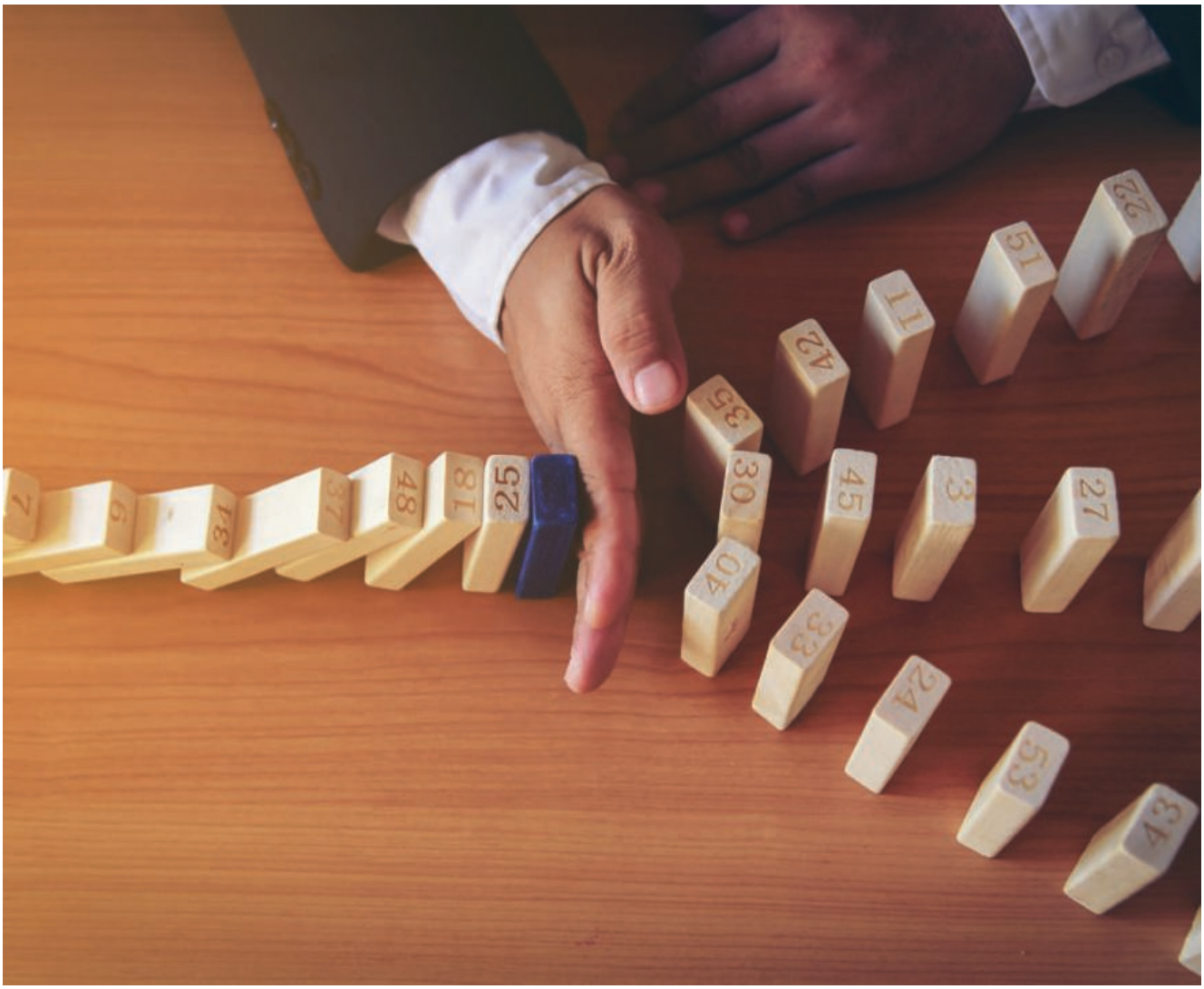
Description: The Company's success depends on its infrastructure and set-up as well as its information technology systems. The LIGHT System is also equipped with the latest generation of propriety software packages developed by third-parties. Information technology systems are vulnerable to damage from a variety of sources, including network failures, malicious human acts and natural disasters. Moreover, despite network security and back-up measures, some of the servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems.

Mitigation: The Company has taken precautionary measures to prevent unanticipated problems, including the implementation of a system of data storage, offsite backup and monitoring of key coding and modelling data. Following the disruption caused by Covid-19 and the necessary need to support remote operations, the Company has invested in servers dedicated to highspeed computation which has significantly reduced the time required to run operations and reduce risks.

Reliance on third parties requires a carefull risk assessment

Description: The Company relies on arrangement with third-parties for manufacturing components of the LIGHT System. As a result, the Company is subject to disruptions, delays, and potential increased costs due to factors beyond its control. Any failure to deliver, install or service future LIGHT Systems in a timely manner may damage the Company's reputation, with the risk of losing customers.

Mitigation: Wherever possible, the Company seeks to have duplicate suppliers to lessen the reliance on a particular vendor. Arrangements with third-parties also encompass an array of protective clauses in favour of the Company.



GOVERNANCE REPORT

ADVANCED ONCOTHERAPY
TEAM

The Executive Team provides input and recommendations to assist the Chief Executive Officer in the day-to-day management of the business and its operations. Team members combine experience and expertise across a range of disciplines.

Dr. Michel Baelen
Director, Regulatory Affairs

- Over 20 years of experience in Regulatory and Quality for proton therapy
- Former Head of Regulatory Affairs and Quality Assurance at IBA
- Former Quality Coordinator at the University Hospital Saint-Luc at the Catholic University of Louvain

Mrs. Bridget Biggar
HR Director

- Fellow of the UK Chartered Institute of Personnel and Development
- Masters in Applied Positive Psychology from the University of Pennsylvania
- 13 years as an employer representative on the Employment Tribunal Board of England and Wales; has been an HR Director in various start-ups

Dr. Jonathan Farr
Chief Clinical Officer

- Over 15 years of Radiation Physics experience across USA and Europe
- Former Chief of Radiation physics and Associate Professor at St. Jude Children's Research Hospital
- Current Privat Dozent at University of Essen-duisburg and chief medical physicist at WPE
- Author of many peer-reviewed publications on advances in proton, other particles and photon radiotherapy

Dr. Manuel Gallas
Technical and Engineering Director

- 15 years' experience managing complex technology product design, innovation, and R&D projects
- Ph.D. in High Energy Physics and an eMBA in Management of Technology, Innovation, and Entrepreneurship
- Fellow then Staff at CERN from 1999 to 2008 working on the PS-DIRAC proton experiment and the ATLAS Large Hadron Collider (LHC), Higgssearching experiment

Mrs. Louise Harley-Smeur
Senior Vice-President, Intellectual Property

- European Patent Attorney and Head of the Intellectual Property Department
- Specialising in IP since 2001, with a focus on medical technology, devices, and business
- Previously worked in various UK hospitals as a medical physicist, specialising in radiotherapy and imaging

Mr. Wim Hulsbergen
Vice-President, IT Services

- Over 20 years experience building IT organisations enabling businesses to drive and enable their strategy
- Specialises in digital transformation, optimising and automating business processes, ERP deployment and organisational transformation

Mr. Moataz Karmalawy
Chief Commercial Officer, President US

- Former General Manager of the Worldwide Particle Therapy Business for Varian Medical Systems, the world's largest manufacturer of radiotherapy equipment
- Grew the order book of Varian to over $1bn and achieved a 50% market share of the global particle therapy products market
- Also worked at Philips Medical Systems, Inc and won a performance excellence award for quality & customer satisfaction industry wide

Mr. Ed Lee
Chief Operating Officer, President Europe

- Former Production and Technical Field Service Director at Optivus Proton Therapy (Loma Linda University Medical Center)
- 30 years manufacturing and operations experience spanning from high-volume/low-mix to low-volume/high-mix industries such as Automotive, Aerospace, Military/ Defence, Nuclear, and Medical Devices

Mrs. Berengere Pons-Chabord
Senior Vice-President, Corporate Finance

- Strong experience in financial analysis, business planning and Board/management reporting
- Previously worked for Lazard as a Vice-President in M&A
- Transaction experience covers a wide range of private and public transactions, including acquisitions, divestitures, and more complex structures

Mr. Graham Pughe
Senior Vice-President, Accounting

- Seasoned finance professional with a strong technical grounding within all areas of the finance spectrum
- Implemented robust and pragmatic solutions for various industries including newspaper publishing, food manufacturing and building materials

Mr. Benoit Raskin
Programme Director

- More than 20 years' experience in proton therapy as project manager and Director at IBA
- Considerable experience of site installation, commissioning, contract acquisition and customer acceptance

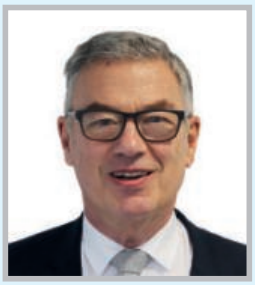
Mr. Julian Tokuta
Director, Supply Chain

- More than 20 years of professional procurement experience at Proxima Group and Accenture
- Substantial expertise delivering supply chain and procurement strategies that address unanticipated business challenges

BOARD OF DIRECTORS

As a Board we have collective responsibility for the long-term success of Advanced Oncotherapy and are accountable to all stakeholders of the Company.

(A) Member of the Audit Committee
(R) Member of the Remuneration Committee
(S) Member of the Strategic Committee
(C) Chairman



Dr. Michael Sinclair (C)

Executive Chairman

Appointed: June 2006

Skills and Experience
Michael brings extensive expertise and experience to the board, drawing on over 40 years founding, building and leading hospitals and healthcare institutions worldwide.

Prior to Advanced Oncotherapy, Michael was the founder and former CEO of Nestor Healthcare and Allied Medical Group Limited; the Chairman and founder of Lifetime Corporation Inc. and US based Atlantic Medical Management LLP; and a Former member of the Board of Overseers of Tufts University Medical School. Michael also previously held a number of appointments at teaching hospitals in London.

Michael has an MB, BS in Medicine and physiology.

External Appointments
Michael currently serves as a Trustee of The London Clinic, Non-Executive Chairman of Symthera Inc, a Non-Executive Director of Opiant Pharmaceuticals Inc., and is a Board member of a number of educational non-profits.

Mr. Michael Bradfield (A) (R)

Non-Executive Director

Appointed: April 2013

Skills and Experience
Michael brings significant corporate leadership experience, with particular expertise in marketing and insurance.

Prior to Advanced Oncotherapy, Michael founded and was the CEO of Hospital Plan Insurance Services, a company sold to AIG in 2000. He was also the Chairman and CEO of Acacia Asset Management Ltd, Hamilton.

Michael has a law degree from LSE.

External Appointments
Michael currently serves as the Chairman of Fairford Medical Ltd, Fairford Medical Services Ltd, Health Imaging Solutions Ltd and Quest Medical UK Ltd, all active in the Diagnostic Medical Imaging field.

He is also on the board of Stockgain Asset Management, Henstridge Properties Ltd, the Vail Foundation, and the Covenant & Conversation Trust (registered charity).

Mr. Hans von Celsing (A) (R) (S)

Non-Executive Director

Appointed: January 2017

Skills and Experience
Hans brings over 35 years of experience launching, managing and developing medical technology businesses with a focus on radiation therapy, as well as developing corporate governance practices for scaling businesses.

Prior to Advanced Oncotherapy, Hans worked in the radiation oncology market where he was an Advisor to Mevion Medical Systems and Executive Vice President of Elekta. In these roles, he was responsible for global operations and international expansion, including Europe and Asia.

Hans has an MBA from Harvard School of Economics.

External Appointments
Hans currently serves as the Executive Chairman of Clinical Laser Thermia Systems AB; Chairman of Gelexir Healthcare Ltd, Peptonic Medical and Partner Fondkommission AB; and part-time consultant at Berkshire Investment Management.

Ms. Lori Cross (S)

Non-Executive Director

Appointed: September 2020

Skills and Experience
Lori brings extensive experience in strategy, innovation, operational scaling, and leadership development, building on a career transforming leading global organisations in the medical technology and life sciences sectors.

Prior to Advanced Oncotherapy, Lori has successfully designed and commercialised numerous disruptive healthcare business models, with executive positions at VIASYS Healthcare (acquired by Cardinal Health), Instrumentarium/GE Medical Systems, Smith & Nephew and Baxter Edwards Laboratories

Lori has a BS in Biomedical Engineering, MBA and Masters of Engineering Biomedical Systems.

External Appointments
Lori currently serves as the President and founder of MindSpan Consulting; and is a Board member of Fastems and Electrosonic.

Prof. Steve Myers
Executive Director and ADAM Executive Chairman

Appointed: November 2015

Skills and Experience
Steve is a world renowned and leading expert on accelerator physics, bringing extensive experience in delivering complex physics projects over 40 years at CERN.

Steve joined CERN in 1972, becoming the leader of the CERN Accelerator Beams Division in 2000 and the Director of Accelerators and Technology in 2009. From 2014 to 2016 he was the Head of CERN Medical Applications.

He has been awarded the IOP Duddell (renamed Gabor) medal and prize, a lifetime achievement award from the Internal Particle Accelerators Committee and shared the EPS Edison Volta Prize.

External Appointments
Steve is an Honorary Member of the European Physical Society and of the Royal Irish Academy.

Dr. Nick Plowman
Non-Executive Director and Chairman of the Medical Advisory Board

Appointed: February 2017

Skills and Experience
Nick has unparalleled clinical experience in using new radiation techniques for paediatric and adult oncology, bringing invaluable expertise regarding the deployment of Advanced Oncotherapy's LIGHT system. Nick has pioneered uses of lens sparing, Gamma Knife, IMRT, Cyberknife, and linac based radiosurgery. He has written over 300 research papers in radiotherapy and clinical oncology and part-funds a laboratory project at Brunel University exploring DNA repair mechanisms, including those relating to irradiated tumours.

His academic qualifications include an MA, MD, FRCP, FRCR.

External Appointments
Nick currently also serves as the Senior Clinical Oncologist to St Bartholomew's Hospital and The Hospital for Sick Children Great Ormond Street, London.

Mr. Nicolas Serandour
Chief Executive Officer

Appointed: September 2014

Skills and Experience
Nicolas was appointed CEO in October 2016, having previously held the roles of Group Finance Director and Chief Operating Officer.

He brings extensive financial management and strategic advisory experience, drawing on 15 years spent at Lazard, Lehman Brothers and JPMorgan where he specialised in advising healthcare businesses worldwide.

He attended ESSEC Management school and has a masters in risk management.

External Appointments
n/a

Dr. Enrico Vanni (A) (R) (S)
Non-Executive Director

Appointed: October 2013

Skills and Experience
Enrico brings extensive advisory and consulting experience, having previously led McKinsey & Co's European pharmaceutical practice, where he advised boards on strategic healthcare transformation and governance matters. He was also a Director of Eclosion2 SA, Alcon Inc. and Actavis Plc.

In his earlier career, Enrico was a research engineer at IBM and an assistant in Chemistry at University of Frankfurt.

Since retiring in 2007, Enrico has continued to support leaders of pharmaceutical and biotechnology companies on core strategic challenges facing the healthcare industry.

External Appointments
Enrico is also Vice-chairman of Novartis; and Board member of Lombard Odier & Cie SA.

Mrs. Renhua Zhang*
Non-Executive Director

Appointed: August 2018

Skills and Experience
Renhua brings considerable healthcare experience and expertise, with a focus on the Chinese medical and pharmaceutical market. She co-founded and was CEO of Realcan Pharmaceutical, a large distributor of medical drugs and equipment in China with access to more than 8,000 hospitals and 33,000 primary medical institutions. Renhua was also the former Director of Nursing for one of China's leading regional Hospital Systems

She graduated in Business Administration from the Shandong Television Broadcast University.

External Appointments
Renhua is also currently CEO and Vice Chairman of the Board of Realcan Pharmaceutical; Supervisor at the Shandong Ruixiang Dental; Supervisor at Shandong Chengen Invst. Co., Ltd; Director and General Manager at Shandong Realcan Pharmaceutical Distribution Co., Ltd; Executive Director at Yantai Ruiyou Invst. Co., Ltd.

** Mr Chunlin Han is an alternate director (unremunerated) for Mrs. Zhang so that he may attend board meetings when Mrs. Renhua Zhang is unable to do so*

MEDICAL ADVISORS

The medical advisory board comprises distinguished scientists and leaders of medical research and physics institutions. It provides insight, scientific direction, and expertise to Advanced Oncotherapy's leadership team.

Prof. Ugo Amaldi
Adviser

- Has been working at CERN since the 1970s; founded the DELPHI Collaboration, at CERN's LEP Accelerator: established TERA, the Italian Foundation for Hadrontherapy
- Led the design effort of the Italian National Centre of Oncological Hadrontherapy (CNAO)
- Awarded the Gold Medal for science and culture by the President of the Republic of Italy
- Appointed Fellow of the European Physics Society

Dr. Jay Loeffler, MD
Adviser

- Herman Suit Professor of Radiation Oncology at Harvard Medical School, Boston
- Chair of the Department of Radiation Oncology at the Massachusetts General Hospital, Boston
- Member of the Institute of Medicine of the National Academies of Science

Dr. Margaret Spittle, OBE
Adviser

- Clinical oncologist at University College London Hospital (UCLH) and consultant adviser in Radiation Medicine to Royal Navy and the Ministry of Defence
- Member of the Nuclear Safety Committee and Medical Adviser Board member to UK All Party Committee on Breast Cancer

Dr. Euan Thomson
Adviser

- Trained as a physicist; nearly 20 years of experience in research, clinical practice, consulting and corporate management and more than 14 years of experience as a CEO
- Operating partner at Khosla Ventures; CEO of AliveCor; Director of the Hospice of the Valley
- Served as global lead of R&D, digital technology and advanced innovation for J&J; previously the CEO of Accuray for 10 years; consultant for other medical device companies including Varian Oncology Systems and Radionics; has served as Chair of the California Division of the Entrepreneur of the Year award

CORPORATE GOVERNANCE REPORT

The Directors recognise the importance of sound corporate governance and are committed to maintaining high standards of corporate governance.

Introduction

The Board of the Company is collectively accountable to the Company's shareholders for good corporate governance, with the Chairman taking a lead on corporate governance matters. Accordingly, and in accordance with the London Stock Exchange's requirement for all AIM-quoted companies to comply with a recognised corporate governance code, the Board of Directors of the Company adopted the Quoted Companies Alliance (QCA) Corporate Governance Code (Code). The Board considered that the Code provides the Company with the framework to help ensure that a strong level of governance is maintained, enabling the Company to embed the governance culture that exists within the organisation as part of building a successful and sustainable business for all its stakeholders.

The Code is constructed around 10 principles, taking key elements of good governance and applying them in a manner which is workable for the needs of a growing company in pursuit of medium to long-term value creation for shareholders. The Board is of the unanimous opinion that the Company complies with the Code and any divergence from the Code are, in the circumstances, reasonable, appropriate and in the best interests of the stakeholders of the Company as a whole.

This statement sets out how we currently comply with the provisions of the QCA Code and – when relevant – the reasons for any departures from it. A full copy of the QCA Code is available from the QCA's website: www.theqca.com

The QCA Code contains the following 10 principles:

- Principle 1 – establish a strategy and business model which promote long-term value for shareholders;
- Principle 2 – seek to understand and meet shareholder needs and expectations;
- Principle 3 – take into account wider stakeholder and social responsibilities and their implications for long-term success;
- Principle 4 – embed effective risk management, considering both opportunities and threats, throughout the organisation;
- Principle 5 – maintain the board as a well-functioning, balanced team led by the chair;
- Principle 6 – ensure that between them the Directors have the necessary up-to-date experience, skills and capabilities;
- Principle 7 – evaluate board performance based on clear and relevant objectives, seeking continuous improvement;
- Principle 8 – promote a corporate culture that is based on ethical values and behaviours;
- Principle 9 – maintain governance structures and processes that are fit for purpose and support good decision-making by the Board;
- Principle 10 – communicate how the company is governed and is performing by maintaining a dialogue with shareholders and other relevant stakeholders.

Principle 1 – Establish a strategy and business model which promote long-term value for shareholders

The Company's ambition and growth prospects are underpinned by a vast unmet medical need, the development of a proton-based medical system that has been tailored

to meet the needs of physicians, an innovative business model and a lean and robust infrastructure to meet future demand and introduce future product upgrades.

The Company's vision is to democratise proton therapy, which – as explained within the previous Strategic Report section, on pages 13 and 14 – is driven through five strategic priorities:

- **solve** customers' need by introducing a turn-key solution that delivers the best outcome for patients whilst making treatments more affordable;
- **support** customers through long-term servicing contracts;
- **scale** the Company's infrastructure to reduce future cost and lead times and increase throughput, the foundation for delivering a fast-growing pipeline;
- **share** a common vision of doing good and well with all stakeholders, including customers and suppliers, in the spirit of aligning interest in the long-term;
- **sustain** the Company's competitive advantages through innovation, investment in talents and a commitment to make a positive impact on society and environment.

Its business model is further detailed on pages 67 and 68.

The Company operates in a highly regulated sector, and this is reflected in the principal risks and uncertainties that may affect the business, which are set out in more detail on pages 73 to 76.

Principle 2 – Seek to understand and meet shareholder needs and expectations

The Board of the Company endeavours to engage in clear and consistent dialogue with both existing and potential shareholders to assess their needs, expectations, and any concerns they may have as well as ensure that the Company's strategy, business model and progress are clearly understood.

This active communication is maintained through a planned programme of investor relations which includes formal presentations, meetings with investors and analysts on a regular basis. Regular communication also takes place through the Company's annual report and website, which contain up-to-date information on the Group's activities. This is complemented with the use of a Regulatory Information Service and social media. The Company has established an email alert service on its website to which shareholders and other interested parties can subscribe to receive company announcements as and when they wish (www.avoplc.com/en-gb/Investors/Investor-Alert-Service). There is also a designated email address for shareholder liaison – ir@advancedoncotherapy.com – and all contact details are included on the investor relations website.

The Board also recognises that the Annual General Meeting (AGM) provides an opportunity to meet shareholders and it values their feedback. All shareholders are given the opportunity to ask questions and raise issues; this can be done formally during the meeting or in writing prior to the meeting. The Notice of the AGM is sent to shareholders at least 21 days before the date of the meeting and all Directors routinely attend the AGM and are available to answer questions raised by shareholders.

Copies of the annual report (which includes the notice of AGM) and the interim report are available to all shareholders and can be downloaded from the investors' section https://www.avoplc.com/en-gb/Investors/Company-Documents. Alternatively, they are available on request by writing to the Company Secretary at Henry.Clarke@avo-adam.com. Other information for shareholders – including the results of the resolutions of the AGM results and the share price performance of the Company – is also provided on the Group's website.

Principle 3 – Take into account wider stakeholder and social responsibilities and their implications for long-term success

The Company recognises that the introduction of LIGHT and more broadly the implementation of innovative health solutions for cancer patients are more likely to be successful when a broad range of stakeholders and decision-makers are part of the process. Involving medical, technical, and other experts to ensure that all aspects of the patient pathway are covered from the outset creates ownership and contributes to the long-term success for the Company as a whole. Therefore, the Board places utmost importance on the feedback from all stakeholders, which is key to frame and adjust the Company's strategy.

The Company is also aware of its corporate social and environmental responsibilities. It is the Group's policy and practice to comply with health, safety and environmental regulations and the requirements of the countries in which it operates to protect its employees, partners, assets, and the environment. A range of processes and systems have also been put in place to ensure that there is close oversight and contact with these key resources and relationships. This commitment is evidenced and underpinned by the vision and values of the Company, described in pages 7 and 8 of the Strategic Report. The Board is committed to harness this mindset to bring the right stakeholders together and connect healthcare providers, patients and information systems in a way that is scalable and sustainable. It remains grounded in the Company's purpose of delivering quality, patient-centred care and the delivery of better outcome for patients. How the Board seeks to engage with all stakeholders and ascertain their feedback is set out in our section 172 statement on pages 71 and 72.

Principle 4 – Embed effective risk management, considering both opportunities and threats, throughout the organisation

Risk assessment and evaluation is an essential part of the Company's planning and control system. This is also critical to safeguard the Company's assets and enable it to meet its strategic objectives. The Company operates in

a highly regulated environment and as such is necessarily subject to stringent medical norms and regulation as well a rigorous health and safety regime.

The Board has delegated the responsibility for reviewing and monitoring the risk management systems to the Audit Committee, which works closely with the management and reports back to the Board. Any such system of financial and operational controls can provide reasonable, but not absolute assurance, against material misstatement or loss. The Board considers that the internal controls in place are appropriate for the size, complexity, and risk profile of the Company. The Group receives regular feedback from its external auditors on the state of its risk management and internal controls, monitoring and reporting to the Board on the Groups performance.

The Company maintains a risk register which is reviewed regularly, and which covers a variety of financial, operational, economic, and regulatory uncertainties. This register allows the Board to appraise external and internal threats to the business and to plan and mitigate accordingly. Principal risks and uncertainties that may affect the business are set out in more detail on pages 73 to 76. Notes 1 and 19 within the Financial Report also expands on the Company's exposure to risk and the steps to control and manage exposure to risk. The Board has a conservative approach to financial risk management and the Group does not use any speculative or non-basic financial instruments.

The Company has adopted a Code of Conduct which sets out the standards that it expects all employees and representatives of the Company to meet. It is the Board's view that encouraging these high working standards helps to mitigate against risks arising in the day-to-day activities.

BNF Insurance Services in the UK and Kessler & Co SA in Switzerland provided insurance services to the Company. Under their guidance, the Company has put in place a scheme of insurance which reflects both the current and medium-term needs of the business and this is continually monitored through periodic reviews with our advisers and our underwriters.

Principle 5 – Maintain the board as a well-functioning, balanced team led by the chair

The Board

The Board currently comprises of six Non-Executive Directors and three Executive Directors. The biographies on pages 81 and 82 include further disclosures in relation to the Directors, their relevant experience, skills and personal qualities and capabilities.

Duties

The Board is collectively responsible for the success of Advanced Oncotherapy and provides entrepreneurial leadership of the Company within the framework of effective controls, which enable tasks to be assessed and managed. It sets out the Company's values and standards and ensures that its obligations to shareholders and other stakeholders are understood and met. In accordance with the Companies Act 2006, the Board complies with the following:

Duty	Further information
Act within their powers	-
Promote the success of the Company	This duty is set out in section 172 of the Act (see pages 71 and 72) and provides that Directors "must act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole"
Exercise independent judgement	See further details below on Independence
Exercise reasonable care, skill and diligence	See further details below on Reasonable care, skill and diligence, Time commitment and Attendance
Avoid conflicts of interest	See further details below on Conflicts of interest and Remuneration
Avoid benefits from third parties	Id.
Declare any interest in a proposed transaction or arrangement	Id.

Further details on the governance structure are set out at Principle 9.

Independence

The Directors are mindful that a balance between Executive and independent Non-Executive Directors should be maintained to facilitate impartial and equitable decision making.

The individual members of the Board have equal responsibility for the overall stewardship, management, and performance of the Group and for the approval of its long-term objectives and strategic plans.

Whilst the Board recognises that having an Executive Chairman is not considered best practice under the QCA Code, it feels that the commitment, expertise, industry connections and enthusiasm the Executive Chairman brings to the role offset this. The role of the Chairman is reviewed periodically by the Board.

The current division of responsibilities between the Executive Chairman and Chief Executive Officer have each been agreed by the Board. Dr Michael Sinclair, the Executive Chairman, is responsible for the running of the Board. Nicolas Serandour, the Chief Executive Officer, has executive responsibility for running the Group's business and implementing its strategy.

All Non-Executive Directors serving at the year-end bring an independent judgement. Mrs. Renhua Zhang (Non-Executive Director) is not considered to be independent as she represents a large shareholder, Liquid Harmony. The Board does not consider the shareholdings of the other Non-Executive Directors as detailed on page 102 to have any effect on their independence. The Executive Chairman and other Non-Executive Directors have other directorships, which are not deemed to conflict with the business of the Company.

Reasonable care, skill, and diligence

Directors have a duty of reasonable care, skill, and diligence. To do so, they take the following into consideration in any decision-making process:

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

Further information on the knowledge, skill and experience of Directors can be found on pages 81 and 82.

Time commitment

Each board member commits sufficient time to fulfil their duties and obligations to the Board and the Company. They attend regular board meetings and join ad-hoc board calls and offer availability for consultation when needed. The contractual arrangements between the Directors and the Company specify the minimum time commitments which are considered sufficient for the proper discharge of their duties. The time commitment is commensurate with the size and complexity of a quoted company. However, in exceptional circumstances all board members understand the need to commit additional time.

Attendance

The Board met six times in 2021, excluding separate ad-hoc meetings and calls. Due to COVID-19 restrictions, the Board and committees have been restricted in their ability to physically meet and have utilised virtual meeting rooms to ensure dialogue, challenge and support has been provided throughout. The record of each Director's attendance at Board meetings is set out thereafter.

Director	*Scheduled Board meetings*	*Ad hoc Board meetings*	*Audit and Remuneration Committees*
Dr. Michael Sinclair	6/6	9	-
Mr. Michael Bradfield	4/6	4	2/5
Mr. Hans von Celsing	6/6	7	5/5
Ms. Lori Cross	6/6	4	-
Prof. Steve Myers, OBE	6/6	7	-
Dr. Nick Plowman	4/6	3	-
Mr. Nicolas Serandour	6/6	10	-
Dr. Enrico Vanni	6/6	6	5/5
Mrs. Renhua Zhang*	4/6	2	-

** Mr Chunlin Han is an alternate director for Mrs. Zhang so that he may attend board meetings when Mrs. Renhua Zhang is unable to do so*

Directors who were unable to attend specific meetings reviewed the relevant papers and provided their comments to the Executive Chairman of the Board or Committee. Any Director who misses a meeting receives, as a matter of course, the minutes of that meeting for reference.

Conflicts of interest

To address the provisions of Section 175 of the Companies Act 2006 relating to conflicts of interest, the Company's Articles of Association allow the Board to authorise situations in which a Director has, or may have, a conflict of interest. Directors are required to give notice of any potential situations or transactional conflicts that are to be considered at the next Board meeting and, if considered appropriate, conflicts are authorised. Directors are not permitted to participate in such considerations or to vote regarding their own conflicts.

Remuneration

The Board considers and determines the remuneration of the Executive and Non-Executive Directors. No Director is involved in setting his or her own remuneration.

Principle 6 – Ensure that between them the Directors have the necessary up-to-date experience, skills and capabilities

The Directors' biographies appear on pages 81 and 82.

The Board feels that it has an appropriate balance between independence, knowledge of the Company's technology, sector experience and professional standing to allow it to discharge its duties and responsibilities well. All Directors are encouraged to constructively challenge strategy, scrutinise performance and use independent judgement based on their respective knowledge and experience on all matters affecting the business.

The Board keeps abreast of ongoing changes relating to governance and compliance, the AIM Rules for Companies,

QCA Code, the Market Abuse Regulation and other statutory and regulatory developments. In that regard, all Directors have access to the Company's NOMAD, Company Secretary, lawyers and auditors are able to obtain advice from other external bodies as and when required, at the Company's expense. Details of the Company's advisors can be found on the website and on page 151 of the annual report.

Principle 7 – Evaluate board performance based on clear and relevant objectives, seeking continuous improvement

The Board seeks to improve the ways in which it interacts, and the way information is presented to it. The processes that have been put in place allow for a consistent approach to reporting, thus aiding analysis by the Board of all matters at hand.

In May 2021, the Board conducted a Board Effectiveness review under the auspices of the Senior Independent Director Hans von Celsing and Non-Executive Director Lori Cross, assisted by the Company Secretary. The Board may utilise the results of the evaluation process when considering the adequacy of the composition of the Board, to identify any training and development needs and for succession planning. Separately to this, the executive Chairman and non-Executive Directors regularly meet and discuss performance with members of the Executive team.

In the context of evaluating the Board performance and aligning this review exercise with the expectations of shareholders, each Director stands for re-election at the AGM and significant emphasis is placed on new appointments:

- Services and re-election – All Executive Directors have service agreements with the Group terminable by either party upon the minimum notice period being met. The notice period is 24 months for Dr. Michael Sinclair and Nicolas Serandour and six months for Prof. Steve Myers. Non-Executive Directors are initially appointed for a three-year term, but their appointment is terminable by either party on three months' written notice. The letters of appointment of all Directors are available for inspection at the Company's registered office during normal business hours. Executive and Non-Executive Directors retire by rotation in accordance with the Company's Articles of Association which prescribe that at every Annual General Meeting one third of the Directors shall retire from office. However, to underline their accountability to shareholders and the Board's commitment to appropriate corporate governance, each Director will stand for re-election at the upcoming AGM. The Board has concluded that each Director is eligible for re-election;
- New appointments – When a new appointment to the Board is made or a removal is being considered, thought is given to the skills, knowledge and experience that could be of benefit to the Board. In the case of a new appointment, a formal process is then undertaken, which may involve external recruitment agencies, with appropriate consideration being given, regarding Executive appointments, to internal and external candidates. Before undertaking the appointment of a Non-Executive Director, the Executive Chairman establishes that the prospective Director can give the time and commitment necessary to fulfil his/her duties, in terms of availability both to prepare for and attend meetings and to discuss matters at other times.

Principle 8 – Promote a corporate culture that is based on ethical values and behaviours

The core principle of the Company is clear: to democratise proton therapy. As such, ethical values – life, safety, quality and innovation – and behaviours are at the heart of what each employee and Director does. The Board seeks to enshrine such ethical values and behaviours throughout the conduct of all of activities of the Company. These values – further outlined in pages 7 and 8 – together with our commitment to provide a positive impact on society and environment – as detailed in pages 11 and 12 – are set out in the Company's policies, working practices and systems.

The Board leads by example. The Board seeks to:

- treat all persons fairly and equitably with a focus on openness and well-being, through clearly defined parameters of operation;
- take the welfare of all employees extremely seriously and invest in people;
- promote diversity;
- ensure values are embedded in a positive and supportive environment through full compliance with norms and certification and the implementation of clear policies.

Treating all persons fairly and equitably with a focus on openness and well-being, through clearly defined parameters of operation

In dealing with each of the Company's principal stakeholders, the Board encourages staff to operate in an honest and respectful manner; it believes that achieving a common awareness across all employees plays a major role in maintaining good employee relations. This culture of honesty and respect – reflected in the continued support and dedication shown by staff to execute the strategic plan – is promoted by listening to and actioning feedback given during the ROADMap process (performance management conversations), and internal HR channels, with immediate attention paid to any concerns raised. The Company is continually improving the support provided to managers to help ensure that they are actively listening and valuing their teams.

Taking the welfare of all employees extremely seriously and investing in people

The Company takes the welfare of all its employees extremely seriously and continues to invest in its people, who are encouraged to develop and grow with the business. Advanced Oncotherapy strives to continually improve the working environment and benefits of its people. The Company's commitment to staff is shown in the significant investment made to upgrade facilities and the working

environment. During the Covid-19 pandemic, the Company has also increased communication and support to all staff with frequent updates about the local situation and measures taken to keep everyone safe. The Company has invested in the training of the HR team to become mental health first aiders to support the increased levels of stress and anxiety some are facing in the light of Covid-19.

Promoting diversity

The Board believes it is crucial for the success of the Company to have a diverse workforce comprised of individuals with different ideas, strengths, interests, and backgrounds. It sees a great benefit in the diversity of employees, as this helps the Company to better fulfil the wishes and multi-faceted demands of customers around the world and provides a higher-performing workplace. The Company strives to create an environment where all employees are heard and appreciated – regardless of gender, nationality, ethnic origin, religion, world view, abilities, age, sexual orientation, or identity.

The Board believes in mixed leadership teams as a competitive advantage and driver of success. By the end of 2021, women made up 38% of the workforce, 22% of those being managers and 40% in technical roles. The management team is represented by 30% women and 5 nationalities. The Group applies fair and equitable employment policies, and these ensure that entry into, and progression within, the Group is determined solely by the fair application of relevant job criteria and by personal ability and competence. The Company actively promotes the career development of its employees. Full and fair consideration (having regard to the person's particular aptitudes and abilities) is given to applications for employment and the career development of disabled persons. The Group will take all practicable steps to ensure that if an employee becomes disabled during the time he/she is employed, his/her employment can continue. It continues to review both performance and potential as a key part of the annual performance management, career development and succession planning processes. Diversity is at the heart of the Group culture, which is characterised by a meritocratic and collaborative ethos. 31 different nationalities are represented in the Group as of 31st December 2021.

Ensuring values are embedded in a positive and supportive environment through full compliance with norms and certification and the implementation of clear policies

The commercialisation of the LIGHT system requires the business to have a robust quality management system which is third-party audited to ISO: 13485 standards. Underpinning this quality management system are processes to ensure that necessary safeguards are in place to ensure the integrity of this system and accordingly the quality of the products under development. Further information can be found on pages 63 to 65.

Policies are also in place covering key matters such as bribery, protection of intellectual property and sensitive information, conflicts of interest, whistleblowing. These are vigorously enforced and monitored. These are further outlined at principle 9.

Principle 9 – Maintain governance structures and processes that are fit for purpose and support good decision-making by the Board

The Board retains full and effective control over the Company and holds regular Board meetings at which financial, operational and other reports are considered and where appropriate voted upon. It has ultimate accountability for good governance and is responsible for monitoring the activities of the management team. The Board is responsible for the Company's strategy and key financial and compliance issues.

The Board is satisfied that the Company's governance structures and processes are consistent with its current size and complexity. The current structure enables the retention of key skill sets within the Company whilst facilitating the enhancement of the senior management base and the continuing development of the Board and the management in line with the QCA Code's key principles. As the Company grows, the Directors will ensure that the governance framework is reviewed and appropriately updated to support the development of the business. The Company continues to look at how to best improve its corporate governance; and as a fast-growing company Advanced Oncotherapy is constantly looking for ways to strengthen its Board, whilst ensuring that the business is led by people with the right experience, passion, and enthusiasm.

Key processes and structures in place include the following:

- clear segmentation of roles and responsibilities with a formal list of matters reserved to the Board's approval;
- internal control focused on safeguarding the Company's assets;
- clear guidelines to support healthy and open debates;
- dedicated Board Committees;
- share dealing policies;
- whistleblowing procedures;
- anti-bribery and corruption policies;
- appointment of a Company Secretary to support the Board and ensure processes are being followed.

Clear segmentation of roles and responsibilities with a formal list of matters reserved to the Board's approval Operational and reserved matters

Day-to-day operational decisions are taken initially by the Executive Directors, in accordance with the Group's strategy. The Executive Directors are also responsible for initiating commercial transactions and approving payments, save for those relating to their own employment.

The Board has a formal schedule of matters specifically reserved for its approval. These matters are delegated to the Board Committees, Executive Directors, executive management team and senior management where appropriate. The schedule of matters reserved for the Board can be found on the website www.avoplc.com. Key

matters include:

- reviewing, approving and guiding corporate strategy, major plans of action, risk appetite and policies, annual budgets and business plans; setting performance objectives; monitoring, implementation and corporate performance; and overseeing major capital expenditures, acquisitions and disposals;
- monitoring the effectiveness of the Company's governance arrangements and practices, making changes as needed to ensure the alignment of the Company's governance framework with current best practices;
- ensuring that appointments to the Board or its Committees are made in accordance with the appropriate governance process;
- monitoring and managing potential conflicts of interest of management, Board members, shareholders, external advisors, and other service providers, including misuse of corporate assets and abuse in related party transactions; and
- overseeing the process of external disclosure and communications. The Board is also responsible for all other matters of such importance as to be of significance to the Group as a whole because of their strategic, financial, or reputational implications or consequences.

Internal control focused on safeguarding the Company's assets

The Board is responsible for ensuring that the Company maintains a system of internal financial controls. The objective of the system is to safeguard assets, ensure proper accounting records are maintained and that the financial information used within the business and for publication is timely and reliable. Given the size of the Group, the Board does not consider it appropriate to have its own internal audit function.

Clear guidelines to support healthy and open debates

Guidelines are in place concerning the content, presentation, and timely delivery of papers by management to Directors for each board meeting so that the Directors have enough information to be properly briefed. Where issues arise at board meetings, the Executive Chairman ensures that all Directors are properly briefed and, when necessary, appropriate further enquiries are made.

Dedicated Board Committees

There are three Board Committees – Audit, Remuneration and Strategic committees (which also cover ESG considerations). The roles and responsibilities of each are detailed on page 92. The terms of reference of the Audit Committee and the Remuneration Committee are set out on the Company's website. All Board Committees report back to the Board following a committee meeting.

Share dealing

The Company has established a Group share dealing code which complies with all applicable legislation, and which is in accordance with the requirements of the Market Abuse Regulation which came into effect in 2016. All the Directors of the Group understand the importance of compliance with the Code. At every Board meeting, Directors are reminded whether they are allowed to trade shares of the Company.

Whistleblowing procedures

The Company has a whistleblowing policy to allow and encourage all employees to bring matters which cause them concern and in strict confidence to the attention of certain persons within the Company and, ultimately, to the attention of the Chairman. These matters include but are not limited to unethical business practices, fraud, misconduct, or wrongdoing.

Anti-bribery and corruption policies

All staff and Directors are bound by the Company's Anti Bribery and Corruption policies. The Company has a zero-tolerance approach with its policies to protect the Company, its employees and those third-parties with which the business engages. These policies are provided to staff upon joining the business to ensure that everyone within the business is aware of the importance of all dealings within the Company being carried out with the highest integrity. All policies are regularly reviewed, and compliance training is given. Each employee is required to sign an agreement to confirm that they understand and will comply with the policies.

Appointment of a Company Secretary to support the Board and ensure processes are being followed

The Company Secretary, Henry Clarke, ensures that the Board procedures are followed, and that applicable rules and regulations are complied with. The Company Secretary attends the Board meetings and reports directly to the Executive Chairman.

Principle 10 – Communicate how the company is governed and is performing by maintaining a dialogue with shareholders and other relevant stakeholders

The importance of engaging with shareholders underpins the essence of the business.

As outlined at principle 2, the Company maintains an active dialogue with its shareholders through a planned programme of investor relations. It places a high priority on transparent and effective communications with shareholders. As an AIM listed company there is a need to provide fair and balanced information in a way that is understandable to all stakeholders. The Board recognises the importance of engaging with all stakeholders including employees, investors, partners, suppliers, media and communities. This is done through a number of channels: The primary communication tool with shareholders is the Company's website, https://www.avoplc.com. This is further supplemented by regular and appropriate Regulatory News Service ("RNS") announcements as well as the release of the annual and interim report. The full year results are audited by an external firm of auditors with the interim statement usually subject to a review by the same external auditors. These reports contain full details of all the principal events of the relevant period together with an assessment of current trading and prospects. The

interim report and other investor presentations are also available on the website. The Company has full electronic communications in place, so that shareholders (unless they elect otherwise) will have access to communications through the Company's website.

Upon conclusion of Shareholder meetings arrangements are made that the outcomes of votes cast by shareholders to be disclosed in a clear and transparent manner. If a significant proportion of votes (20%+) was ever cast against a resolution, the Company would provide, on a timely basis, an explanation of what actions it intends to take to understand the reasons behind that vote result, and, where appropriate, any different action it has taken, or would take, as a result of the vote.

	Audit Committee	Remuneration Committee	Strategic Committee
Primary responsibility	• Review the financial statements and the accounting principles and practice underlying them; the ultimate responsibility for approving the annual financial statements and interim statements remains with the Board • Liaise with the external auditors • Review the effectiveness of internal controls	• Determine and recommend to the Board the remuneration of Executive Directors, the Chair and the other members of the Executive Committee • Monitor, review and approve the levels and structure of remuneration for other senior managers and employees • Determine the headline targets for any performance-related bonus or pay schemes • Determine specific targets and objectives for any performance-related bonus or pay schemes for the Executive Directors and the other members of the Executive Committee • Review and approve any material termination payment	• Review and deliver a concrete strategic 3-year base plan and 7-year growth plan • Prepare for next-tier growth catalysts • Invest in best high-return initiative assessments
Members	• Mr. Hans von Celsing • Mr. Michael Bradfield • Dr. Enrico Vanni	• Dr. Enrico Vanni • Mr. Michael Bradfield • Mr. Hans von Celsing	• Ms. Lori Cross • Mr. Hans von Celsing • Dr. Enrico Vanni
Number of meetings in 2021	3	2	1
Matters considered	• Reviewed and approved the annual report and financial statements for the year and half-year end, including the results announcements • Considered the reports from the external auditors identifying any accounting or judgemental issues requiring the Board's attention and the auditors' assessment of internal controls • Reviewed any changes to accounting policies • Discussed with the external auditors to confirm their independence and scope for audit work • Considered the adequacy of the whistleblowing facility and the anti-bribery policy	• Determined the Company's policy on the remuneration for the Executive Chairman, Executive Directors and any senior management • Supervised the Company's share incentive and SAYE schemes and set performance conditions	• Reviewed the Company's competitive value propositions • Prepared a recommended prioritised list of clinical targets based on the clinical and technical advantages of LIGHT • Reviewed the product development roadmap options – new capabilities and possible timeframes • Set-up a roadmap for operations/ manufacturing/ cost strategies as well as IP and business model

Note: Attendance is expressed by the number of meetings attended / number eligible to attend. Attendance of Directors at other Board Committees – as outlined at Principle 9 – can be found on page 88

STATEMENT OF DIRECTORS' RESPONSIBILITIES

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

Company law requires the Directors to prepare financial statements for each financial year. Under that law the Directors have prepared the consolidated financial statements in accordance with International Financial Reporting Standards (IFRS) as adopted by the European Union (IFRSs as adopted by the EU) and have elected to prepare the Company financial statements in accordance with UK Generally Accepted Accounting Practice (Accounting Standards and applicable law, comprising FRS 101 'Reduced Disclosure Framework').

In preparing the Group financial statements, International Accounting Standard 1 requires that Directors:

- properly select and apply accounting policies;
- make judgements and estimates that are reasonable, relevant, reliable and prudent;
- for the Group financial statements, state whether they have been prepared in accordance with IFRSs as adopted by the EU;
- for the parent Company financial statements, state whether applicable UK accounting standards have been followed, subject to any material departures disclosed and explained in the parent company financial statements;
- use the going concern basis of accounting unless they either intend to liquidate the Group or the parent Company or to cease operations, or have no realistic alternative but to do so.

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

They are responsible for such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error, and have general responsibility for taking such steps as are reasonably open to them to safeguard the assets of the Group and to prevent and detect fraud and other irregularities.

Under applicable law and regulations, the Directors are also responsible for preparing a strategic report, Directors' report, Directors' remuneration report and corporate governance statement that complies with that law and those regulations.

The Directors are responsible for the maintenance and integrity of the corporate and financial information included on the company's website. Legislation in the UK governing the preparation and dissemination of financial statements may differ from legislation in other jurisdictions.

Provision of information to the auditor

Each Director in office at the date the Directors' Report is approved confirms that:

- so far as the Director is aware, there is no relevant audit information of which the Company's auditor is unaware; and
- he/she has taken all the steps that he/she ought to have taken as Director to make himself/herself aware of any relevant audit information and to establish that the Company's auditor is aware of that information.

Responsibility statement of the Directors in respect of the annual financial report

We confirm that to the best of our knowledge:

- the financial statements, prepared in accordance with the applicable set of accounting standards, give a true and fair view of the assets, liabilities, financial position and profit or loss of the Company; and
- the strategic report includes a fair review of the development and performance of the business, together with a description of the principal risks and uncertainties that they face.

We consider the annual report and accounts, taken as a whole, is fair, balanced and understandable and provides the information necessary for shareholders to assess the Group's position and performance, business model and strategy.

By order of the board

Dr Michael Sinclair
Executive Chairman
30 June 2022

AUDIT COMMITTEE REPORT

Hans von Celsing
Chairman of the Audit Committee

Introduction

As Chairman of the Audit Committee, I am pleased to present the report of the Audit Committee for the year ended 31 December 2021.

This report sets out the work of the Audit Committee over the past year and offers insight into how the Audit Committee has discharged the responsibilities delegated to it by the Board and the key areas of focus is has considered in doing so.

In meeting its responsibilities, the Audit Committee continues to consider the provisions of the UK Corporate Governance Code and the FRC Guidance on Audit Committees. The Audit Committee's Terms of Reference are available on www.avoplc.com.

Composition and meetings

The composition of the Audit Committee and attendance is shown on page 92. The members of the Audit Committee are independent Non-Executive Directors who possess the necessary depth of financial and commercial expertise to fulfil their role. Detailed information on the experience, skills and qualifications of all Committee members can be found on pages 81 and 82. The Board is satisfied that the Committee Chair, Hans von Celsing, has recent and relevant financial experience.

Although not members of the Audit Committee, the CEO, the SVPs (Finance and Accounting) and the Company Secretary are also invited to attend meetings, unless they have a conflict of interest. Other senior members of the business are invited to attend meetings as appropriate. Representatives of the external auditors meet with the Audit Committee at least once a year without Executive Directors or management being present.

Primary responsibility and matters considered

This is further outlined on page 92.

Fair, balanced and understandable

The Audit Committee undertook an assessment as to whether, in its view, the Annual Report and Accounts were fair, balanced and understandable, and provided the necessary information for shareholders to assess the position, performance, business model and strategy of the Company. In forming its opinion, the Audit Committee considered the results of management's assessment of going concern, reviewed the Annual Report and Accounts as a whole, and assessed the results of processes undertaken by management to provide assurance that the Group's financial statements were fairly presented. These processes included, but were not limited to:

- Review by senior management of the Annual Report to ensure that the information presented was accurate and that the narrative was consistent with the fact pattern, including appropriate disclosure of material or significant items necessary to aid a reader's understanding and appropriate balance of reported and adjusted performance measures;
- Board meetings where the financial projections were reviewed to ensure that the business performance was appropriately assessed and understood.
- Discussion with senior management and a review of any significant judgements or estimates made by management in preparing the Annual Report.

The views of the external auditors on this matter were also considered by the Audit Committee. Having completed its assessment, the Audit Committee reported to the Board that it was able to make the corresponding confirmation in its Directors' responsibility statement.

In conclusion, the Audit Committee reported to the Board that it considers the Annual Report for the year ended 31 December 2021 to be fair, balanced and understandable.

Risks

The Audit Committee oversees the effectiveness of the Group's risk management and reviews and monitors the key risks in order to eliminate or mitigate against those risks. The Audit Committee has assured itself that a risk management framework is in place and effective; it is satisfied that risks are within the risk appetite of the Group and, where mitigating actions are undertaken, they are proportionate.

In relation to financial reporting, the Audit Committee has discussed areas of risk with the auditors and agreed for

the following areas of heightened risk to be reviewed and assessed in the audit of the Group's performance in the financial year to 31 December 2021:

- Carrying value of intangibles;
- Carrying value of inventory;
- Accounting for convertible loan agreements; and
- Going concern.

For each of the above areas the Audit Committee considered the key facts and judgements outlined by management. Key findings are provided in the Independent Auditor's Report on pages 105 to 108. The Audit Committee was satisfied that there are relevant accounting policies in place in relation to these key areas and management have correctly applied these policies.

External auditors

Role of the external auditors

The Audit Committee monitors the relationship with its external auditors, RPG Crouch Chapman LLP, to ensure that auditor independence and objectivity are maintained.

Audit process

The external auditors prepare an audit plan for review of the full-year financial statements. The audit plan sets out the scope of the audit, specific areas of risk to target and the audit timetable. This plan is reviewed and agreed in advance by the Audit Committee. Following completion of audit fieldwork the external auditors present their findings to the Audit Committee for discussion, including accounting judgements undertaken in respect of various matters such as research and development capitalisation.

Non-audit fees

Any non-audit services require approval by the Audit Committee. Non-audit fees comprised predominantly fees for tax compliance and ad hoc tax work. Non-audit fees amounted to £8,750 (2020: £8,500) compared to £56,350 (2020: £54,750) of audit fees.

Tax compliance services provided by RPG Crouch Chapman LLP do not involve the making of any decisions and are carried out by a separate team not involved with the audit work. The company has informed management in place that make all tax related decisions. The tax disclosures are also drafted before the completion of the tax compliance work and RPG Crouch Chapman LLP play no part in the drafting of these disclosures.

Auditor effectiveness and appointment

RPG Crouch Chapman LLP has served as external auditors of the Company since 2011. Periodic rotation of key audit partners is also required. This is the first year that Mark Wilson has acted as the audit partner for the group. Mark brings his experience of working with listed groups and reporting under IFRS.

In line with its Terms of Reference, the Audit Committee undertakes an annual assessment of the effectiveness, value and independence of the external auditors. This assessment incorporates the views of management in addition to the Non-Executive Directors to facilitate continued improvement in the external audit process.

The assessment considered:

- Audit risk identification whereby this is a key factor in the delivery of a thorough, robust and efficient global audit in accordance with pre-set timescales. These risks remained broadly consistent with the prior financial year;
- Provision of accurate, robust and perceptive advice on key accounting and audit judgements, technical issues and best practice;
- The level of professionalism and technical expertise consistently demonstrated and maintenance of continuity within the core audit team; and
- Strict adherence to independence policies and other regulatory requirements.

RPG Crouch Chapman's objectivity, independence and performance are considered to remain strong and the Audit Committee has recommended to the Board that RPG Crouch Chapman's be re-appointed as external auditors for the next financial year, subject to approval at the AGM.

Internal audit

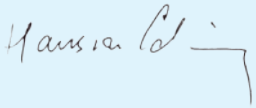
At present the Company does not have a formal internal audit function; the Audit Committee presently considers this to be appropriate given the close involvement of the Executive Directors and senior management on a day-to-day operational basis. The Audit Committee will keep this matter under review as the Group's activities expand.

Conclusions

The Audit Committee's oversight of financial reporting, external audit, and the further development of the control and risk environments have been areas of significant focus. These are likely to remain so for the next financial year as the Company grows and develops in line with its strategy.

The Audit Committee remains focused on ensuring that finance and risk capability is enhanced appropriately to manage in an increasingly complex business and an increasingly regulated environment.

I am confident that the Audit Committee has the necessary skills and experience to continue to meet the challenges ahead.



Hans von Celsing
Chairman of the Audit Committee
30 June 2022

REMUNERATION COMMITTEE REPORT

Enrico Vanni
Chairman of the Remuneration Committee

Introduction

As Chairman of the Remuneration Committee, I am pleased to present the report of the Remuneration Committee for the year ended 31 December 2021.

This report does not constitute a Directors' remuneration report in accordance with the Companies Act 2006. As a company whose shares are admitted to trading on AIM, the Company is not required by the Companies Act to prepare such a report. However, the Remuneration Committee is committed to complying with the principles of good corporate governance in relation to the design of the Directors' remuneration policy. As such, our policy takes account of the UK Corporate Governance Code and the QCA Corporate Governance Code (against which the Company formally reports compliance). The Remuneration Committee also considers other best practice guidance (for example, the QCA Remuneration Committee Guide and the Investment Association's Principles of Remuneration), as far as is appropriate to the Company's management structure, size and listing.

The Remuneration Committee's Terms of Reference are available on www.avoplc.com.

Composition and meetings

During the past year, the Remuneration Committee, chaired by Enrico Vanni, was exclusively composed of independent Non-Executive Directors. The Executive Chairman and the Chief Executive Officer are invited to attend meetings where appropriate. The Remuneration Committee met three times in 2021. The composition of the Remuneration Committee and attendance can be found on page 92.

Primary responsibility and matters considered

This is further outlined on page 92.

Remuneration policy

The remuneration policy of the Company is to:

- provide a suitable remuneration package to attract, motivate and retain Executive Directors and the wider Executive team who will run the Group successfully; and
- ensure that all long-term incentive schemes for the Directors are consistent with the shareholders' interests.

The Remuneration Committee reviews overall levels of pay and the operation of the incentive arrangements for Executive Directors to ensure they remain appropriate in light of the current business strategy and the interests of shareholders. More specifically, these reviews are framed around the following key principles:

- total rewards will be set at levels that are sufficiently competitive to enable the recruitment and retention of high-calibre executives;
- total incentive-based rewards will be earned through the achievement of demanding performance conditions consistent with shareholder interests;
- incentive plans, performance measures and targets will be structured to operate soundly throughout the business cycle;
- the design of long-term incentives will be prudent and will not expose shareholders to unreasonable financial risk;
- in considering the market positioning of reward elements, account will be taken of the performance of the Group and of each individual senior team member; and
- reward practice will conform to best practice standards as far as reasonably practicable.

No Director or senior manager is involved in any decisions about their own remuneration. The Remuneration Committee is, however, responsible for making recommendations to the Directors on matters relating to the Company's remuneration structure, including pension rights, the policy on compensation for Executive Directors and their terms of employment. In order to achieve the overall aim of attracting and retaining high-quality people, the Remuneration Committee has continued to provide a suitable balance of short-term and long-term incentives.

The policy on each element of remuneration and how it operates, is also detailed on the following page. The main elements of the remuneration packages are as follows.

Basic annual salary and pension

Base salary is based on a number of factors, including market rates, benchmarking to peers, as well as the individual Director's experience, responsibilities and performance. Individual salaries are subject to annual review.

All Executive Directors, along with other employees, are able to take part in the Company's pension scheme, where they receive a pension contribution from the Group of up to 10% of salary together with employer's National

Insurance saved on employee pension contributions. This complies with legal requirements, with both the employee and employer making contributions under automatic enrolment provisions.

Other benefits

All employees benefit from life assurance and medical health insurance. Other benefits may also be provided to employees once they have met eligibility criteria.

Discretionary bonus

The purpose of the annual bonus is to incentivise the Executive Directors, members of the Executive team and senior management to deliver strategic and financial success, as well as long-term growth to the benefit of the Company and its shareholders. Bonus awards take into account Company and individual performance. They are either related to the achievement of personal, departmental and/or Group targets/milestones.

In addition, the Remuneration Committee has the discretion to settle an element of any bonus in shares or share options in lieu of cash considerations. The extent of such discretions and the maximum opportunity for performance metrics is set out on page 99. To ensure the efficient administration of the variable incentive plans outlined, the Remuneration Committee applies certain operational discretions which include the following:

- selecting the participants in the plans on an annual basis;
- determining the timing of grants of awards and/or payments;
- determining the quantum of awards and/or payments;
- determining the extent of vesting based on the assessment of performance as well as taking into account the experience of shareholders and other stakeholders over the vesting period;
- determining 'good leaver' status for incentive plan purposes and applying the appropriate treatment; and
- undertaking the annual review of weighting of performance measures and setting targets for the annual bonus plan and other incentive schemes, where applicable, from year to year.

Long-term incentive plan and save as you earn scheme

In 2020 the Remuneration Committee established a Long-Term Incentive Plan ("LTIP"). In 2018 the Remuneration Committee set-up a Save As You Earn ("SAYE") scheme. The Executive team and certain key individuals in the Company were invited to join the LTIP and SAYE scheme. The purpose of the LTIP and the SAYE scheme are to provide a long-term performance and retention incentive, linking long-term share rewards to the creation of long-term sustainable shareholder value by delivering on the Company's agreed strategic objectives.

Details can be found on page 99.

Differences in the remuneration policy of the executive directors and the general employees

There are no material differences in the structure of remuneration arrangements for the Executive Directors and senior management, aside from quantum and participation levels in incentive schemes, which reflect the fact that a greater emphasis is placed on performance-related pay for Executive Directors and the most senior individuals in the management team.

Non-executive Directors

Fees for Non-Executive Directors are determined by the Board on the recommendation of the Remuneration Committee, based on market comparisons with positions of similar responsibility and scope in companies of a similar size and in comparable industries. Non-Executive Directors are not eligible for pension scheme membership or to participate in the Company's LTIP; and do not participate in any of the Company's bonus schemes or receive any other benefits.

As with the Executive Directors, Non-Executive Directors' fees are designed to attract and retain individuals who have the expertise, responsibility and the time commitment to be able to contribute to an effective Board and deliver long-term sustainable shareholder value. The Company reimburses Non-Executive Directors for reasonable expenses incurred such as travel and hotel accommodation.

Most Non-Executive Directors have historically elected to receive their fees in shares of the Company. Please refer to Directors' shareholding on page 102 and options on page 124.

In addition to an annual fixed fee of £30,000, Non-Executive Directors are paid additional fees for memberships of Board Committees. Fees for Non-Executive Directors are set by the Board.

- Committee Chairmanship fee: £15,000
- Other Committee Membership fee: £10,000

Conclusion

The Board firmly believes that the remuneration policy of the Company effectively rewards and incentivises the executive and senior management team in pursuit of the Company's strategic aims and that these incentives align with long-term stakeholder value creation.

Enrico Vanni
Chairman of the Remuneration Committee
30 June 2022

Element of pay	Link to remuneration policy and strategy	Key features/operation	Potential value	Performance metrics
Base salary	To provide an appropriate level of fixed basic income To aid recruitment and retention	Normally reviewed annually Set initially at a level required to recruit suitable executives, reflecting their experience and expertise Any subsequent increase influenced by scope of the role, experience and personal performance in the role, average change in total workforce salary, performance of the Company, external economic conditions, such as inflation Account taken of practice in comparable companies (e.g. those of a similar size and complexity)	Annual increases will generally be restricted to those of the average of the wider workforce Increases beyond those awarded to the wider workforce (in percentage of salary terms) may be awarded in certain circumstances, such as where there is a change in responsibility or experience, or a significant increase in the scale or complexity of the role and/or size and value of the Company	None
Benefits	To provide a competitive benefits package	Executive Directors may receive benefits including healthcare, income protection and life assurance, as well as other standard group-wide benefits offered by the Company from time to time	The value of benefits may vary from year to year depending on the cost to the company	None
Pensions	To aid recruitment and retention To provide an appropriate level of fixed income	The Company contributes to executives' existing personal pension schemes Cash payments in lieu of pension are available in the event an executive has exceeded his/her personal pension allowance	Between 7% and 10% of basic salary	None
Performance related bonus	To reward the annual delivery of short to medium-term objectives relating to the business strategy	All bonus payments are at the discretion of the Remuneration Committee Not pensionable Targets are set and/or reviewed annually Bonus can be settled in shares or share options in lieu of cash considerations	Payments capped at 100% of salary Additional discretionary bonus can be awarded subject to specific contributions, roles and performance of individuals	Takes into account Company and individual performance, which are related to the achievement of personal, departmental and/ or Group targets/milestones
Long-Term Incen-tive Plan ("LTIP")	Intended to align the long-term interests of senior executives with those of shareholders To incentivise the delivery of key strategic objectives over the longer term	Awards are normally granted in the form of nominal cost options Ability to exercise can be dependent on performance targets being met	n.a.	Awards vest based on challenging targets measured over a multi-year period Prior to each award, the Remuneration Committee will set threshold and stretch targets along with an intermediate vesting range. Latest grant of LTIP options announced in October 2020; options to vest at the discretion of the Remuneration Committee, based on four vesting conditions: (i) the LIGHT system is fully; (ii) operational at 230MeV; (iii) the first patient has been treated; (iv) the LIGHT system has been certified; and (v) the Company's share price has been in excess of £1.00 for 30 consecutive calendar days
Savings related share option scheme or SAYE (Save As You Earn) plan	To encourage ownership and align the interests of employees and external shareholders and build long-term value	Open to all employees with more than one month's service Participants can make monthly contributions of up to £500 on a three-year savings account	Maximum monthly savings of £500 As per this SAYE plan, the Board granted options over a total of 908,150 new shares	None

GROUP DIRECTORS' REPORT

Corporate details

Advanced Oncotherapy plc is a public limited company incorporated and registered in England and Wales under the Companies Act with registered number 05564418. Its registered office is Level 17, Dashwood House, 69 Old Broad Street, London EC2M 1QS.

Advanced Oncotherapy plc owns 100% of ADAM S.A.

Principal activity

Advanced Oncotherapy is a provider of particle therapy with protons that harnesses the best in modern technology. Advanced Oncotherapy's team "ADAM," based in Geneva, focuses on the development of a proprietary proton accelerator called, Linac Image Guided Hadron Technology (LIGHT). LIGHT's compact configuration delivers proton beams in a way that facilitates greater precision and electronic control.

Advanced Oncotherapy will offer healthcare providers affordable systems that will enable them to treat cancer with innovative technology as well as expected lower treatment-related side effects.

Advanced Oncotherapy continually monitors the market for any emerging improvements in delivering proton therapy and actively seeks working relationships with providers of these innovative technologies. Through these relationships, the Company will remain the prime provider of an innovative and cost-effective system for particle therapy with protons.

Directors – power, protection and interests

Description

The Directors and brief biographies are detailed on pages 81 and 82. Information on the election and re-election of Directors can be found in Principle 7 of the QCA Code on page 89.

Powers

The Directors are responsible for the management of the business of the Company and may exercise all powers of the Company subject to UK legislation and the Company's Articles of Association, together with any specific authorities that may be given to the Directors by shareholders from time to time (for example the authority to allot or purchase shares in the Company).

Qualifying third-party indemnity provisions

The Company has entered into indemnity deeds with all its current Directors containing qualifying indemnity provisions, as defined in Section 234 of the Companies Act 2006, under which the Company has agreed to indemnify each Director in respect of certain liabilities, which may be attached to them as Directors or as former Directors of the Company or any of its subsidiaries. All such indemnity provisions are in force as at the date of this Directors' report.

Directors' and Officers' insurance

The Company maintains liability insurance for its Directors and Officers to cover any claim for wrongful acts in connection with their positions with the exceptions of events whereby a Director or Officer is proved to have acted fraudulently or dishonestly.

Interests

The beneficial interests of the Directors in the Ordinary Shares of the Company on 31st December 2021 and 31st

December 2020 are set out below:

Holdings by Directors or Holdings Under Their Control	31st December 2021	31st December 2020
Mrs. Renhua Zhang*	**45,503,765**	45,000,000
Dr. Michael Sinclair & Family	**8,810,814**	8,280,604
Mr. Michael Bradfield	**7,558,240**	7,443,240
Dr. Nick Plowman	**4,515,304**	4,412,804
Dr. Enrico Vanni	**3,396,361**	2,796,361
Mr. Nicolas Serandour	**2,177,134**	1,760,467
Prof. Steve Myers	**1,400,569**	983,902
Mr. Hans von Celsing	**689,167**	512,500
Ms. Lori Cross	**60,417**	0

** Includes shares owned by Liquid Harmony and related parties*

In the financial year, the Company expensed through the income statement £140,000 (2020: £40,000) in relation to research and development costs; these largely relate to ADAM physics consultancy costs not capitalised as an intangible asset. Additionally, £12.5 million (2020: £5.8 million) of development costs were capitalised.

At the date of this report, there is no contract or arrangement with the Company or any of its subsidiaries that is significant in relation to the business of the Company in which a Director of the Company is materially interested.

Further information – including details on non-beneficial interests and Directors' share options – are contained in the Directors' remuneration report set out on pages 97 to 99 and in Note 8 on page 124.

The Directors have a statutory duty under the Companies Act 2006 to avoid situations in which they have, or can have, a direct or indirect interest that conflicts, or may conflict, with the interests of the Company. Details on conflict of interests can be found on page 87 (Principle 5 of the QCA Code).

Business activity and review

Business review

The Company is still pre-revenue and continues to invest in the development and assembly of the first LIGHT machine through expenditure on intangible assets and inventory. It recorded a comprehensive loss of £30.2 million in the year ended 31st December 2021 (2020: £23.4 million), with shareholder funds as at 31st December 2021 of £61.4 million (2020: £44.1 million). Cash and cash equivalents at the year-end were £4.3million (2020: £2.3 million), although these year-end figures do not take into account post period financing agreements. The Company has funded its operations through borrowings and equity raises.Further details of the results for the year are set out in the Consolidated Income Statement and in the related notes forming part of the Consolidated Financial Statements. The Chairman's letter and the Chief Executive Officer's Review – which are included in the Strategic Report – report on the performance of the Group's business during the year and on future developments.

Dividends

The Directors do not recommend the payment of a dividend (2020: no dividend) so that cash is retained in the Company for assembling the first LIGHT machine and capital expenditures that are required for the rapid growth of the business.

Donations

During the year, the Company made no charitable donations (2020: nil).

Likely future developments

The outlook is available on pages 6, 37, 38 and 49 to 52.

Going concern

The Group has made a loss before tax of £29.5m (2021: £23.4m) and is presently pre-revenue and, as such, has relied upon equity and debt funding to progress its development plans. Post year end, the Group has successfully raised £11.5m in equity and £1.5m in short term loans as detailed further in Note 29.

The Directors regularly review cash flow forecasts to determine whether the Group has sufficient cash reserves to meet its future working capital requirements and development plans. The Group's plans indicate that they need to raise further finance and the Directors are confident based on past history of successful fundraising and discussions with investors that the Group will be successful in raising these funds. Additionally, they consider they can defer settlement of creditors, reduce short term expenditure and obtain short-term finance should there be any delay in completing any such fundraising to allow continuance of their plans. They therefore consider it appropriate to prepare the Group's financial statements on a going concern basis.

However, as at the date of approval of these financial statements, there are no legally binding agreements in place in relation to any fundraising or extension of terms with creditors and as the success of any finance raising is outside the control of the company there can be no certainty that additional funds will be forthcoming, which indicates the existence of a material uncertainty which may cast doubt about the Group's ability to continue as a going concern and therefore it may be unable to realise its assets and discharge its liabilities in the normal course of business. The financial statements do not include the adjustments that would result if the Group was unable to continue as a going concern.

Share structure

Share capital

As at 31st December 2021, the Company had an allotted and fully paid up share capital of 451,612,211 ordinary shares of 25 pence each with an aggregate nominal value of £113 million. Further details of the authorised and issued share capital, together with details of the movements in the Company's issued share capital during the year are

set out in Note 20 to the consolidated financial statements.

The Company has one class of ordinary shares which are listed on the Alternative Investment Market ("AIM") and trade under the ticker symbol: LON: AVO.

Rights of shareholders
The rights attached to the ordinary shares of the Company are defined in the Company's Articles. Each share carries the right to one vote at general meetings of the Company but has no right to fixed income.

Shareholders are entitled to attend and vote at any general meeting of the Company. It is the Company's practice to hold a poll on every resolution at general meetings. Every member present in person or by proxy has, upon a poll, one vote for every share held. In the case of joint holders of a share the vote of the senior who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other joint holders and, for this purpose, seniority shall be determined by the order in which the names stand in the Register of Members in respect of the joint holding.

No person has any special rights of control over the Company's share capital.

Transfer of shares
There are no specific restrictions on the size of a holding, nor on the transfer of shares which are both governed by the general provisions of the Company's Articles and prevailing legislation.

Shareholder agreement
The Directors are not aware of any agreements between holders of the Company's shares that may result in restrictions on the transfer of securities or on voting rights at any meeting of the Company.

Major shareholdings
As at 30th March 2022, the Company had been notified under the FCA's Disclosure, Guidance and Transparency Rule of the following interests in its total voting rights of 3% or more:

Holder	Number of Shares	% of Total in Issue
Mr Philippe Glatz	45,659,162	**9.9%**
Liquid Harmony Limited(1)	45,503,765	**9.8%**
Celeste Mgt SA	28,333,333	**6.1%**
DNCA Investments	22,625,000	**4.9%**
Nerano Capital Limited(2)	22,500,000	**4.9%**
Odey Asset Management	20,126,443	**4.3%**
Lombard Odier AM(3)	18,127,584	**3.9%**
Jarvis Investment Mgt	18,063,026	**3.9%**

(1) Includes shares owned by Mrs Renhua Zhang and related parties
(2) Controlled by Mr Seamus Mulligan. Mr Seamus Mulligan also controls Barrymore Investments which owns 7,905,721 shares in the Company's ordinary share capital
(3) Lombard Odier Darier Hentsch & Cie

On 27th May 2022, the Company was informed that Odey Asset Management LLP had a total beneficial interest in 20,281,159 ordinary shares in the Company, representing 4.3% of the Company's issued share capital at that time.

Employees
Diversity
The Company is committed to encouraging diversity, promoting a diverse culture where everyone is treated with respect and valued for their individual contribution and creating a work environment free of bullying, harassment, victimisation, and unlawful discrimination. The Company has policies in place to ensure that selection for employment, promotion, development, or any other benefit is on the basis of merit and ability and does not impact negatively upon diversity. It is a key objective to ensure that all employees are helped and encouraged to fulfil their potential.

Equal opportunities
It is the Company's policy to ensure equal opportunity in recruitment, selection, promotion, employee development, training and reward policies and we have an equal opportunity and diversity policy in place. It is a key objective to ensure that successful candidates for appointment and promotion are selected taking account of individual ability, skills, and competencies without regard to age, gender, race, religion, disability or sexual orientation. Every effort is also made to retain and support employees who have a disability during their employment, including flexible working to assist their re-entry into the workplace and making alternative suitable provisions.

Involvement of employees
Employees are key to the Company's success, and the Company relies on a committed workforce to help achieve the business objectives. Employees are encouraged to operate in an open environment, embracing teamwork and aligning personal development with the strategy of the business and their behaviours with Company values. Directors are keen to engage Company's employees by providing an environment where they can contribute their own ideas and challenge those of others. Directors are committed to involving employees and consider that good communication helps to achieve this. Further information – including the way in which Directors discharge the duty of taking into consideration the interests of employees and other stakeholders – can be found on page 86 (Principle 3 of the QCA Code) and on pages 71 and 72.

Employee share plans
To aid in retention, a benefits package encompassing death in service and medical insurance, together with a contributory pension scheme, is offered to all employees, in addition to salary. Discretionary bonus scheme can also be available subject to the satisfaction of any applicable performance conditions at the time. The Company operates several employee share plans, details of which are set out on page 99.

Health, safety, and environment

The Directors are committed to ensuring the highest standards of health and safety for the employees of the Group. The Directors are also committed to minimising the impact of the Group's operations on the environment. Please refer to pages 11 and 63 to 65 for further information.

Risk management

The Board is responsible for the Group's system of risk management and continues to develop policies and procedures that reflect the nature and scale of the Group's business. Further details of the key areas of risk to the business identified by the Group are included on pages 73 and 76.

Cautionary statement regarding forward-looking information

Forward-looking statements are subject to assumptions, inherent risks and uncertainties, many of which relate to factors that are beyond the Company's control or precise estimate. Directors caution investors that a number of important factors, including those referred to in the Company's annual report, could cause actual results to differ materially from those expressed or implied in any forward-looking statement. Such factors include, but are not limited to, those discussed in the Risk section on pages 73 and 76. Any forward-looking statements made by or on behalf of the Company speak only as of the date they are made and are based upon the knowledge and information available to the Directors on the date of this report.

Events after the reporting period

Since the year end, the Group has raised additional equity through the issue of shares:

	Number of Shares	Equity (£)
January	500,000	125,000
February	3,100,000	775,000
March	8,000,000	2,000,000
April	3,400,000	850,000
May	3,540,000	885,000
June	3,200,000	800,000
Announced June	24,090,000	6,022,500
Total	**45,830,000**	**11,457,500**

On 23 March 2022, the Company entered into a new short term loan agreement of £1.5 million with Nerano Pharma Ltd, a company owned and controlled by Seamus Mulligan, a significant shareholder in the Company, with an interest rate of 1.25 per cent per month (the "Loan"). The Loan is repayable by the Company on 24 June 2022. As part of the agreement, the Company issued 6,382,978 warrants to Nerano Pharma Ltd with an exercise price of 28.20 pence per share, exercisable up until 24 March 2025.

As at the date of publication of the annual accounts, the Loan remains outstanding. Nerano Pharma has agreed to not seek repayment at the current time and are in discussions with the Company surrounding the potential to convert the Loan into New Ordinary Shares. At the current time no agreement has been entered into in relation to varying the terms of the Loan nor have the terms of any variation been, as yet, agreed. In the event that the terms cannot be agreed between Nerano Pharma and the Company, the Company would seek to repay the amounts owed pursuant to the Loan.

Independent auditor

RPG Crouch Chapman LLP have expressed willingness to continue in office for the year ending 31st December 2021 and a resolution to re-appoint them will be proposed at the forthcoming AGM.

Articles of association, annual general meeting and recommendation

The Company's Articles of Association may only be amended by special resolution at a general meeting of the shareholders.

The Company's Annual General Meeting (AGM) will be held on Friday, 29 July 2022 at 2.00pm at the offices of Advanced Oncotherapy plc, Third Floor, 4 Tenterden Street, London W1S 1TE. Full details of the business to be transacted at the AGM can be found in the Notice of the AGM on pages 147 to 149 of this report.

The Board are of the opinion that all resolutions which are to be proposed at the 2021 AGM are in the best interests of its shareholders as a whole and, accordingly, unanimously recommend that they vote in favour of all the resolutions as the Board intends to do in respect of their own holdings.

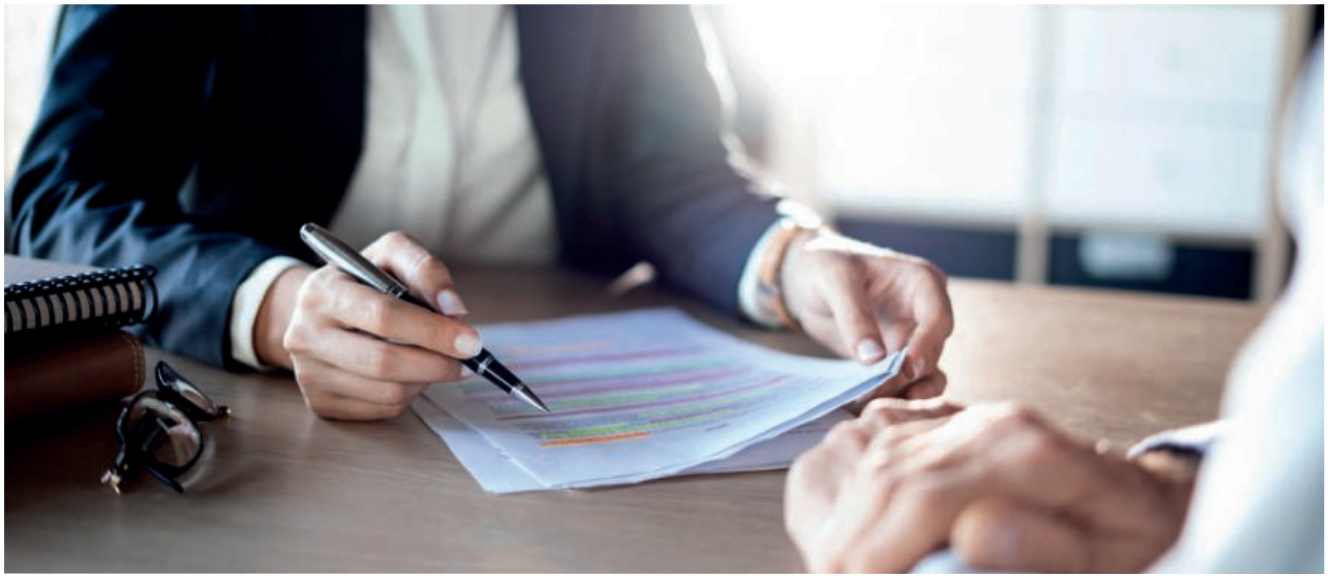
Cross references

All information cross referenced in this report forms part of the Report of the Directors.

This Directors' Report was approved by the Board and was signed on its behalf on 30 June 2022.

Dr Michael Sinclair
Executive Chairman
Registered Office: Level 17, Dashwood House, 69 Old Broad Street, London EC2M 1QS

INDEPENDENT AUDITOR'S REPORT



Opinion

We have audited the financial statements of Advanced Oncotherapy plc (the 'Company') and its subsidiaries (the 'Group') for the year ended 31 December 2021 which comprise the Consolidated statement of comprehensive income, the Consolidated statement of financial position, the Consolidated statement of changes in equity, the Consolidated statement of cash flows, the Company statement of financial position, the Company statement of changes in equity, and notes to the financial statements, including a summary of significant accounting policies.
The financial reporting framework that has been applied in the preparation of the Group financial statements is applicable law and International Financial Reporting Standards as adopted in the United Kingdom (IFRS). The Company financial statements have been prepared in accordance with applicable law and United Kingdom Accounting Standards, including FRS 101 Reduced Disclosure Framework (UK GAAP).

In our opinion:

- the financial statements give a true and fair view of the state of the Group's and of the 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 IFRS;
- the Company financial statements have been properly prepared in accordance with UK GAAP; and
- the financial statements have been prepared in accordance with the requirements of the Companies Act 2006.

Basis for audit 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 in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, 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.

Material uncertainty related to going concern

We draw attention to Note 1b in the accounting policies, concerning the Group's ability to continue as a going concern. The matters explained in Note 1b indicate that the Group needs to raise further finance to fund its working capital needs and development plans. As at the date of approval of these financial statements there are no legally binding agreements relating to securing the required funds. These events or conditions along with the matters set forth in Note 1b indicate the existence of a material uncertainty which may cast significant doubt over the Group's ability to continue as a going concern. Our opinion is not modified in respect of this matter.

We have highlighted going concern as a key audit matter. 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 the Parent Company's ability to continue to adopt the going concern basis of accounting included:

- Analysing Management's and the Directors' cashflow forecast which forms the basis of their assessment that the going concern basis of preparation remains appropriate for the preparation of the Group and Company financial statements for a period of at least twelve months from the date of approval of these financial statements;

- Testing the integrity of the cashflow model;
- Assessing costs included within the cashflow forecast and where available agreeing these costs to other evidence obtained during the course of our audit work is in line with our expectations;
- Obtaining details of post year ends fundraisings and agreeing supporting documentation and cash received;
- We reviewed loan agreements and ensured the repayments were appropriately included in the forecasts;
- Discussing with Management and the Board the Group's strategy to continue to ensure funds are available to the Group to fund its plans;
- Sensitising the cash flows for changes in key assumptions and considering the impact on headroom; and
- Reviewing and considering the adequacy of the disclosure within the financial statements relating to the Directors' assessment of the going concern basis of preparation.

Our approach to the audit

In planning our audit, we determined materiality and assessed the risks of material misstatement in the financial statements. In particular, we looked at where the Directors made subjective judgements, for example in respect of significant accounting estimates. As in all of our audits, we also addressed the risk of management override of internal controls, including evaluating whether there was evidence of bias by the Directors that represented a risk of material misstatement due to fraud.

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

We performed full-scope audits of the material components of the Group, being Advanced Oncotherapy Plc and ADAM S.A.. The remaining components of the Group were considered nonsignificant and we performed limited review procedures as deemed necessary.

Key audit matters

Key audit matters are those matters that, in our professional judgement, 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 we identified (whether or not due to fraud), including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. The matter identified was addressed in the context of our audit of the financial statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters. The use of the Going Concern basis of accounting was assessed as a key audit matter and has already been covered in the previous section of this report. The other key audit matters identified are listed below.

Key audit matter	Our audit work included:
Intangible asset valuation The Group's Intangible assets consist of direct costs relating to the internal development of the proton therapy technology and machines. Please refer to Note 10. As an intangible asset not yet ready for use, Management and the Board are required to perform an annual impairment review. Given the materiality of the assets in the context of the Group's consolidated statement of financial position and the judgement involved in making this assessment we consider this to be a key audit matter.	***Our audit work included:*** • Reviewing the impairment model provided and checking that the value in use model is appropriate; • Testing the integrity of the cashflow model; • Discussing with Management the assumptions used and obtaining details to support the key assumptions; and • Sensitising the cash flow for assumptions and considering if the disclosures in the financial statements reflect appropriately the requirement to disclosure key judgements and estimates.
Carrying value of inventories Inventory comprise the costs incurred to date to assemble machines being constructed for sale. There is judgement involved in the assessment of whether the carrying value is the lower of cost or net realisable value. We therefore consider this to be a key audit matter.	***Our audit work included:*** • Confirming costs to date are accurate by reference to invoices; • Confirming costs to complete to budgets and supporting documents; • Considering whether the budget is reasonable based on costs to date against original budget; and • Considering sales price of similar equipment or indicated sales price in correspondence with potential customers.

Our application of materiality

We apply the concept of materiality both in planning and performing our audit, and in evaluating the effect of misstatements. We consider materiality to be the magnitude by which misstatements, including omissions, could influence the economic decisions of reasonable users that are taken on the basis of the financial statements.

In order to reduce to an appropriately low level the probability that any misstatements exceed materiality, we use a lower materiality level, performance materiality, to determine the extent of testing needed. Importantly, misstatements below these levels will not necessarily be evaluated as immaterial as we also take account of the nature of identified misstatements, and the particular circumstances of their occurrence, when evaluating their effect on the financial statements as a whole.

We have based materiality on 1.25% of reported gross assets for the significant components, which is consistent with the prior year. This benchmark is considered the most appropriate because assets are the key item for an entity in the development phase. Overall materiality for the Group was therefore set at £1.7m (2020: £1.5m). For each component, the materiality set was lower than the overall group materiality. For the Company, materiality was set at £1.3m (2020: £1.2m).

We agreed with the Audit Committee that we would report on all differences in excess of 5% of materiality relating to the Group financial statements. We also report to the Audit Committee on financial statement disclosure matters identified when assessing the overall consistency and presentation of the consolidated financial statements.

Other information

The Directors are responsible for the other information. The other information comprises the information included in the annual report, other than the financial statements and our auditor's report thereon. Our opinion on the financial statements does not cover the other information and, except to the extent otherwise explicitly stated in our report, we do not express any form of assurance conclusion thereon.

In connection with our audit of the financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements or our knowledge obtained in the audit or otherwise appears to be materially misstated. If we identify such material inconsistencies or apparent material misstatements, we are required to determine whether there is a material misstatement in the financial statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact.

We have nothing to report in this regard.

Opinions on other matters prescribed by 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 the 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 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 Group or the Company, or returns adequate for our audit have not been received from branches not visited by us; or
- the Group or the Company financial statements 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 93 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's and the parent company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the Directors either intend to liquidate the group or the parent company or to cease operations, or have no realistic alternative but to do so.

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 our opinion in an auditor's report. Reasonable assurance is a high level of assurance, but does not

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 aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of the financial statements.

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

We gained an understanding of the legal and regulatory framework applicable to the Group and the industry in which it operates and considered the risk of acts by the group which were contrary to applicable laws and regulations, including fraud. These included but were not limited to compliance with Companies Act 2006 and applicable accounting standards.

We designed audit procedures to respond to the risk, recognising that 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.

We focused on laws and regulations that could give rise to a material misstatement in the financial statements. Our tests included, but were not limited to:

- agreement of the financial statement disclosures to underlying supporting documentation;
- enquiries of management;
- review of minutes of board meetings throughout the period; and
- obtaining an understanding of the control environment in monitoring compliance with laws and regulations.

Because of the inherent limitations of an audit, there is a risk that we will not detect all irregularities, including those leading to a material misstatement in the financial statements or non-compliance with regulation. This risk increases the more that compliance with a law or regulation is removed from the events and transactions reflected in the financial statements, as we will be less likely to become aware of instances of non-compliance. The risk is also greater regarding irregularities occurring due to fraud rather than error, as fraud involves intentional concealment, forgery, collusion, omission or misrepresentation.

A further description of our responsibilities for the audit of the financial statements is located on the Financial Reporting Council's website at: 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.

Mark Wilson MA FCA
Senior Statutory Auditor
For and on behalf of RPG Crouch Chapman LLP
Chartered Accountants

Statutory Auditor
5th Floor, 14-16 Dowgate Hill
London
EC4R 2SU

30 June 2022

CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME

For the year ended 31 December 2021 - Financials in £

	Note	Group 2021	Group 2020
Revenue		**-**	-
Cost of sales	2	**-**	-
Gross loss		**-**	-
Administrative expenses	2	**(23,736,754)**	(20,269,788)
Operating loss	3	**(23,736,754)**	(20,269,788)
Finance income	2,4	**-**	3,297
Finance costs	2,5	**(5,755,981)**	(5,032,981)
Loss on ordinary activities before taxation		**(29,492,735)**	(25,299,472)
Taxation	6	**-**	-
Loss after taxation		**(29,492,735)**	(25,299,472)
Loss for the period			
Equity of shareholders of the parent company		**(29,492,735)**	(25,299,472)
Non-controlling interests		**-**	-
		(29,492,735)	(25,299,472)
Other comprehensive income			
Items that will or may be subsequently re-classified as to profit or loss:			
Exchange differences on translation of foreign operations		**(772,061)**	1,902,660
Total comprehensive loss for the year net of tax		**(30,264,796)**	(23,396,812)
Total comprehensive loss attributable to:			
Equity of shareholders of the parent Company		**(30,264,796)**	(23,396,812)
Non-controlling interests		**-**	-
		(30,264,796)	(23,396,812)
Loss per ordinary share			
Basic and diluted	10	**(7.71)p**	(8.75)p
Weighted average number of shares (000's)	10	**382,479**	288,981

The accompanying Notes on pages 115 to 138 form part of the financial statements.

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

As at 31 December 2021 - Financials in £

	Note	Group 2021	Group 2020
Non-current assets			
Intangible assets	11	**68,577,370**	56,869,415
Property, plant and equipment	12	**7,871,939**	6,710,777
Right of use assets	13	**33,183,516**	31,437,161
Trade and other receivables	14	**927,414**	934,834
		110,560,239	95,952,187
Current assets			
Inventories	16	**25,826,665**	22,138,323
Trade and other receivables	14	**643,319**	1,885,224
Cash and cash equivalents	15	**4,260,490**	2,317,451
		30,730,474	26,340,998
Total assets		**141,290,713**	122,293,185
Current liabilities			
Trade and other payables	17	**(5,347,169)**	(6,438,217)
Lease liabilities	13	**(745,315)**	(1,407,853)
Borrowings	18	**(10,025,497)**	(10,039,316)
		(16,117,981)	(17,885,386)
Non-current liabilities			
Licence fee received	17	**(16,500,000)**	(16,500,000)
Lease liabilities	13	**(32,201,824)**	(30,928,876)
Borrowings	18	**(10,382,520)**	(8,258,435)
Embedded derivative	18	**(4,718,960)**	(4,578,210)
		(63,803,304)	(60,265,521)
Total liabilities		**(79,921,284)**	(78,150,907)
Net assets		**61,369,428**	44,142,278
Equity			
Share capital	20	**112,903,053**	83,359,894
Share premium reserve	22	**71,087,838**	61,442,782
Share option reserve	23	**15,722,018**	7,675,332
Reverse acquisition reserve	24	**11,038,204**	11,038,204
Exchange movements reserve	25	**2,120,125**	2,892,186
Accumulated losses		**(151,501,810)**	(122,266,120)
Equity attributable to shareholders of the Parent Company		**61,369,428**	44,142,278
Total equity funds		**61,369,428**	44,142,278

These consolidated financial statements have been approved and were authorised for issue by the Board of Directors on 30 June 2022.

Dr Michael Sinclair
Executive Chairman

Nicolas Serandour
Chief Executive Officer

CONSOLIDATED STATEMENT OF CHANGES IN EQUITY

For the year ended 31 December 2021 - Financials in £

	Share capital	Share premium reserve	Share option reserve	Reverse acquisition reserve	Exchange movement reserve	Accumulated losses	Total equity share holders interest
Balance at 01 January 2020	61,105,852	60,452,065	7,853,803	11,038,204	989,526	(98,504,386)	42,935,064
Loss for the year	-	-	-	-	-	(25,299,472)	(25,299,472)
other comprehensive income exchange movement	-	-	-	-	1,902,660	-	1,902,660
Total comprehensive income	-	-	-	-	1,902,660	(25,299,472)	(23,396,812)
Shares Issued in the period	22,254,042	2,003,103	-	-	-	-	24,257,145
Expenses deducted from share premium	-	(1,012,386)	-	-	-	-	(1,012,386)
Lapsed options	-	-	(510,950)	-	-	510,950	-
Lapsed warrants	-	-	(1,026,788)	-	-	1,026,788	-
Share based payments							
- Share option charge	-	-	704,533	-	-	-	704,533
- Share warrants charge	-	-	654,734	-	-	-	654,734
Balance at 31 December 2020	83,359,894	61,442,782	7,675,332	11,038,204	2,892,186	(122,266,120)	44,142,278
Balance at 01 January 2021	83,359,894	61,442,782	7,675,332	11,038,204	2,892,186	(122,266,120)	44,142,278
Loss for the year	-	-	-	-	-	(29,492,735)	(29,492,735)
other comprehensive income exchange movement	-	-	-	-	(772,061)	-	(772,061)
Total comprehensive income	-	-	-	-	(772,061)	(29,492,735)	(30,264,796)
Shares Issued in the period	29,543,159	16,514,884	-	-	-	-	46,058,043
Expenses deducted from share premium	-	(1,194,556)	-	-	-	-	(1,194,556)
Cost of warrants deducted from share premium	-	(5,675,272)	5,675,272	-	-	-	-
Lapsed options	-	-	-	-	-	-	-
Lapsed warrants	-	-	(257,045)	-	-	257,045	-
Share based payments							
- Share option charge	-	-	2,421,599	-	-	-	2,421,599
- Share warrants charge	-	-	206,859	-	-	-	206,859
Balance at 31 December 2021	**112,903,053**	**71,087,838**	**15,722,018**	**11,038,204**	**2,120,125**	**(151,501,810)**	**61,369,429**

The accompanying Notes on pages 115 to 138 form part of the financial statements.

CONSOLIDATED STATEMENT OF CASH FLOWS

As at 31 December 2021 - Financials in £

	Group 2021	Group 2020
Cash flow from operating activities		
Loss after taxation	**(29,492,735)**	(25,299,472)
Adjustments to cash flows from non-cash items		
Depreciation of property, plant and equipment	**1,044,530**	1,000,115
Amortisation of right of use assets	**1,294,725**	1,331,698
Finance income	**-**	(3,297)
Finance expense	**3,603,480**	5,032,981
Taxation	**-**	-
Share based payment expense	**2,628,458**	1,340,949
Foreign exchange	**3,272,736**	471,204
Cash flows from operations before changes in working capital	**(17,648,807)**	(16,125,822)
Changes in inventories	**(9,188,342)**	(7,090,095)
Change in trade and other receivables	**1,249,325**	235,537
Change in trade and other payables	**(3,982,181)**	968,798
Cash (used) / generated from operations	**(29,570,005)**	(22,011,582)
Corporation tax receipt	**-**	1,768,591
Cash flows from operating activities	**(29,570,005)**	(20,242,991)
Cash flows from investing activities		
Interest received	**-**	3,297
Purchase of buildings, plant and equipment	**(2,222,647)**	(1,656,335)
Capital expenditure on intangible assets	**(12,572,083)**	(5,781,884)
Proceeds from disposal of investment property	**-**	-
Cash flows from investment activities	**(9,294,730)**	(7,434,922)
Cash flows from financing activities		
Proceeds from issue of ordinary shares	**43,564,416**	18,040,021
Costs of share issue	**1,299,072**	(728,853)
Interest paid	**(294,494)**	(327,086)
Long term loan receipts	**-**	7,621,951
Lease payments	**(3,781,009)**	(1,865,946)
Short term loan receipts	**7,850,000**	4,000,000
Short term loan repayments	**(7,850,000)**	-
Cash flows from financing activities	**40,787,985**	26,740,087
Increase/(decrease) in cash and cash equivalents	**1,923,249**	(937,825)
Exchange gain/(loss) on cash and cash equivalents	**19,789**	20,109
Cash and cash equivalents at 01 January 2021	**2,317,451**	3,235,167
Cash and cash equivalents at 31 December 2021	**4,260,490**	2,317,451

The accompanying Notes on pages 115 to 138 form part of the financial statements.

NOTES FORMING PART OF THE FINANCIAL STATEMENTS

Consolidated

Company

NOTES TO THE ACCOUNTS – GROUP

Continued - Financials in £

1. Principal accounting policies – Group

a. Accounting convention, basis of preparation and going concern
These financial statements have been prepared under accordance with international accounting standards in conformity with the requirements of the Companies Act 2006. The financial statements have been prepared on the historical cost basis modified to include certain assets and liabilities at fair value.

The Directors have taken advantage of the exemption offered by Section 408 of the Companies Act 2006 not to prepare a separate statement of comprehensive income for the Parent Company.

Advanced Oncotherapy PLC ("the Company") is a public limited company incorporated and domiciled in the UK. The nature of the operations and principal activities of the Company and its subsidiary undertakings (the "Group") are set out in the Strategic Report on pages 1 to 76 and the Directors' report on pages 101 to 104. These consolidated financial statements are presented in pounds sterling because that is the predominant currency of the economic environment in which the Group operates.

Use of estimates and judgements
The preparation of financial statements in conformity with IFRS requires management to make judgements, estimates and assumptions that affect the application of policies and reported amounts of assets and liabilities, income and expenses. The estimates and associated assumptions are based on historical experience and opinions or statements received from competent professional advisors. The assumptions used are considered to be reasonable under the circumstances and the results of which form the basis of making judgements about the carrying values of assets and liabilities that are readily apparent from other sources. Actual results may differ from these estimates.

Estimates and assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognised in the period in which the estimates are revised if the revisions affects only that period.

Critical estimates and judgements that have the most significant effect on the amounts recognised in the financial statements and/or have a significant risk attached to:

1. The values ascribed to Intangible assets. The Directors carried out an impairment review of the Intangible assets and found that no impairment is necessary. At 31 December 2021, the Group held intangible assets currently still being developed, for which the most sensitive assumption is the probability of technical success and, given their nature, impairment adjustments triggered by future events that have yet to occur which may be material. In addition, there is a significant risk that impairments recognised in any one period may be subject to material adjustments in future periods. See Note 10 and Note w below.

2. Inventory. The Directors have made significant accounting estimates in respect of the carrying value of inventory at the year-end both in respect of estimated selling prices and costs to complete the inventory. These estimates have been based on quoted amounts from suppliers and on discussions with or signed contracts with potential customers. An impairment provision of £nil (2020: £1.9m) has been provided. Some sales values are contractually agreed thus a 20% reduction in those not agreed would lead to an impairment of £1.1m. An increase in expected costs of 20% would lead to an impairment of £4.3m.

3. Incremental interest rates on Leases. On adoption of IFRS 16, the Group recognised lease liabilities in relation to leases which had previously been classified as 'operating leases' under the principles of IAS 17 Leases. These liabilities were measured at the present value of the remaining lease payments, discounted using the lessee's incremental borrowing rate as of 1 January 2020. The weighted average lessee's incremental borrowing rate applied to the lease liabilities on 1 January 2020 was 3.0%. The determination of applicable incremental borrowing rates at the commencement of new lease contracts also requires judgement. The Group determines its incremental borrowing rates by obtaining interest rates from various external financing sources and makes certain adjustments to reflect the terms of the lease. The Group considers the relevant market interest rate, based on the weighted average of the timing of the lease payments under the lease obligation.

4. Going concern – refer to Note 1b for judgments in respect of the going concern basis of preparation.

5. Valuation of share based payments – the estimation related to share based payments includes the selection of an appropriate valuation option pricing model, consideration as to the inputs into the valuation model chosen and the estimation of the number of the awards that will ultimately vest. Inputs subject to estimation relate to the future volatility of the share price based on historically observed volatility from trading in the Company's shares, over a historical period between the date of grant and the date of exercise. Management has used a Monte Carlo model to calculate the fair value of the awards which include market based conditions. Further disclosure of inputs relevant to the calculations is set out in Note 21.

6. Accounting for loan agreements and valuation of embedded derivative – management have applied judgement in accounting for the loan received from Nerano. In determining the appropriate accounting, they have considered the terms of the arrangement and identified that the loan contains an embedded derivative that needs to be recognised separately from the host contract. Additionally, they have applied judgement in determining which of the cash flows arising from the arrangement can be estimated reliably in determining what should be included in the amortised cost calculation.

   The fair value of the embedded derivative has been determined through a range of inputs and modelling the results of the change in these inputs. Inputs are determined based on past performance, comparable instruments and management's determination of the suspected future time horizons for the conversion of the instruments. These forecasted values are by their nature estimates and therefore there is uncertainty with relation to the valuation of these instruments. Further details in relation to the valuation of these instruments can be found in Note 18.

1. Principal accounting policies – Group continued

A summary of the Group accounting policies is set out below, together, where relevant, with an explanation of where changes have been made to previous policies on the adoption of new accounting standards in the year. Certain new standards, amendments and interpretations to existing standards have been published that are mandatory for the Group's accounting periods beginning on or after 01 January 2021 and these have been adopted in the financial statements.

b. Going concern
The Group has made a loss before tax of £29.5m (2021: £23.4m) and is presently pre-revenue and, as such, has relied upon equity and debt funding to progress its development plans. Post year end, the Group has successfully raised £11.5m in equity and £1.5m in short term loans.

The Directors regularly review cash flow forecasts to determine whether the Group has sufficient cash reserves to meet its future working capital requirements and development plans. The Group's plans indicate that they need to raise further finance and the Directors are confident based on past history of successful fundraising and discussions with investors that the Group will be successful in raising these funds. Additionally, they consider they can defer settlement of creditors, reduce short term expenditure and obtain short-term finance should there be any delay in completing any such fundraising to allow continuance of their plans. They therefore consider it appropriate to prepare the Group's financial statements on a going concern basis.

However, as at the date of approval of these financial statements, there are no legally binding agreements in place in relation to any fundraising or extension of terms of with creditors and as the success of any finance raising is outside the control of the company and is thus considered to be a material uncertainty. There can be no certainty that additional funds will be forthcoming which indicates the existence of a material uncertainty which may cast doubt about the Group's ability to continue as a going concern and therefore it may be unable to realise its assets and discharge its liabilities in the normal course of business. The financial statements do not include the adjustments that would result if the Group was unable to continue as a going concern.

c. Basis of consolidation
The consolidated financial information includes financial information in respect of the Group and all of its subsidiary undertakings.

The results of subsidiaries acquired or disposed of during the year are included in the consolidated statement of comprehensive in-come from the effective date of acquisition or up to the effective date of disposal, as appropriate. All intra-group transactions, balances, income and expenses are eliminated on consolidation.

The consolidated financial statements consolidate the financial statements of the Company and its subsidiary undertakings (together "the Group") drawn up to 31 December 2021.

A subsidiary is an entity controlled by the Company. Control is achieved where the Company:
- has power over the investee;
- is exposed, or has rights, to variable returns from its involvement with the investee; and
- has the ability to use its power to affect its returns

Consolidation of a subsidiary begins when the Company obtains control over the subsidiary and ceases when the Company loses con-trol of the subsidiary. Specifically, income and expenses of a subsidiary acquired or disposed of during the year are included in the con-solidated statement of profit or loss and other comprehensive income from the date the Company gains control until the date when the Company ceases to control the subsidiary.

Where necessary, adjustments are made to the financial statements of subsidiaries to bring their accounting policies into line with those used by the Group.

The purchase method of accounting is used to account for business combinations that result in the acquisition of subsidiaries by the Group. The cost of a business combination is measured as the fair value of the assets given, equity instruments issued and liabilities incurred or assumed at the date of exchange, plus costs directly attributable to the business combination. Identifiable assets acquired and liabilities and contingent liabilities assumed in a business combination are measured initially at their fair values at the acquisition date. Any excess of the cost of the business combination over the acquirer's interest in the net fair value of the identifiable assets, liabilities and contingent liabilities recognised is recorded as goodwill.

Inter-company transactions, balances and unrealised gains on transactions between the Company and its subsidiaries, which are related parties, are eliminated in full.

d. Intangible assets-research and development
Development activities involve a plan or design for the production of new and innovative proton beam cancer therapy machines. Development expenditure is capitalised only if development costs can be measured reliably, the proton therapy machine is technically and commercially feasible, future economic benefits are probable, and the Group has sufficient resources available to complete development and to use, lease or sell the asset. The expenditure capitalised includes only the cost of gross direct labour that is directly attributable to preparing the asset for its intended use or third-party costs incurred directly on the development activities above. Capitalised development expenditure is measured at cost less accumulated amortisation and accumulated impairment losses. Other research and development expenditure not meeting the above criteria is recognised in the income statement as incurred. Capitalised development costs are amortised over the period from the date the development generates revenue. As at 31 December 2021 the proton therapy machines are still in the development phase and therefore no amortisation has been recognised

Continued - Financials in £

1. Principal accounting policies – Group continued

in the income statement. Management estimates the useful economic life of the proton machines to be 20 years once development has been completed.

e. Property, Plant and Equipment
Depreciation is provided at the following annual rates in order to write off each asset over its estimated useful life:

Fixtures and fittings	20% of cost
Plant - equipment	14 % to 20% of cost
Plant - LIGHT development equipment	20% of cost
Computer equipment	33.3% to 50% of cost
Leasehold Improvements	are written off over the term of the lease

Property, plant and equipment are stated at cost less accumulated depreciation and accumulated impairment losses. Where parts of an item of property, plant and equipment have different useful lives, they are accounted for as separate items of property, plant and equipment.

f. Cash and cash equivalents
Cash and cash equivalents are carried in the balance sheet at cost. For the purposes of the cash flow statement, cash and cash equivalents comprise cash on hand, deposits with banks and other short-term highly liquid investment maturities of three months or less, net of short term bank overdrafts.

g. Trade and other receivables
Trade and other receivables are recognised initially at the transaction price. They are subsequently measured less any provision for impairment in relation to expected credit losses. At each reporting date the Group assesses the expected credit losses and changes in credit risk since initial recognition of the receivable and a provision for impairment is recognised when considered necessary.

h. Trade and other payables
Trade and other payables are recognised initially at the transaction price and subsequently measured at amortised cost using the effective interest method.

i. Holiday Pay Accrual
A liability is recognised to the extent of any unused holiday pay entitlement which is accrued at the Statement of Financial Position date and carried forward to future periods. This is measured at the undiscounted salary cost of the future holiday entitlement.

j. Government Grants
Grants have been received from the UK and US governments to assist with staff furlough and payroll costs during the COVID pandemic. The grants are included in the financial statements to the extent that they have been received for the reporting period and confirmation has been received that they will become repayable at any point. No other forms of government assistance have been received.

k. Inventories
Stocks are stated at the lower of cost and realisable value. Cost is based on the first-in first-out principle. Net realisable value is the estimated selling price in the ordinary course of business, less the estimated costs of selling expenses. Any write down to net realisable value is recorded in cost of sales.

Work in progress is valued at the cost charged for material supplies and the cost charged by sub-contractors for work completed or in progress with those sub-contractors. No element of Group overhead or finance cost has been included.

l. Revenue recognition
During prior periods, the company received an amount of £16.5m for an exclusive distribution agreement issued to Liquid Harmony Ltd. This amount is fully repayable if the entity does not complete the development of the products and have regulatory approval in China within 5 years of the signing of the agreement. As a result of the conditions attached requiring full repayment no revenue, has been recognised.

m. Income taxes
The charge for current taxation is based on the results for the year as adjusted for items which are non-assessable or disallowed.

Deferred tax is provided using the balance sheet liability method in respect of temporary differences between the carrying amount of assets and liabilities in the financial statements and the corresponding tax bases used in computation of taxable profit.

Deferred tax is determined using tax rates that have been enacted or substantially enacted by the balance sheet date and are expected to apply when the related deferred tax asset is realised or the deferred tax liability is settled. It is recognised in profit or loss except when it relates to items credited or charged directly to equity, in which case the deferred tax is also dealt with in equity.

Deferred tax is determined using tax rates that have been enacted or substantially enacted by the balance sheet date and are expected to apply when the related, deferred tax asset is realised or the deferred tax liability is settled. It is recognised in profit or loss except when it relates to items credited or charged directly to equity, in which case the deferred tax is also dealt with in equity.

Deferred tax assets are recognised to the extent that it is probable that future taxable profit will be available against which the

1. Principal accounting policies – Group continued

temporary difference can be utilised. Deferred tax assets and liabilities are offset only when they relate to taxes levied by the same authority, with a legal right to set off and when the Group intends to settle them on a net basis.

n. Pensions
The Group makes defined contributions to employees' personal pension plans. Contributions payable to the employees' schemes are recognised as an expense in the statement of comprehensive income as incurred.

o. Share based payments
The cost of granting share options and other share based remuneration to employees and Directors is recognised through the statement of comprehensive income on a straight-line basis over the vesting period, based on the Group's estimate of shares that will eventually vest. These share based payments are measured at fair value at the date of grant by use of an option pricing mode. Where the share options only contain service conditions or non-market conditions, a Black – Scholes model is used. Where the share options contain market conditions, a Monte Carlo simulation model is used and reflected the in the fair value of the options granted. Details of the assumptions used in those models are included in Note 21 Share based payments.

For equity-settled transactions with non-employees, the costs are recognised through the statement of comprehensive income with measurement based on the fair value of goods or services received.

p. Foreign currencies
Transactions in currencies other than the entity's functional currency are recorded at the exchange rate prevailing at the transaction dates. Foreign exchange gains and losses resulting from settlement of these transactions and from retranslation of monetary assets and liabilities denominated in foreign currencies are recognised in profit or loss.

The assets and liabilities of foreign entities are translated into sterling at the rate of exchange ruling at the balance sheet date and their statements of comprehensive income and cash flows are translated at the average rate for the period. Exchange differences arising are transferred to reserves as a separate component of equity.

The Group's presentational currency is GBP.

q. Financial instruments
The Group's activities expose it primarily to the financial risks of changes in foreign currency exchange rates and interest rates.

Loans are initially recognised net of associated transaction costs. Subsequent to initial recognition, they are stated at amortised cost.

r. Loans and Borrowings
Loans and borrowings are recorded at amortised cost using the effective interest method using the expected cash flows attached to the financial instrument, with interest-related charges recognised as an expense in finance cost in the statement of comprehensive income. In rare circumstances, where cash flows are not possible to be predicted the contractual cash flows over the contractual term of the financial instrument are used.

Where the loan includes a convertible feature, resulting in the possible settlement through issue of shares management consider if the conversion would result in a fixed loan amount being settled with a fixed number of shares. Where this is the case, the cash flows attached to the financial instrument are discounted at a market rate of interest and the difference between cash proceeds and the present value of cash flows being recorded in equity. If the conversion feature does not result in the settlement of a fixed loan amount with a fixed number of shares, the financial instrument is assessed as containing a host financial liability held at amortised cost and a financial liability held at fair value through profit and loss.

The fair value of the derivative component held at fair value through profit and loss is derived at draw down date and recognised separately from the host contract which is held at amortised cost. The derivative component is subsequently measured at fair value at each reporting date with the changes being recorded in profit and loss.

s. Equity instruments
Equity instruments issued by the Group are recorded at the proceeds received, net of direct issue costs.

t. Financial liability and equity
Financial liabilities and equity instruments are classified according to the substance of the contractual arrangements entered into. An equity instrument is any contract that evidences a residual interest in the assets of the Company after deducting all of its liabilities.

u. Borrowing costs
All borrowing costs are recognised in profit or loss in the period in which they are incurred.

v. Segmental reporting
As the Group's business activities were not complex, being the development and building of the LIGHT system, and the management of a healthcare related property, management reviews information based on different locations and, accordingly, the operating segments are based on such a geographical split.

w. Impairment of non-current assets
The Group's main asset is it development costs which are not yet ready for use. As a result an annual impairment revenue review is

Continued - Financials in £

1. Principal accounting policies – Group continued

performed which involves estimating the recoverable amount of the assets, which is the higher of its fair value less costs to sell and its value in use, is estimated in order to determine the extent of the impairment loss. Where the carrying value of an asset exceeds its recoverable amount (i.e. the higher of value in use and fair value less costs to sell), the asset is written down accordingly. Impairment charges are included in profit or loss, except to the extent they reverse gains previously recognised in other comprehensive income.

x. Leases

Identifying Leases

The Group accounts for a contract, or a portion of a contract, as a lease when it conveys the right to use an asset for a period of time in exchange for consideration. Leases are those contracts that satisfy the following criteria:

(a) There is an identified asset;
(b) The Group obtains substantially all the economic benefits from use of the asset; and
(c) The Group has the right to direct use of the asset.

The Group considers whether the supplier has substantive substitution rights. If the supplier does have those rights, the contract is not identified as giving rise to a lease.

In determining whether the Group obtains substantially all the economic benefits from use of the asset, the Group considers only the economic benefits that arise use of the asset, not those incidental to legal ownership or other potential benefits.

In determining whether the Group has the right to direct use of the asset, the Group considers whether it directs how and for what purpose the asset is used throughout the period of use. If there are no significant decisions to be made because they are pre-determined due to the nature of the asset, the Group considers whether it was involved in the design of the asset in a way that predetermines how and for what purpose the asset will be used throughout the period of use. If the contract or portion of a contract does not satisfy these criteria, the Group applies other applicable IFRSs rather than IFRS 16.

On adoption of IFRS 16, the Group recognised lease liabilities in relation to leases which had previously been classified as 'operating leases' under the principles of IAS 17 Leases. These liabilities were measured at the present value of the remaining lease payments, discounted using the lessee's incremental borrowing rate as of 1 January 2020. The weighted average lessee's incremental borrowing rate applied to the lease liabilities on 1 January 2020 was 3.0%. The determination of applicable incremental borrowing rates at the commencement of new lease contracts also requires judgement. The Group determines its incremental borrowing rates by obtaining interest rates from various external financing sources and makes certain adjustments to reflect the terms of the lease. The Group considers the relevant market interest rate, based on the weighted average of the timing of the lease payments under the lease obligation.

y. Changes in Accounting Policy

(i) New and amended standards adopted by the Group:

The accounting policies adopted are consistent with those of the previous financial year. New or amended financial standards or interpretations adopted during the year are detailed below:

- Amendments to IFRS 9 Financial Instruments, IAS 39 Financial Instruments: Recognition and Measurement, IFRS 7 Financial Instruments: Disclosures, and IFRS 16 Leases – Interest Rate Benchmark Reform (Phase 2)
- Amendments to IFRS 16 Leases – Covid-19-Related Rent concessions beyond 30 June 2021.

No material impact has arisen as a result of applying these standards.

(ii) The following standards, amendments and interpretations, which are effective for reporting periods beginning after the date of these financial statements, have not been adopted early:

Standard	Description	Effective date
IFRS 1	Amendments resulting from Annual Improvements to IFRS Standards 2018–2020 (subsidiary as a first-time adopter)	01 January 2022
IFRS 3	Amendments updating a reference to the Conceptual Framework	01 January 2022
IFRS 9	Amendments resulting from Annual Improvements to IFRS Standards 2018–2020 (fees in the '10 per cent' test for derecognition of financial liabilities)	01 January 2022
IAS 1	Amendments regarding the classification of liabilities	01 January 2023
IAS 1	Amendment to defer the effective date of the January 2020 amendments	01 January 2023
IAS 1	Amendments regarding the disclosure of accounting policies	01 January 2023
IAS 8	Amendments regarding the definition of accounting estimates	01 January 2023
IAS 12	Amendments regarding deferred tax on leases and decommissioning obligations	01 January 2023
IAS 16	Amendments prohibiting a company from deducting from the cost of property, plant and equipment amounts received from selling items produced while the company is preparing the asset for its intended use	01 January 2022
IAS 37	Amendments regarding the costs to include when assessing whether a contract is onerous	01 January 2022

In reviewing the above standards, the Company does not believe that there will be a material impact on the financial statements.

2. Segment reporting

	Notes	2021 Development of Proton Therapy - UK	Development of Proton Therapy - Switzerland	Development of Proton Therapy - USA	Group
Revenue		**-**	**-**	**-**	**-**
Cost of sales		**-**	**-**	**-**	**-**
Gross Loss		**-**	**-**	**-**	**-**
Administrative expenses		**(14,192,526)**	**(8,446,846)**	**(1,097,382)**	**(23,736,754)**
Operating loss		**(14,192,526)**	**(8,446,846)**	**(1,097,382)**	**(23,736,754)**
Finance income	4	**-**	**-**	**-**	**-**
Finance costs	5	**(5,742,537)**	**(13,444)**	**-**	**(5,755,981)**
Loss on ordinary activities before taxation		**(19,935,063)**	**(8,460,290)**	**(1,097,382)**	**(29,492,735)**
Capital Expenditure					
Intangible assets	11	**1,872,420**	**5,199,663**	**-**	**7,072,083**
Property, plant and equipment	12	**2,021,294**	**201,353**	**-**	**2,222,647**
Total assets		**97,194,588**	**43,887,118**	**209,007**	**141,290,713**
Total liabilities		**(76,632,688)**	**(3,246,897)**	**(41,699)**	**(79,921,284)**
Net assets/(liabilities)		**20,561,900**	**40,640,221**	**167,308**	**61,369,428**

During 2021 the Group operated in one business segment: Proton Therapy.

	Notes	2020 Development of Proton Therapy - UK	Development of Proton Therapy - Switzerland	Development of Proton Therapy - USA	Group
Revenue		-	-	-	-
Cost of sales		-	-	-	-
Gross Loss		-	-	-	-
Administrative expenses		(11,104,749)	(8,279,694)	(885,345)	(20,269,788)
Operating loss		(11,104,749)	(8,279,694)	(885,345)	(20,269,788)
Finance income	4	3,297	-	-	3,297
Finance costs	5	(5,032,884)	(97)	-	(5,032,981)
Loss on ordinary activities before taxation		(16,134,336)	(8,279,791)	(885,345)	(25,299,472)
Capital Expenditure					
Intangible Assets	11	501,546	5,280,338	-	5,781,884
Property, Plant and Equipment	12	1,315,203	340,282	850	1,656,335
Total assets		82,073,874	40,194,549	24,762	122,293,185
Total liabilities		(74,862,311)	(3,246,897)	(41,699)	(78,150,907)
Net assets/(liabilities)		7,211,563	36,947,652	(16,937)	44,142,278

For the year ended 31 December 2021 - Financials in £

3. Operating loss

	Note	2021	2020
Operating loss is arrived at after charging:			
Depreciation	12	**1,044,530**	1,000,115
Amortisation of right of use assets	13	**1,294,725**	1,331,698
Foreign exchange loss or (gain)		**139,915**	471,204
Amounts payable to the Group's Auditor and their associates for:			
- audit of the Group's annual accounts		**22,875**	22,250
- audit of the Group's subsidiaries		**33,475**	32,500
- taxation compliance		**8,750**	8,500

4. Finance income

	2021	2020
Interest receivable on deposits	**-**	3,297
Total	**-**	3,297

5. Finance costs

	2021	2020
Interest expense on unsecured facilities	**264,552**	291,408
Interest expense on secured loans	**3,448,116**	2,557,025
Interest expense on lease liabilities	**1,349,247**	1,322,763
Costs of raising finance	**553,316**	-
Embedded derivative cost	**140,750**	861,785
Total	**5,755,981**	5,032,981

Refer to Note 18 for information on the secured loan interest rates.

6. Taxation on profit for ordinary activities

(a) Tax (credit) / charge comprises	2021	2020
Current tax		
UK corporation tax charge/(credit) for the year	-	-
UK corporation tax charge/(credit) for the previous year	-	-
Deferred tax		
Origination and reversal of temporary differences	-	-
Total tax credit	-	-

(b) Factors affecting tax credit for the year

The tax assessed for the year differs from the standard rate of corporation tax in the UK (19.0%) (2020: 19.0%)
The differences are explained below:

	2021	2020
Loss on ordinary activities before tax	**(29,492,735)**	(25,299,472)
Loss on ordinary activities multiplied by the standard rate of corporation tax in the UK at 19.00% (2020: 19.0%)	**(5,603,620)**	(4,806,900)
Effects of:		
Permanent differences	**273,572**	360,518
Capital allowances in excess of depreciation	**(31,827)**	90,655
Short term timing differences	**491,814**	573,215
Unprovided losses carried forward	**4,870,061**	3,782,511
Tax credit for the year	-	-

(c) Unprovided deferred tax assets at 19.0% (2020: 19.0%)	2021	2020
Losses carried forward	**(34,903,630)**	(20,915,823)
R&D tax credit on Intangible assets	**11,198,869**	7,545,825
Accelerated capital allowances	**1,363,307**	1,083,814
Total	**(22,341,454)**	(12,286,184)

No deferred tax asset has been recognised on the above item on the grounds that it is uncertain when taxable profits will arise against which losses carried forward may be utilised.

NOTES TO
THE ACCOUNTS – GROUP

Continued - Financials in £

7. Staff costs

	2021	2020
Wages and salaries	**13,444,972**	12,917,614
Social security costs	**1,378,526**	1,130,903
Pension costs	**1,005,420**	933,981
Other benefits	**345,108**	350,672
Share based payments	**1,051,754**	1,340,949
Total	**17,225,781**	16,674,119

Staff costs include amounts of £5,080,607 (2020:£5,240,672) which have been capitalised within development projects during the year.
Government grants of £ nil (2020: 89,535) have been included in Wages and Salaries. The amounts in 2020 were received to assist with the costs of furloughing two employees in the UK and a lump sum for assistance in the US.
Details of employee share options are set out in Note 21.

The monthly average number of persons employed during 2021 was 157 (2020: 139), categorised as follows:

	2021	2020
Managerial	**10**	10
Operational	**24**	18
Product Development	**62**	60
Technical	**36**	31
Administrative	**25**	20
Total	**157**	139

8. Directors' remuneration

The salaries and benefits of the Directors of the Group payable by the Company or any of the Group companies for the year ended 31 December 2021 were as follows:

	2021							
	Appointed	Resigned	Base salary (£)	Bonus (£)	Committee Membership (£)	Pension (£)	Other benefits (£)	**Total (£)**
Dr Michael Sinclair, Executive Chairman	16 Jun 06		252,240	166,667*	-	-	15,509	**434,416**
Nicolas Serandour, CEO	27 Aug 14		300,000	166,667*	-	30,000	6,298	**502,965**
Prof Steve Myers	26 Jan 17		229,256	166,667*	-	-	1,794	**397,716**
Michael Bradfield	26 Apr 13		30,000	-	20,000	-	-	**50,000**
Lori Cross	29 Sep 20		30,000	-	15,000	-	-	**45,000**
Dr Nick Plowman	09 Feb 17		30,000	-	10,000	-	-	**40,000**
Dr Enrico Vanni	01 Oct 13		30,000	-	32,500	-	-	**62,500**
Hans Von Celsing	26 Jan 17		30,000	-	37,500	-	-	**67,500**
Renhua Zhang	28 Aug 18		30,000	-	-	-	-	**30,000**
Total			961,496	500,000	115,000	30,000	23,601	**1,630,097**

** As per the market announcement dated 11 August 2021*

Mchael Bradfield, Lori Cross, Nick Plowman, Enrico Vanni, Renhua Zhang and Hans von Celsing elected to take their remuneration to June 2021 in shares. Amounts due for July to December 2021 are included in creditors. Dr Sinclair took part of his salary in shares.

Chunlin Han, a former Director, represents Renhua Zhang at Board Meetings and is, therefore, registered at Companies House as a Director. He receives no remuneration.

8. Directors' remuneration continued

	2020							
	Appointed	Resigned	Base salary (£)	Bonus payment (£)	Pension (£)	Medical Board Fees (£)	Other benefits (£)	**Total (£)**
Dr Michael Sinclair, Executive Chairman	16 Jun 06		270,147	-	-	-	18,623	**288,770**
Nicolas Serandour, CEO	27 Aug 14		300,000	-	-	30,000	6,298	**336,298**
Prof Steve Myers	26 Jan 17		264,599	-	-	-	2,914	**267,513**
Michael Bradfield	26 Apr 13		26,400	96,100	-	-	-	**122,500**
Lori Cross	29 Sep 20		7,500	-	-	-	-	**7,500**
Dr Nick Plowman	09 Feb 17		30,000	96,100	6,000	-	-	**132,100**
Dr Enrico Vanni	01 Oct 13		30,000	96,100	-		-	**126,100**
Hans Von Celsing	26 Jan 17		30,000	96,100	-	-	-	**126,100**
Renhua Zhang	28 Aug 18		29,113	-	-	-	-	**29,113**
Chunlin Han^	28 Aug 18	31 Jul 20	17,863	-	-	-	-	**17,863**
Yuelong Huang	28 Aug 18	31 Jul 20	17,863	-	-	-	-	**17,863**
Peter Sjöstrand	28 Aug 18	31 Jul 20	17,500	-	-	-	-	**17,500**
Gabriel Urwitz	28 Aug 18	31 Jul 20	16,800	-	-	-	-	**16,800**
Total			1,057,785	384,400	6,000	30,000	27,835	**1,506,020**

^ Mr Chunlin Han is an alternate director (unremunerated) for Mrs. Zhang so that he may attend board meetings when Mrs. Renhua Zhang is unable to do so

Directors' share options

	At 01 Jan 2021	Granted during the year	Lapsed or expired during the year	Exercised during the year	**At 31 Dec 2021**	Option price pence	Date of grant	Earliest exercise date	Expiry date
Prof Steve Myers	**215,000**	-	-	-	**215,000**	100.0p	20 Feb 19	20 Feb 19	20 Feb 24
	1,500,000	-	-	-	**1,500,000**	50.0p	01 Oct 20	Note[1]	04 Oct 25
Nicolas Serandour	**1,400,000**	-	-	-	**1,400,000**	100.0p	20 Feb 19	20 Feb 19	20 Feb 24
	6,500,000	-	-	-	**6,500,000**	50.0p	01 Oct 20	Note[1]	04 Oct 25
Dr Michael Sinclair	**545,000**	-	-	-	**545,000**	100.0p	20 Feb 19	20 Feb 19	20 Feb 24
	5,500,000	-	-	-	**5,500,000**	50.0p	01 Oct 20	Note[1]	04 Oct 25
Total	**15,660,000**	**-**	**-**	**-**	**15,660,000**	**56.9p**			

Note[1] See vesting conditions in Note 21

The fair value of these options has been charged to the Consolidated Statement of Comprehensive Income.

Directors' share warrants

	At 01 Jan 2021	Granted during the year	Lapsed or expired during the year	Exercised during the year	**At 31 Dec 2021**	Warrant price pence	Date of grant	Earliest exercise date	Expiry date
Dr Enrico Vanni	**40,816**	-	-	-	**40,816**	100.0p	31 Aug 18	31 Aug 18	31 Aug 23
Hans von Celsing	**6,000**	-	-	-	**6,000**	100.0p	31 Aug 18	31 Aug 18	31 Aug 23
Dr Nick Plowman	**61,224**	-	-	-	**61,224**	100.0p	31 Aug 18	31 Aug 18	31 Aug 23
Total	**108,040**	**-**	**-**	**-**	**108,040**	**100.0p**			

As disclosed above no warrants have been issued to the Directors during in the year (2020: nil).

The fair value of services received in return for share options and warrants is measured by reference to the fair value of the share options and warrants granted. This estimate is based upon a Black-Scholes model or Monte Carlo simulations based on the terms of options. The inputs into the Black-Scholes model for Options and Warrants granted in the year are shown in Note 21.

Continued - Financials in £

9. Pensions

The Group operates a defined contribution pension scheme. Contributions payable for the period of £1,005,420 (2020: £901,485) are charged in the statement of comprehensive income. One Director (2020: One) accrued retirement benefits during the year. A charge of £30,000 (2020: £30,000) has been included in the year for the Directors.

10. Loss per share

Basic loss per share is calculated by dividing the loss for the period by the weighted average number of ordinary shares in issue during the year. This is disclosed on page 109 on the income statement. An alternative to this is the loss per share based on the comprehensive loss attributable to the equity holders of the group. This is shown below.

	2021	2020
Loss attributable to equity holders of the Group (£'s)	**(29,492,735)**	(25,299,472)
Weighted average number of ordinary shares in issue (000s)	**382,479**	288,981
Loss per share (pence per share)	**(7.71)p**	(8.75)p

Diluted loss per share
The Group has two categories of dilutive potential ordinary shares - share options and warrants. Both the Group's share options and warrants have been excluded from the calculation of diluted loss per share as the entity is loss making and they would be anti-dilutive. These instruments could potentially be dilutive in the future.

Events after reporting period
As at 30 June 2022 the Company had 473,352,211 ordinary shares in issue. Assuming the same loss for the year ended 31 December 2021 the basic loss per share for the year ended 31 December 2021 divided by the current number of shares in issue would decrease to (6.23)p per share.

11. Intangible assets

	LIGHT Accelerator	Treatment Software	Total
Development costs			
At 01 January 2020	33,644,841	15,538,587	49,183,428
Foreign exchange difference	1,301,955	602,148	1,904,103
Additions	3,938,402	1,843,482	5,781,884
At 31 December 2020	38,885,198	17,984,217	56,869,415
Development costs			
At 01 January 2021	38,885,198	17,984,217	56,869,415
Foreign exchange difference	(590,859)	(273,269)	(864,128)
Reclassification of assets - Inventory	5,500,000	-	5,500,000
Additions	3,712,622	3,359,461	7,072,083
At 31 December 2021	**47,506,961**	**21,070,408**	**68,577,370**

For the purpose of impairment testing of intangible assets, the Group's continuing operations are regarded as a single cash-generating unit relating to the development and operation of the LIGHT technology.

The recoverable amount is based on value in use using discounted risk-adjusted projections of the Group's pre-tax cash flows over 10 years and then at a flat rate into perpetuity which is considered by the Board as a reasonable period given the long development and expected operational life cycle of the LIGHT technology. The projections include assumptions about the number of units to be sold in each financial year, expected unit selling price and production cost, pipeline conversion, competition from rival products and pricing policy as well as the possibility of new technology entering the market. In setting these assumptions the Directors consider their own past experience, external sources of information (including information on expected increases and ageing of the populations in our established markets and the expanding patient population in newer markets), our knowledge of competitor activity and our assessment of future changes in the proton beam industry. The 10 year period is covered by internal budgets and forecasts. Given that internal budgets and forecasts are prepared for all projections, no general growth rates are used to extrapolate internal budgets and forecasts for the purposes of determining value in use. The methods used to determine recoverable amounts have remained consistent with the prior year. The weighted average pre-tax discount rate used was approximately 12.5% (2020: 12.5%).

As a further check, the market capitalisation is compared to the book value of the Group's net assets: as of the date of this report, the market capitalisation is higher than the book value of the net assets.

No impairment was found necessary.

The Group has also performed sensitivity analysis calculations on the projections used and discount rate applied. By their nature, the value in use calculations are sensitive to the underlying methods, assumptions and estimates. Consistent with prior years, as part of the impairment review process, management has not identified that reasonably possible changes in certain key assumptions may cause the carrying amount of the intangible assets to exceed the recoverable amount. At 31 December 2021, the Group held intangible assets currently still being developed, for which the most sensitive assumption is the probability of final technical success, and given their nature, impairment adjustments triggered by future events that have yet to occur may be material. In addition, there is a significant risk that impairments recognised in any one period may be subject to material adjustments in future periods.

Continued - Financials in £

12. Plant and equipment

	Leasehold property	Computer hardware and software	Fixtures, fittings and equipment	Total
Cost				
At 01 January 2020	5,377,959	456,351	2,015,835	7,850,145
Foreign exchange difference	12,360	14,886	104,957	132,203
Additions	543,583	274,895	837,857	1,656,335
At 31 December 2020	5,933,902	746,132	2,958,649	9,638,683
Depreciation				
At 01 January 2020	296,536	306,743	1,244,366	1,847,645
Foreign exchange difference	234	9,249	70,663	80,146
Charge for the year	415,638	131,806	452,671	1,000,115
At 31 December 2020	712,408	447,799	1,767,699	2,927,906
Net book value				
At 01 January 2020	5,081,423	149,608	771,469	6,002,500
At 31 December 2020	5,221,494	298,333	1,190,950	6,710,777
Cost				
At 01 January 2021	5,933,902	746,132	2,958,649	9,638,683
Foreign exchange difference	(5,040)	(11,029)	(43,324)	(59,393)
Additions	1,737,099	86,112	399,436	2,222,647
At 31 December 2021	**7,665,961**	**821,214**	**3,314,761**	**11,801,937**
Depreciation				
At 01 January 2021	712,408	447,799	1,767,699	2,927,906
Foreign exchange difference	(566)	(5,873)	(35,998)	(42,437)
Charge for the year	545,007	153,944	345,579	1,044,530
At 31 December 2021	**1,256,849**	**595,869**	**2,077,280**	**3,929,998**
Net book value				
At 01 January 2021	5,221,494	298,333	1,190,950	6,710,777
At 31 December 2021	**6,409,112**	**225,345**	**1,237,481**	**7,871,939**

13. Leases

	Land & Buildings	
	2021	2020
Right-of-Use Assets		
At the beginning of the period	**31,437,161**	32,528,667
Additions	**3,062,048**	144,664
Amortisation	**(1,294,725)**	(1,331,698)
Foreign exchange movements	**(20,969)**	95,528
At the end of the period	**33,183,516**	31,437,161

13. Leases continued

	2021	2020
Lease liabilities		
At the beginning of the period	**32,336,729**	32,641,518
Additions	**3,062,048**	145,195
Interest expense	**1,349,647**	1,322,763
Lease payments	**(2,781,009)**	(1,865,946)
Lease incentive payments	**(1,000,000)**	-
Foreign exchange movements	**(20,276)**	93,199
At the end of the period	**32,947,138**	32,336,729
The maturity profile of discounted lease payments		
Repayable within one year	**745,315**	1,407,853
Current liabiities	**745,315**	1,407,853
Repayable in two to five years	**2,545,242**	2,570,751
Repayable in more than five years	**29,656,582**	28,358,125
Non-current liabilities	**32,201,824**	29,604,809
Total borrowings	**32,947,138**	32,336,729

Break clauses

The only lease that provides a break clause that has not already passed is for the property at STFC Daresbury. The earliest date at which the break clause could take effect is July 2023, management currently does not intend to exercise this break option.

14. Trade and other receivables

	2021	2020
Due greater than 1 year		
Property rent deposits	**577,414**	584,834
Property decommissioning deposits	**350,000**	350,000
Total due greater than 1 year	**927,414**	934,834
Current receivables		
VAT recoverable	**185,061**	661,286
Advance payments to suppliers	**-**	238,848
Employee loans	**4,462**	-
Property and other deposits	**35,500**	9,943
Prepayments	**418,296**	975,147
	643,319	1,885,224
Total current receivables	**643,319**	1,885,224

15. Cash and cash equivalents

		2021	2020
Cash and cash equivalents		**4,260,490**	2,317,451
Amounts in foreign exchange denominated by	Swiss Franc	**184,440**	122,280
	Euro	**34,341**	234,527
	US Dollar	**229,949**	32,481
	Sterling	**3,811,760**	1,928,163
Cash included above which is pledged as security. See Note 18.		**500,000**	500,000

Continued - Financials in £

16. Inventories

	2021	2020
Work in progress - LIGHT		
At the beginning of the period	**22,138,323**	15,048,228
Reclassification of assets to Intangible Assets	**(5,500,000)**	-
Purchases - Work in progress - LIGHT	**9,188,342**	7,090,095
Total	**25,826,665**	22,138,323

All of the above items of Inventory have been valued at cost.

Costs included in Inventory are for finished components of the LIGHT machine that will be sold as part of future LIGHT installations.

17. Trade and other payables

	2021	2020
Due greater than 1 year		
Licence Fee Received	**16,500,000**	16,500,000
Total due greater than 1 year	**16,500,000**	16,500,000

The agreement under which the license fee was received in 2018 from our Chinese partner, Liquid Harmony, a shareholder, requires certain milestones to be met within a five year from receiving the fee including development of the products and obtaining regulatory approval in China within 5 years. If these conditions are not met the amount will be fully repayable.

	2021	2020
Current		
Trade payables	**2,450,064**	1,598,315
Other taxes and social security	**1,938,942**	1,358,372
Accruals and deferred income	**958,163**	3,481,530
Total	**5,347,169**	6,438,217

18. Borrowings

	2021	2020
Amounts falling due within one year		
Secured loans	**10,025,497**	10,039,316
Leases	**745,315**	2,731,920
Total amounts falling due within one year	**10,770,812**	12,771,236
Amounts falling due over one year		
Secured loans	**10,382,520**	8,258,435
Leases	**32,201,824**	29,604,809
Total amounts falling due over one year	**42,584,344**	37,863,244
Total borrowings	**53,355,155**	50,634,480
The maturity profile of gross debt is as follows		
Repayable within one year	**10,770,812**	12,771,236
Repayable in two to five years	**12,927,762**	15,724,559
Repayable in more than five years	**29,656,582**	22,138,684
Total borrowings	**53,355,155**	50,634,480

A debt facility with Credit Suisse AG ("Credit Suisse") for £10 million is secured against an aggregated amount of £10.5 million, Nerano Pharma Ltd ("Nerano Pharma") acting as Third Party Pledgor having placed £10 million in a pledged account, with the remaining £0.5 million placed in a pledged account by the Company. Interest rate payable on the Loan is 2 percent above SONIA (Sterling Overnight

18. Borrowings continued

Index Average) per annum. In May 2021, the Company extended the repayment date of the £10 million loan facility on a rolling quarterly basis at the sole discretion of Advanced Oncotherapy through to 11 November 2022. The loan is repayable in cash.

Nerano Pharma is the ultimate parent company of Nerano Capital, a shareholder of the Company. A loan from Nerano Pharma of £4 million was received in a prior year and interest accrues at 12 per cent per annum for annual payment or 15 per cent per annum if paid at the end of the loan.

On 28 June 2020, the Company entered into an interest-bearing secured convertible facility with Nerano Pharma for up to $30 million with the Company being able to issue drawdown requests at any time during the three-year term.

A rate of interest of 5 per cent. per annum will accrue on all amounts drawn under the Nerano Facility, paid annually in cash on each anniversary of the Nerano Facility with the option for the Company to defer payment of that interest until the maturity date of the Nerano Facility on 29 June 2023. On the maturity date all amounts drawn under the Nerano Facility and any interest accrued thereon shall be repayable by the Company. The Facility provides an option for the Company to voluntarily repay part, or all, of the loan (along with any accrued interest) prior to the maturity date. The Nerano Facility is secured on the LIGHT components being built in Daresbury and Geneva, associated intellectual property and the property at Harley St. Nerano Pharma will be entitled to a share of the profit generated by the Harley Street Centre for up to 15 years.

Nerano Pharma may convert any amount that the Company has opted to voluntarily prepay during the life of the Nerano Facility and at maturity of the Nerano Facility in June 2023, any outstanding loan amounts and interest payable, in each case, into new ordinary shares in Advanced Oncotherapy at a price of 25 pence per ordinary share.

On 17 August 2020 the company drew down $10m of the loan facility. Although convertible, the loan does not meet the fixed number of shares for a fixed loan value and therefore the convertible feature has been separated from the host contract and recognised as an embedded derivative. The below table shows the movement in the loans.

	2021	2020
Host Loan		
At the beginning of the period	**3,506,862**	-
Proceeds received	**-**	7,621,951
Recognition of embedded derivative	**-**	(3,716,425)
Costs including warrants	**-**	(654,734)
Interest accrued	**1,462,537**	399,243
Foreign exchange	**(51,536)**	(143,173)
At the end of the period	**4,917,863**	3,506,862
Embedded Derivative		
At the beginning of the period	**4,578,210**	-
Recognition of embedded derivative	**-**	3,716,425
Fair value adjustment	**140,750**	861,785
Total amounts falling due within one year	**4,718,960**	4,578,210

The fair value of the embedded derivative was designated as a level 3 in accordance with fair value hierarchy as per financial instruments note. The fair value has been determined in conjunction with a third party valuation firm, using a Monte Carlo simulation forecasting the share price at the date the conversion is exercised. The following assumptions were used in the calculation of the derivative option:

	2021	2020
Assumptions		
Share price	**38.0p**	36.0p
Exchange rate	**1.354**	1.366
Volatility share price	**42%**	50%
Volatility exchange rate	**7.5%**	9.5%
Time period	**1.49**	2.49
A change in foreign exchange rates of -/+ 5% would move the derivative valuation by approximately	**235,948**	200,000
Whilst a -/+ 5% movement on the share price would move the valuation by approximately	**7,038**	400,000

Continued - Financials in £

19. Financial instruments

The Group's principal financial instruments comprise short-term receivables and payables, lease liabilities and borrowings, short-term bank deposits and cash. There is currently no material difference between the carrying value of financial assets and liabilities and their fair value. The prime objectives of the Group's policy towards financial instruments are to maximise returns on the Group's cash balances, manage the Group's working capital requirements and finance the Group's ongoing operations.

Capital management
The Group's objectives when maintaining capital are:

- to safeguard the entity's ability to continue as a going concern, so that it can continue to provide returns for shareholders and benefits for other stakeholders, and
- to provide an adequate return to shareholders.

The Group does not yet have any significant recurring revenues and finances its operations through the issue of new shares and loans. The Group's capital resources are managed to ensure it has resources available to invest in operational activities designed to generate future income. These resources were represented by £4,260,490 of cash as at 31 December 2021. During 2021 the Group utilised a number of short and longer term debt facilities in order to provide liquidity to the Group.

	2021	2020
Assets		
Total assets	**141,290,713**	122,293,185
Debt		
Secured loans	**20,408,017**	18,297,751
Lease liabilities	**71,625,650**	69,363,818
	92,033,667	87,661,569
Equity		
Share capital and share premium	**183,990,891**	144,802,676
Reserves	**(122,621,463)**	(100,660,398)
	61,369,428	44,142,278
Total capital	**153,403,095**	131,803,847
Debt as a % of total capital	**60.0%**	66.5%
Debt as a % of total assets	**65.1%**	71.7%

Management of financial risk
The main risks associated with the Group's financial instruments have been identified as interest rate risk, liquidity risk, exchange rate risk, and credit risk. The Board is responsible for managing these risks and the policies adopted, which have remained largely unchanged throughout the year, are set out below.

Interest rate risk
The Group has debts which are the subject of fixed interest rate agreements and, therefore, there is no interest rate risk arising.

Liquidity risk
The Group has financed operations to date through the issue of equity and debt. All of the financial instruments are measured at amortised cost with the exception of the embedded derivative which is measured at fair value. In connection with its business plan, management anticipates additional increases in operating expenses, working capital requirements, and capital expenditures in line with the growth of its business, relating to the lease for the assembly site, the purchase of additional inventory, the hiring of personnel, and marketing expenses. It expects that those will continue to be funded through a combination of existing funds and further issuances of shares, and debt issuances. Thereafter, it is expected that the Group will need to raise additional capital and generate revenues to meet long-term operating requirements. Additional issuances of equity will result in dilution to current shareholders.

19 . Financial instruments continued

All of the Group's Trade and Other Payables are due within three months.

The Credit Suisse loan of £10m was due for repayment in May 2021 however the date has been extended to November 2022.

The Licence Fee received will only be repayable if certain milestones, as indicated in Note 17, are not met.
The maturity of Liabilities is:

	Due in less than one year	Due between two and five years	Due over five years
Trade and other payables	5,347,169	-	-
Borrowings	10,025,497	10,382,520	-
Lease liabilities (undiscounted)	2,089,378	7,730,573	61,805,699
Total	**17,462,044**	**18,113,093**	**61,805,699**

Exchange rate risk
Foreign exchange risk arises when individual Group entities enter into transactions denominated in a currency other than their functional currency. The Group's policy is, where possible, to allow Group entities to settle liabilities denominated in their functional currency). Where Group entities have liabilities denominated in a currency other than their functional currency (and have insufficient reserves of that currency to settle them), cash already denominated in that currency will, where possible, be transferred from elsewhere within the Group.

As of 31 December 2021, the Group's net monetary assets by functional currency of the Group's entities were as follows:

	Functional currency of entity				
Currency denomination of monetary assets/liabilities	GBP	CHF	EUR	USD	**Total**
GBP	(8,793,970)	(12,868)	-	(1,985)	**(8,808,823)**
CHF	17,253	(1,233,799)	-	-	**(1,216,546)**
Euro	(264,455)	26,511	8,543	-	**(229,401)**
USD	(9,675,119)	(11,968)	-	17,895	**(9,669,192)**
Total	**(18,716,291)**	**(1,232,124)**	**8,543**	**15,910**	**(19,923,962)**

The Directors consider that a movement of 10% of GBP and USD represents the entities exposure to foreign exchange risk and do not consider the impact to be material therefore no sensitivity analysis is presented.

Credit risk
The Group is not currently trading and has limited financial assets and therefore the Directors' do not consider that credit risk is material.

Cash at bank is held only with reputable banks with high quality external credit ratings which represents the maximum credit exposure. This represents the maximum credit risk to the Group.

NOTES TO THE ACCOUNTS – GROUP

Continued - Financials in £

20. Equity share capital

Ordinary shares of 25p each	Number	Share Capital	Share Premium	Total	p/Share
As at 01 January 2020	244,423,407	61,105,852	60,452,065	121,557,917	49.73p
Shares Issued in the period	89,016,167	22,254,042	2,003,103	24,257,145	27.25p
Expenses deducted from Share Premium	-	-	(1,012,386)	(1,012,386)	-
Total for year 2020	**89,016,167**	**22,254,042**	**990,717**	**23,244,759**	**26.11p**
As at 31 December 2020	**333,439,574**	**83,359,894**	**61,442,782**	**144,802,676**	**43.43p**
Shares Issued in the period	118,172,637	29,543,159	16,514,884	46,058,043	38.98p
Warrants cost deducted from Share Premium	-	-	(5,675,272)	(5,675,272)	-
Expenses deducted from Share Premium	-	-	(1,194,556)	(1,194,556)	-
Total for year 2021	**118,172,637**	**29,543,159**	**9,645,056**	**39,188,215**	**33.16p**
As at 31 December 2021	**451,612,211**	**112,903,053**	**71,087,838**	**183,990,891**	**40.74p**

Shares issued in the period					
Jan-21	15,101,040	3,775,260	1,905,369	5,680,629	37.62p
Feb-21	500,000	125,000	-	125,000	25.00p
Mar-21	361,111	90,278	39,722	130,000	36.00p
Apr-21	7,296	1,824	803	2,627	36.00p
May-21	425,709	106,427	25,543	131,970	31.00p
Aug-21	500,000	125,000	-	125,000	25.00p
Sep-21	100,300,046	25,075,012	7,612,978	32,687,989	32.59p
Nov-21	500,000	125,000	-	125,000	25.00p
Dec-21	477,435	119,359	60,641	180,000	37.70p
Total	**118,172,637**	**29,543,159**	**9,645,056**	**39,188,215**	**33.16p**

Shares issued in the prior period					
May-20	61,947,835	15,486,959	108,470	15,595,429	25.18p
Oct-20	27,068,332	6,767,083	882,247	7,649,330	28.26p
Total	**89,016,167**	**22,254,042**	**990,717**	**23,244,759**	**26.11p**

In January 2021, 15,101,040 shares were issued under authority from the July 2020 AGM, raising £5.7 million of equity.

In February 2021, 500,000 shares were issued under authority from the July 2020 AGM, raising £0.1 million of equity.

In March 2021, 361,111 shares were issued under authority from the July 2020 AGM, raising £0.1 million of equity.

In April 2021, 7,296 shares were issued under authority from the July 2020 AGM, raising £2,627 of equity.

In May 2021, 425,709 shares were issued under authority from the July 2020 AGM, raising £131,970 of equity.

In August 2021, 500,000 shares were issued under authority from the July 2021 AGM, raising £125,000 of equity.

The Directors were authorised at a General Meeting in July 2021 to allot and issue up to 104,950,419 shares.

The Directors were further authorised at a General Meeting in August 2021 to allot and issue up to 184,883,807 shares. 100,000,046 were issued as shares in October 2020 raising £32.6 million of equity. In September 2021 84,883,761 were issued as warrants.

In September 2021, 300,000 shares were issued under authority from the July 2021 AGM, raising £75,000 of equity.

In November 2021, 500,000 shares were issued under authority from the July 2021 AGM, raising £125,000 of equity.

In December 2021, 477,435 shares were issued under authority from the July 2021 AGM, for advisory services received by the Company.

21. Share based payments

(a) Share Options

The Group's shares options are detailed in note a below. The options in issue are all equity options and vest over a term of 1 to 5 years. They do not have performance conditions attached other than the 24m shares options issued on 01 October 2020 under the LTIP scheme.

The vesting conditions attached to the issue are detailed below:

- 6m on the LIGHT System being fully operational
- 6m on first patient treated
- 6m on the LIGHT system being certified
- 6m if the share price is above £1 for 30 consecutive days.

The first three of these are non-market conditions and are reflected in the number of options expected to vest in accordance with the accounting policy. The vesting period is assessed by management based on their expectation of the conditions being satisfied based on the project timeline. Management expect these all to fully vest over a two year period. The inputs in the Black and Scholes model are detailed later in this note.

The latter item is a non-market condition and is reflected in the fair value of the options in accordance with the accounting policy. The inputs in the Monte Carlo simulation are detailed later in this note.

Share Options

Share options held by Directors are disclosed in Note 8. The total number of options outstanding at the year end are as follows:

Grant date	Maximum date of exercise	Exercise price	Outstanding at start of period 01 January 2021	Issued in the period	Lapsed in the period	**Share options as at 31 December 2021**
13-Feb-17	12-Feb-22	200.00p	400,000	-	-	**400,000**
29-Aug-17	28-Aug-22	130.00p	400,000	-	-	**400,000**
20-Feb-19	20-Feb-24	100.00p	3,720,000	-	(140,000)	**3,580,000**
01-Mar-19	31-Aug-22	40.00p	1,404,324	-	(358,848)	**1,045,476**
01-Oct-20	31-Oct-25	50.00p	24,000,000	-	-	**24,000,000**
01-Oct-20	31-Oct-25	100.00p	600,000	-	-	**600,000**
01-Feb-21	31-Jul-24	40.00p	-	962,162	(54,012)	**908,150**
Total			30,524,324	962,162	(552,860)	**30,933,626**

The number and weighted average exercise prices of share options are as follows:

	2021		2020	
	Weighted average exercise price	**Number of options**	Weighted average exercise price	Number of options
Outstanding at the beginning of the period	**59.63p**	**30,524,324**	107.36p	7,304,324
Lapsed during the period	**55.19p**	**(552,860)**	162.32p	(1,380,000)
Exercised during the period	**-**	**-**	-	-
Issued during the period	**40.00p**	**962,162**	51.22p	24,600,000
Outstanding at the end of the period	**59.10p**	**30,933,626**	59.63p	30,524,324
Exercisable at the end of the period	**111.50p**	**4,520,000**	110.16p	5,120,000

(b) Warrants

Warrants held by Directors are disclosed in Note 8. The total number of warrants outstanding at the year end are as follows:

Exercise period	Note	Maximum date of exercise	Exercise price	Share warrants held at 01 January 2021	Issued in the period	Lapsed in the period	Exercised in the period	**Share warrants held at 31 December 2021**
22-Feb-17		21-Feb-21	86.00p	302,325	-	(302,325)	-	**-**
26-Apr-17		25-Apr-21	36.00p	722,223	-	(353,816)	(368,407)	**-**
24-May-17		23-May-21	31.00p	834,474	-	(408,765)	(425,709)	**-**
24-May-17		23-May-22	25.00p	21,768,687	-	-	(2,100,000)	**19,668,687**
26-Apr-18		25-Apr-23	70.00p	1,000,000	-	-	-	**1,000,000**
31-May-18		11-Jun-22	50.00p	450,000	-	-	-	**450,000**
31-Aug-18		31-Aug-23	100.00p	2,617,312	-	-	-	**2,617,312**
07-May-19		07-May-24	100.00p	3,500,000	-	-	-	**3,500,000**
31-Oct-19		31-Aug-24	100.00p	385,000	-	-	-	**385,000**
28-Jun-20		28-Jun-25	50.00p	5,000,000	-	-	-	**5,000,000**
03-Mar-22		28-Feb-25	60.00p	-	82,383,761	-	-	**82,383,761**
01-Apr-22	*Note[1]*	31-Mar-25	60.00p	-	2,500,000	-	-	**2,500,000**
11-Nov-21	*Note[1]*	11-Nov-24	60.00p	-	3,750,000	-	-	**3,750,000**
Total				**36,580,021**	**88,633,761**	**(1,064,906)**	**(2,894,116)**	**121,254,760**

Note[1] Warrants were attached to a shares issue in September 2021 share issue, one warrant for every one share subscribed to be awarded to the subscriber provided that they still hold the subscribed shares six months after the admission of the shares to AIM, and as such are accounted for in 2021.

Continued - Financials in £

21. Share based payments continued

The number and weighted average exercise prices of share warrants are as follows:

	2021		2020	
	Weighted average exercise price	**Number of warrants**	Weighted average exercise price	Number of warrants
Outstanding at the beginning of the period	**44.14p**	**36,580,021**	53.73p	34,159,896
Lapsed during the period	**48.28p**	**(1,064,906)**	184.59p	(2,544,326)
Exercised during the period	**27.28p**	**(2,894,116)**	25.71p	(35,549)
Issued during the period	**60.00p**	**88,633,761**	50.00p	5,000,000
Outstanding at the end of the period	**56.10p**	**121,254,760**	44.14p	36,580,021
Exercisable at the end of the period	**47.00p**	**36,370,999**	44.14p	36,580,021

The fair value of services received in return for share options and warrants is measured by reference to the fair value of the share options and warrants granted. For issues without market performance conditions, this estimate is based upon a Black Scholes model. Where the awards include market conditions, a Monte Carlo simulation model is used. The inputs into the various models for options and warrants granted in the year are as follows:

Options

Expected life	First vesting date	Risk free rate	Exercise price	Share price	Volatility of share price	Options Vested	Options Granted	Expiry	Fair Value
Black-Scholes									
3	01-Feb-24	0.10%	40p	41.5p	56.10%	-	962,162	31-Jul-24	23,133
Total							**962,162**		**23,133**

Warrants

Expected life	First vesting date	Risk free rate	Exercise price	Share price	Volatility of share price	Warrants Vested	Warrants Granted	Expiry	Fair Value
3	11-Nov-21	0.10%	60p	36.0p	88.89%	-	3,750,060	11-Nov-24	206,859
3	03-Mar-22	0.10%	60p	40	88.30%	-	82,383,761	28-Feb-25	5,504,217
3	01-Apr-22	0.10%	60p	40	88.30%	-	2,500,000	31-Mar-25	171,055
Total							**88,633,821**		**5,882,131**

Volatility was determined with reference to the Company's share price movements over a period equivalent to the expected lives of the options and warrants retrospectively from the date of issue.

The Group recognised the following share-based payment expense during the period:

Charged to the profit and loss account	**2021**	2020
Expense arising from fair value of share options currently in issue	**2,421,599**	704,533
Expense arising from fair value of warrants currently in issue	**206,859**	-
Expense arising on employee services paid in shares	**1,612,319**	636,416
Expense arising on third party services paid in shares	**180,000**	-
Expense on settlement of financial liability	**-**	1,297,174
Total charge to the profit and loss account	**4,420,777**	2,638,123

Charged to long term loans	**2021**	2020
Expense arising from fair value of warrants currently in issue	**-**	654,734
Total	**-**	654,734

22. Share premium reserve

Company law restricts the use of the share premium reserve of £71,087,838 (2020:£61,442,782), which may only be applied in paying unissued shares of the Company in respect of capitalisation issues and in writing off the expenses of, or the commission paid or discount allowed on, any issue of shares or debentures of the Company.

23. Share option reserve

The share option reserve of £15,722,018 (2020: £7,675,332) arises owing to the provision in respect of IFRS 2 "Share based payments".

24. Reverse acquisition reserve

The reverse acquisition reserve of £11,038,204 was created on 31 July 2006 when the Company became the legal parent of CareCapital Limited ("CCL") by way of a share exchange agreement. The business combination was regarded as a reverse acquisition under IFRS 3 whereby CCL, the legal subsidiary, is the acquirer and has the power to govern the financial and operating policies of the legal parent so as to obtain benefits from its activities.

25. Exchange movement reserve

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

26. Capital commitments

The Group and its subsidiaries had capital commitments of £4,060,397 (2020: £1,554,283). This was in respect of building modifications and equipping of the Daresbury site.

27. Contingent liabilities

The Directors are not aware of any contingent liabilities at the 31 December 2021 (2020: £nil).

Continued - Financials in £

28. Related party transactions

The following related party transactions are required to be disclosed in accordance with IAS24.

	2021	2020
A family member of Dr Michael Sinclair, Executive Chairman, was employed by the Group. The remuneration and benefits payable under the contract, excluding Company statutory and other costs, were:	**183,547**	198,440
The Group received services from Berkshire Investment Management Limited, a company controlled by Hans von Celsing, a Group Director	**-**	54,955
The balance due to Berkshire Investment Management Limited as at 31 December 2020 was:	**-**	24,000

		Price	Quantity
In September 2021, the following shares were issued:			
Michael Sinclair (Director)	Subscription	40.00p	50,000
Michael Sinclair (Director)	Salary	40.00p	63,543
Michael Sinclair (Director)	Bonus payment	40.00p	416,667
Nicolas Serandour (Director)	Bonus payment	40.00p	416,667
Prof Steve Myers (Director)	Bonus payment	40.00p	416,667
Michael Bradfield (Director)	NED Fees	40.00p	115,000
Lori Cross (Director)	NED Fees	40.00p	60,417
Dr Nick Plowman (Director)	NED Fees	40.00p	102,500
Enrico Vanni (Director)	NED Fees	40.00p	100,000
Enrico Vanni (Director)	Subscription	40.00p	500,000
Hans von Celsing (Director)	NED Fees	40.00p	176,667
Renhua Zhang (Director)	NED Fees	40.00p	214,449
Chunlin Han (Former Director)	NED Fees	40.00p	144,658
Yuelong Huang (Former Director)	NED Fees	40.00p	144,658

Directors' remuneration is detailed in Note 8.

	2021	2020
Remuneration of key management personnel	**2,375,159**	1,924,007

The Group has taken advantage of the exemption available under IAS 24 'Related Party Disclosures' not to disclose details of transactions between Group undertakings which are eliminated on consolidation in the Group Financial Statements.

29. Post balance sheet events

Since the year end, the Group has raised additional equity through the issue of shares:

	No of Shares	Equity
January	500,000	125,000
February	3,100,000	775,000
March	8,000,000	2,000,000
April	3,400,000	850,000
May	3,540,000	885,000
June	3,200,000	800,000
Announced June	24,090,000	6,022,500
Total	**45,830,000**	**11,457,500**

On 23 March 2022, the Company entered into a three-month loan agreement of £1.5 million with Nerano Pharma Ltd, a company owned and controlled by Seamus Mulligan, a significant shareholder in the Company, with an interest rate of 1.25 per cent per month (the "Loan"). The Loan is repayable by the Company on 24 June 2022. As part of the agreement, the Company issued 6,382,978 warrants to Nerano Pharma Ltd with an exercise price of 28.20 pence per share, exercisable up until 24 March 2025.

As at the date of publication of the annual accounts, the Loan remains outstanding. Nerano Pharma has agreed to not seek repayment at the current time and are in discussions with the Company surrounding the potential to convert the Loan into New Ordinary Shares. At the current time no agreement has been entered into in relation to varying the terms of the Loan nor have the terms of any variation been, as yet, agreed. In the event that the terms cannot be agreed between Nerano Pharma and the Company, the Company would seek to repay the amounts owed pursuant to the Loan.

30. Supporting statements of cash flows - Analysis of net debt

		Cash flows	Principal repaid in shares	Costs paid in shares	Fair value of warrants cost	Recognition of embedded derivative	New lease liability recognised	Accrued interest	Foreign exchange	Total
	At 1 January 2020									**At 31 December 2020**
Cash at bank and in hand	3,235,167	(937,825)	-	-	-	-	-	-	20,109	2,317,451
Lease liabilities	(32,641,518)	1,865,946	-	-	-	-	(145,195)	(1,322,763)	(93,199)	(32,336,729)
Borrowings	(13,864,384)	(11,294,865)	4,000,000	-	654,734	3,716,425	-	(1,652,834)	143,173	(18,297,751)
Total	**(43,270,735)**	**(10,366,744)**	**4,000,000**	**-**	**654,734**	**3,716,425**	**(145,195)**	**(2,975,597)**	**70,083**	**(48,317,029)**
	At 1 January 2021									**At 31 December 2021**
Cash at bank and in hand	2,317,451	1,923,250	-	-	-	-	-	-	19,789	4,260,490
Lease liabilities	(32,336,729)	3,781,009	-	-	-	-	(3,062,048)	(1,349,647)	20,276	(32,947,138)
Borrowings	(18,297,751)	-	-	-	-	-		(2,110,266)	(51,536)	(20,459,553)
Short term borrowings	-	7,850,000	-	-	-	-	-	-	-	7,850,000
Short term borrowing repayments	-	(7,850,000)	-	-	-	-	-	-	-	(7,850,000)
Total	**(48,317,029)**	**5,704,259**	**-**	**-**	**-**	**-**	**(3,062,048)**	**(3,459,913)**	**(11,470)**	**(49,146,201)**

COMPANY STATEMENT OF FINANCIAL POSITION

As at 31 December 2021 - Financials in £

	Notes	2021	2020
Non-current assets			
Intangible assets	B	**27,141,345**	19,768,925
Property, plant and equipment	C	**7,202,948**	5,964,648
Right of use assets	D	**32,966,270**	30,515,239
Investment in subsidiaries	E	**81,921,564**	8,052,458
Trade and other receivables	F	**608,461**	59,214,302
		149,840,589	123,515,572
Current assets			
Inventories	H	**25,791,157**	22,139,087
Trade and other receivables	F	**508,908**	1,765,183
Corportion tax R&D refund	F	**-**	-
Cash and cash equivalents		**3,856,807**	2,193,430
		30,156,872	26,097,700
Total assets		**179,997,461**	149,613,272
Current liabilities			
Trade and other payables	G	**(3,282,451)**	(4,015,017)
Lease liabilities	D	**(603,647)**	(1,968,945)
Borrowings	I	**(10,025,497)**	(10,039,316)
		(13,911,595)	(16,023,278)
Non-current liabilities			
Licence fee received	G	**(16,500,000)**	(16,500,000)
Lease liabilities	D	**(32,191,481)**	(29,475,974)
Borrowings	I	**(10,382,520)**	(8,258,435)
Embedded derivative	18	**(4,718,960)**	(4,578,210)
		(63,792,961)	(58,812,619)
Total liabilities		**(77,704,556)**	(74,835,897)
Net assets		**102,292,905**	74,777,376
Equity			
Share capital		**112,903,053**	83,359,894
Share premium reserve		**71,087,838**	61,442,782
Share option reserve		**15,722,018**	7,675,332
Accumulated losses		**(97,420,004)**	(77,700,632)
Total equity		**102,292,905**	74,777,376

The Company's loss for the financial year was £19,976,416 (2020: £15,105,395 loss)

These financial statements have been approved and were authorised for issue by the Board of Directors on 30 June 2022.
Signed on behalf on the Board of Directors by

Dr Michael Sinclair
Executive Chairman

Nicolas Serandour
Chief Executive Officer

Registered number: 05564418
The accompanying Notes on pages 141 to 146 form part of the financial statements.

COMPANY STATEMENT OF CHANGES IN EQUITY

For the year ended 31 December 2021 - Financials in £

	Share capital	Share premium reserve	Share options reserve	Accumulated losses	Total
Balance as at 01 January 2020	61,105,852	60,452,065	7,853,803	(64,132,975)	65,278,745
Loss for the year	-	-	-	(15,105,395)	(15,105,395)
Total comprehensive income	-	-	-	(15,105,395)	(15,105,395)
Shares Issued in the period	22,254,042	2,003,103	-	-	24,257,145
Expenses deducted from share premium	-	(1,012,386)	-	-	(1,012,386)
Lapsed options	-	-	(510,950)	510,950	-
Lapsed warrants	-	-	(1,026,788)	1,026,788	-
Share based payments					
- Share option charge	-	-	704,533	-	704,533
- Share warrants charge	-	-	654,734	-	654,734
Balance at 31 December 2020	**83,359,894**	**61,442,782**	**7,675,332**	**(77,700,632)**	**74,777,376**
Balance at 01 January 2021	**83,359,894**	**61,442,782**	**7,675,332**	**(77,700,632)**	**74,777,376**
Loss for the year	-	-	-	(19,976,416)	(19,976,416)
Total comprehensive income	-	-	-	(19,976,416)	(19,976,416)
Shares Issued in the period	29,543,159	16,514,884	-	(0)	46,058,043
Expenses deducted from share premium	-	(1,194,556)	-	-	(1,194,556)
Cost of warrants dedicted from share premium	-	(5,675,272)	5,675,272	-	-
Lapsed options	-	-	-	(0)	(0)
Lapsed warrants	-	-	(257,045)	257,045	-
Share based payments					
- Share option charge	-	-	2,421,599	-	2,421,599
- Share warrants charge	-	-	206,859	-	206,859
Balance as at 31 December 2021	**112,903,053**	**71,087,838**	**15,722,018**	**(97,420,004)**	**102,292,905**

The accompanying Notes on pages 141 to 146 form part of the financial statements.

NOTES TO
THE ACCOUNTS – COMPANY

As at 31 December 2021 - Financials in £

A. Principal accounting policies

(i) Company
The separate financial statements of the Company are presented as required by the Companies Act 2006 and in accordance with FRS 101 United Kingdom generally accepted accounting practice.

In these financial statements, the Company has applied the exemptions available under FRS 101 in respect of the following disclosures:

- Disclosures regarding revenue;
- Disclosures regarding the cash flow statement;
- Disclosures in respect of transactions with wholly owned subsidiaries;
- Disclosures in respect of capital management;
- The effects of new but not yet effective IFRSs; and
- Disclosures in respect of the compensation of Key Management Personnel

(ii) Investment in subsidiaries
Investments in subsidiaries are carried in the Company's statement of financial position at cost less, where appropriate, accumulated impairment.

(iii) Amounts owed by subsidiaries
Amounts owed by subsidiaries are held at amount remitted less an allowance for expected credit losses.

B. Intangible assets

Development Costs

At 01 January 2020	19,267,379
Additions	501,546
At 31 December 2020	**19,768,925**

At 01 January 2021	**19,768,925**
Reclassification of assets - inventory	**5,500,000**
Additions	**1,872,420**
At 31 December 2021	**27,141,345**

In accordance with IAS 38, £1,872,420 (2020: £501,546) of costs relating to the development of the LIGHT proton therapy machine were capitalised during the year.

C. Property, plant and equipment

	Leasehold property	Computer hardware and software	Fixtures, fittings and equipment	Total
2020				
Cost				
At 01 January 2020	5,177,881	207,439	316,783	5,702,103
Additions	534,353	44,425	736,424	1,315,203
At 31 December 2020	**5,712,234**	**251,864**	**1,053,207**	**7,017,306**
Depreciation				
At 01 January 2020	292,737	149,698	100,524	542,959
Charge for the year	393,822	31,781	84,096	509,699
At 31 December 2020	**686,559**	**181,479**	**184,620**	**1,052,658**
Net book value				
At 01 January 2020	4,885,144	57,741	216,259	5,159,144
At 31 December 2020	**5,025,675**	**70,385**	**868,588**	**5,964,648**

C. Property, plant and equipment continued

	Leasehold property	Computer hardware and software	Fixtures, fittings and equipment	Total
2021				
Cost				
At 01 January 2021	5,712,234	251,864	1,053,207	7,017,306
Additions	1,737,099	47,108	237,087	2,021,294
At 31 December 2021	**7,449,333**	**298,972**	**1,290,294**	**9,038,600**
Depreciation				
At 01 January 2021	686,559	181,479	184,620	1,052,658
Charge for the year	523,344	45,972	213,678	782,994
At 31 December 2021	**1,209,903**	**227,451**	**398,298**	**1,835,652**
Net book value				
At 01 January 2021	5,025,675	70,385	868,588	5,964,648
At 31 December 2021	**6,239,430**	**71,521**	**891,997**	**7,202,948**

D. Leases

	Land and buildings	
	2021	2020
Right-of-Use Assets		
At the start of the period	**30,515,239**	30,982,270
Additions	**3,062,047**	144,664
Amortisation	**(611,016)**	(611,695)
At the end of the period	**32,966,270**	30,515,239
Lease liabilities		
At the start of the period	**31,444,919**	31,123,470
Additions	**3,062,048**	144,664
Interest expense	**1,333,546**	1,284,749
Lease payments	**(2,045,385)**	(1,107,964)
Lease incentive payments	**(1,000,000)**	-
At the end of the period	**32,795,128**	31,444,919
The maturity profile of discounted lease payments		
Repayable within one year	**603,647**	1,968,945
Current liabilities	**603,647**	1,968,945
Repayable in two to five years	**2,535,220**	7,332,380
Repayable in more than five years	**29,656,261**	22,143,594
Non-current liabilities	**32,191,481**	29,475,974
Total borrowings	**32,795,128**	31,444,919

Break clauses

The only lease that provides a break clause that has not already passed is for the property at STFC Daresbury. The earliest date at which the break clause could take effect is July 2023, management currently do not intend to exercise this break option.

NOTES TO
THE ACCOUNTS – COMPANY

As at 31 December 2021 - Financials in £

E. Investment in subsidiaries

	2020
At 01 January	8,052,458
At 31 December	**8,052,458**

	2021
At 01 January	**8,052,458**
Transfer from amounts owed by subsidiary undertakings	**73,869,106**
At 31 December	**81,921,564**

The Company owned the following principal subsidiary companies as at 31 December 2021:

Subsidiary Company		Country of Incorporation	Share class	% Holding
ADAM S.A.		Switzerland	Ordinary	100%
Advanced Oncotherapy Americas Inc		USA	Ordinary	100%
Advanced Oncotherapy B.V.	1	The Netherlands	Ordinary	100%
Advanced Oncotherapy Resources Ltd	1	United Kingdom	Ordinary	100%
APTS Harley Street Ltd	1	United Kingdom	Ordinary	100%
Advanced Oncotherapy (China) Ltd	1	United Kingdom	Ordinary	100%
Advanced Oncotherapy Proton Therapy Services Ltd	1	United Kingdom	Ordinary	100%
Oncotherapy UK Ltd	1	United Kingdom	Ordinary	100%
The London Proton Therapy Centre Ltd	1	United Kingdom	Ordinary	100%
CareCapital Ltd	1	United Kingdom	Ordinary	100%
CareCapital (Southampton) Ltd	1 2	United Kingdom	Ordinary	100%
The Women's Cancer Centre Ltd	1 2	United Kingdom	Ordinary	100%
CareCapital Gesundheitsimmobilien GmbH	1 2	Germany	Ordinary	90%
CareCapital Gesundheitsimmobilien Vervaltungs GmbH	1 2	Germany	Ordinary	90%
GESUNDHEITSZENTRUM ADLERSHOF 2 MINDERHEITSBETEILIGUNGS GMBH	1 2	Germany	Ordinary	100%
Gesundheitszentrum Königs Wusterhausen 2 GmbH & Co. KG	1 2	Germany	Ordinary	100%

Notes
[1] Dormant [2] Indirectly held

F. Trade and other receivables

	2021	2020
Due greater than 1 year		
Property rent deposits	**258,461**	258,461
Property decommissioning deposits	**350,000**	350,000
Amounts owed by subsidiary undertakings	**-**	58,605,841
Total	**608,461**	59,214,302

In accordance with IFRS 9, the Company has considered the impairment of loans due from its primary subsidiary company. During the year amounts due were transferred to the investment cost as show in Note E above. There were no amounts due from subsidiaries at the year end.

	2021	2020
Increase in provision during the year	**-**	-

	2021	2020
Current		
VAT recoverable	**135,030**	581,723
Advance payments to suppliers	**-**	238,848
Property rent deposits	**4,462**	2,819
Other debtors	**5,574**	103,910
Prepayments	**363,842**	837,883
	508,908	1,765,183
Corporation Tax	**-**	-
Total	**508,908**	1,765,183

G. Trade and other payables

	2021	2020
Non current		
Licence fee received	**16,500,000**	16,500,000
Total	**16,500,000**	16,500,000
Current		
Trade payables	**2,249,419**	1,339,126
Social security and other taxes	**286,465**	225,788
Other creditors	**255,364**	183,410
Accruals and deferred income	**491,203**	2,266,693
Total	**3,282,451**	4,015,017

H. Inventories

	2021	2020
Inventories		
Work in progress - LIGHT	**22,139,087**	15,048,228
Reclassification of assets to Intangible Assets	**(5,500,000)**	-
Purchases - Work in progress - LIGHT	**9,152,070**	7,090,859
Total	**25,791,157**	22,139,087

All of the above items of Inventory have been valued at cost.

Costs included in Inventory are for finished components of the LIGHT machine that will be sold as part of future LIGHT installations.

I. Borrowings

	2021	2020
Amounts falling due within one year		
Secured loans	**10,025,497**	10,039,316
Total	**10,025,497**	10,039,316

		2021	2020
Amounts falling due over one year			
Secured loans	See Note 18	**10,382,520**	8,258,435
Total		**10,382,520**	8,258,435

See Note 18 for details of liabilities and securities given.

NOTES TO
THE ACCOUNTS – COMPANY

As at 31 December 2021 - Financials in £

J. Related party transactions

The following related party transactions are required to be disclosed in accordance with IAS24.
There are no employees considered as key management other than the Directors whose remuneration is detailed in Note 8.

	2021	2020
A family member of Dr Michael Sinclair, Executive Chairman, was employed by the Group. The remuneration and benefits payable under the contract, excluding Company statutory and other costs, were:	**183,547**	198,440
The Company received services from Berkshire Investment Management Limited, a company controlled by Hans von Celsing, a Group Director.	**-**	54,955
The balance due to Berkshire Investment Management Limited as at 31 December 2021 was:	**-**	24,000

		Price	Quantity
In October 2020, as disclosed in Note 7, the following options were issued:			
Michael Sinclair (Director)		50.00p	5,500,000
Nicolas Serandour (Director)		50.00p	6,500,000
Steve Myers (Director)		50.00p	1,500,000
In September 2021, the following shares were issued:			
Michael Sinclair (Director)	Subscription	40.00p	50,000
Michael Sinclair (Director)	Salary	40.00p	63,543
Michael Sinclair (Director)	Bonus payment	40.00p	416,667
Nicolas Serandour (Director)	Bonus payment	40.00p	416,667
Prof Steve Myers (Director)	Bonus payment	40.00p	416,667
Michael Bradfield (Director)	NED Fees	40.00p	115,000
Lori Cross (Director)	NED Fees	40.00p	60,417
Dr Nick Plowman (Director)	NED Fees	40.00p	102,500
Enrico Vanni (Director)	NED Fees	40.00p	100,000
Enrico Vanni (Director)	Subscription	40.00p	500,000
Hans von Celsing (Director)	NED Fees	40.00p	176,667
Renhua Zhang (Director)	NED Fees	40.00p	214,449
Chunlin Han (Former Director)	NED Fees	40.00p	144,658
Yuelong Huang (Former Director)	NED Fees	40.00p	144,658

The Group has taken advantage of the exemption available under IAS 24 'Related Party Disclosures' not to disclose details of transactions between Group undertakings which are eliminated on consolidation in the Group Financial Statements.

K. Financial instruments

The Company's activities expose it primarily to the financial risks of changes in foreign currency exchange rates and interest rates.

Management of risks
Credit risk is managed as follows:

Cash at bank is held only with reputable banks with high quality external credit ratings. The Company's financial assets and liabilities are classified as follows:

	Amortised cost	
	2021	2020
Trade and other payables	**(3,282,451)**	(4,015,017)
Trade and other receivables	**508,908**	1,765,183
Cash and cash equivalents	**3,856,807**	2,193,430
Borrowings	**(20,408,017)**	(18,297,751)
Total	**(19,324,753)**	(18,354,155)

	Fair value	
	2021	2020
Trade and other payables	**(3,282,451)**	(4,015,017)
Trade and other receivables	**508,908**	1,765,183
Cash and cash equivalents	**3,856,807**	2,193,430
Borrowings	**(20,408,017)**	(18,297,751)
Embedded derivative	**(4,718,960)**	(4,578,210)
Total	**(24,043,713)**	(22,932,365)

Regarding liquidity risk, the Company, in the future, may need to raise further equity or debt funds to fulfil its objectives and/or finance working capital requirements through future stages of development.

NOTICE OF
ANNUAL GENERAL MEETING

NOTICE IS HEREBY GIVEN that the Annual General Meeting ("AGM") of Advanced Oncotherapy plc, registered in England and Wales with the registered number 05564418 (the 'Company'), will be held at the offices of Advanced Oncotherapy plc, Third Floor, 4 Tenterden Street, London W1S 1TE on Friday, 29 July 2022 at 2.00pm for the following purposes:

ORDINARY RESOLUTIONS
To consider, and if thought fit, to pass the following resolutions which will be proposed as Ordinary Resolutions:

1. To receive the audited financial statements and the Auditor's and Directors' reports for the year ended 31st December 2021.
2. To re-appoint Michael Bradfield as a Director of the Company.
3. To re-appoint Hans von Celsing as a Director of the Company.
4. To re-appoint Lori Cross as a Director of the Company.
5. To re-appoint Prof. Steve Myers as a Director of the Company.
6. To re-appoint Dr Nick Plowman as a Director of the Company.
7. To re-appoint Nicolas Serandour as a Director of the Company.
8. To re-appoint Dr Michael Sinclair as a Director of the Company.
9. To re-appoint Dr Enrico Vanni as a Director of the Company.
10. To re-appoint Renhua Zhang as a Director of the Company.
11. To re-appoint RPG Crouch Chapman LLP as Auditors of the Company to hold office until the conclusion of the next AGM at which accounts are laid before the Company.
12. To authorise the Directors to determine the remuneration of the Auditors.
13. THAT the Directors be and are hereby generally and unconditionally authorised for the purposes of section 551 of the Companies Act 2006 ("the Act"), to exercise all the powers of the Company to allot shares in the Company and/ or to grant rights to subscribe for, or to convert any securities into shares in the Company, and/or the grant of rights to subscribe for or to convert any securities into Ordinary Shares up to a maximum aggregate nominal amount of £37,292,063 (the equivalent of up to 149,168,252 Ordinary Shares), this authority to expire on the earlier of fifteen months from the date of the passing of this resolution or the conclusion of the next AGM of the Company to be held in 2023 unless previously renewed, varied or revoked by the Company in general meeting, save that the Company may before such expiry make any offer or agreement which would or might require shares in the Company to be allotted and/or rights to subscribe for or to convert any securities into shares in the Company to be granted after such expiry and the Directors may allot shares in the Company, or grant rights to subscribe for or to convert any securities into shares in the Company, in pursuance of any such offer or agreement as if the authority conferred hereby had not expired.

SPECIAL RESOLUTION
14. THAT, subject to the passing of Resolution 13 above, in substitution for all previous powers to the extent unused, the Directors be and are hereby unconditionally empowered pursuant to sections 570 and 571 of the Act to allot equity securities (as defined in section 560 of the Act) pursuant to the authority granted to the Directors pursuant to Resolution 13 above as if section 561 of the Act did not apply to any such allotment, provided that this power shall be limited to:

    a) the allotment of equity securities in connection with a rights issue, open offer or equivalent offer in favour of the holders of Ordinary Shares and such other equity securities of the Company as the Directors may determine in which such holders are offered the right to participate in proportion (as nearly as may be) to their respective holdings of such equity securities or in accordance with the rights attached thereto but subject to such exclusions or other arrangements as the Directors may consider necessary or expedient in connection with shares representing fractional entitlements or on account of either legal or practical problems arising in connection with the laws of any territory, or of the requirements of any recognised regulatory body or stock exchange in any territory;

    b) other than pursuant to sub-paragraph 14(a) above, the allotment of equity securities up to an aggregate nominal amount of £37,292,063 (the equivalent of up to 149,168,252 Ordinary Shares). This power shall expire on the earlier of fifteen months from the date of passing of this Resolution and upon the conclusion of the next AGM of the Company to be held in 2023 unless previously renewed, varied or revoked by the Company in general meeting, save that the Company may before such expiry make any offer or agreement which would or might require equity securities to be allotted after such expiry and the Directors may allot equity securities in pursuance of any such offer or agreement as if the power conferred hereby had not expired.

By order of the Board

Dr Michael Sinclair
Executive Chairman

Registered Office: Level 17, Dashwood House,
69 Old Broad Street, London EC2M 1QS
30 June 2022

NOTES
1. COVID-19
    The board takes its responsibility to safeguard the health of its shareholders, stakeholders and employees very seriously. At the time of preparing this document, there are no legal COVID-19 restrictions in place in England. We therefore look forward to welcoming shareholders to our AGM in person again.

    We encourage shareholders who wish to attend the AGM in person to wear face coverings while inside the meeting venue, including for the duration of the meeting.

    Due to the constantly evolving nature of the pandemic, it is possible that physical participation may be restricted. We will notify any changes post-publication of this document via our website. Shareholders are encouraged to check our website in the days leading up to the AGM to ensure they are informed of any changes.

    Shareholders wishing to vote on any of the matters of business are urged to do so through completion of a proxy form online which can be completed and submitted in accordance with the instructions thereon. We strongly recommend voting electronically at www.signalshares.com as your vote will automatically be counted. To be effective, the proxy vote must be submitted at www.signalshares.com so as to have been received by the Company's registrars not less than 48 hours (excluding weekends and public holidays) before the time appointed for the meeting or any adjournment of it. By registering on the Signal shares portal at www.signalshares.com, you can manage your shareholding, including:

    - cast your vote
    - update your address
    - select your communication preference.

    It is strongly recommended that the Chairman of the meeting

is appointed as proxy by shareholders as it is unlikely that any other persons will be admitted to the meeting other than the second participant in the quorum based on the current measures being implemented by the Government in the United Kingdom.

If you need help with voting online, or require a paper proxy form, please contact our Registrar, Link Group by email at enquiries@linkgroup.co.uk, or you may call Link on 0371 664 0391. Calls are charged at the standard geographic rate and will vary by provider. Calls outside the United Kingdom will be charged at the applicable international rate. Link Group are open between 09:00 - 17:30, Monday to Friday excluding public holidays in England and Wales. Submission of a Proxy vote shall not preclude a member from attending and voting in person at the meeting in respect of which the proxy is appointed or at any adjournment thereof.

2. The AGM is to be held at the Company's administrative head office at Level 3, 4 Tenterden Street, London W1S 1TE.

3. Please indicate on your proxy how you wish your votes to be cast in respect of the resolutions to be proposed at the said meeting. If you do not indicate how you wish your proxy to use your votes, the proxy will exercise his/her discretion both as to how he/she votes and as to whether or not he abstains from voting. Your proxy will have the authority to vote at his/her discretion on any amendment or other motion proposed at the meeting, including any motion to adjourn the meeting. Any power of attorney or other authority under which the proxy is submitted must be returned to the Company's Registrars, Link Group, PXS1, 10th Floor, Central Square, 29 Wellington Street, Leeds, LS1 4DL. If a paper form of proxy is requested from the registrar, it should be completed and returned to Link Group, PXS1, 10th Floor, Central Square, 29 Wellington Street, Leeds, LS1 4DL to be received not less than 48 hours before the time of the meeting.

4. In the case of joint holders, the signature of the holder whose name stands first in the relevant register of members will suffice as the vote of such holder and shall be accepted to the exclusion of the votes of the other joint holders. The names of all joint holders should, however, be shown.

5. If a member is a corporation, the form must be executed either under its common seal or under the hand of an officer or agent duly authorised in writing. In the case of an individual the proxy must be signed by the appointor or his/her agent, duly authorised in writing. CREST members should use the CREST electronic proxy appointment service and refer to Note 6 below in relation to the submission of a proxy appointment via CREST.

   In each case the proxy appointment must be received with any authority (or a notarially certified copy of such authority) under which it is signed.

6. CREST members who wish to appoint a proxy or proxies through the CREST electronic proxy appointment service may do so for the AGM to be held on the above date and any adjournment(s) thereof by using the procedures described in the CREST manual. CREST personal members or other CREST sponsored members who have appointed a voting service provider(s), will be able to take the appropriate action on their behalf.

   In order for a proxy appointment or instruction made using the CREST service to be valid, the appropriate CREST message (a "CREST proxy instruction") must be properly authenticated in accordance with Euroclear UK and Ireland Limited's specifications and must contain the information required for such instructions as described in the CREST manual. The message, regardless of whether it constitutes the appointment of a proxy or an amendment to the instruction given to a previously appointed proxy must, in order to be valid, be transmitted so as to be received by the Company's agent (ID: RA10) by the latest time(s) for receipt of proxy appointments specified in the notice of meeting. For this purpose, the time of receipt will be taken to be the time (as determined by the time stamp applied to the message by the CREST applications host) from which the Company's agent is able to retrieve the message by enquiry to CREST in the manner prescribed by CREST. After this time any change of instructions to proxies appointed through CREST should be communicated to the appointee through other means.

   CREST members and, where applicable, their CREST sponsors or voting service providers should note that Euroclear UK and Ireland Limited does not make available special procedures in CREST for any particular messages. Normal system timings and limitations will therefore apply in relation to the input of CREST proxy instructions. It is the responsibility of the CREST member concerned to take (or, if the CREST member is a CREST personal member or sponsored member or has appointed a voting service provider(s), to procure that his/her CREST sponsor or voting service provider(s) take(s) such action as shall be necessary to ensure that a message is transmitted by means of the CREST system by any particular time. In this connection, CREST members and, where applicable, their CREST sponsors or joint service providers are referred, in particular, to those sections of the CREST manual concerning practical limitations of the CREST system and timings.

   The Company may treat as invalid a CREST proxy instruction in the circumstances set out in regulation 35(5) (a) of the Uncertificated Securities Regulations 2001.

   Pursuant to regulation 41 (1) of the Uncertificated Securities Regulations 2001 (2001 No. 3755) the Company has specified that only those members registered on the register of members of the Company at close of business on 19 July 2022 shall be entitled to attend and vote at the AGM in respect of the number of Ordinary Shares registered in their name at the time. Changes to the register of members after close of business on 19 July 2022 shall be disregarded in determining the rights of any person to attend and vote at the AGM.

7. Under Section 319 of the Act, the Company must answer any question relating to the business being dealt with at the meeting put by a member attending the meeting unless:

   a. answering the question would interfere unduly with the preparation for the meeting or involve the disclosure of confidential information;

   b. the answer has already been given on a website in the form of an answer to a question; or

   c. it is undesirable in the interests of the Company or the good order of the meeting that the question be answered.

8. The following documents will be available for inspection at the Company's registered office during normal business hours on any weekday (Saturdays, Sundays and English public holidays excluded) from the date of this notice of the Annual General Meeting until the date of the Annual General Meeting and at the place of the meeting at least 15 minutes prior to the commencement of the Annual General Meeting until its conclusion:

   a. copies of the Directors' contracts of service;

   b. copies of the Non-Executive Directors' letters of appointment;

   c. a copy of the Articles of Association of the Company is available on the Investor Relations section of the Advanced Oncotherapy website (www.avoplc.com) on the Company Documents page.

EXPLANATORY NOTES TO THE NOTICE OF ANNUAL GENERAL MEETING

This year, Resolutions are proposed at the Annual General Meeting and the purpose of each of the Resolutions is as follows:

ORDINARY BUSINESS

Resolution 1: The Report and Accounts

The Directors will present their report and the audited financial statements to 31st December 2021, together with the auditors' report therein.

Resolutions 2-10: Re-appointment of retiring Directors

The Articles of Association of the Company stipulate that any Director shall only hold office until the conclusion of the next annual general meeting following the date of his/her appointment. Furthermore, the articles require that one third of the Directors retire at each Annual General Meeting. Corporate Governance guidance recommends that each of the Directors retire and offer themselves for re-appointment. Biographical details relating to each of the Directors can be found on the Group's website: www.avoplc.com

Resolution 11: Appointment of Auditors

The Company is required to appoint auditors at each Annual General Meeting at which accounts are laid before shareholders, and for them to hold office until the next such meeting. This Resolution proposes RPG Crouch Chapman LLP be re-appointed as auditors for the current year.

Resolution 12: Auditors' remuneration

This Resolution authorises the Directors to determine the auditors' remuneration.

SPECIAL BUSINESS

Resolution 13: Authority to allot shares

Section 549 of the Companies Act 2006 stipulates that Directors cannot allot shares or rights to subscribe for shares in the Company (other than the shares allotted in accordance with an employee share scheme) unless they are authorised to do so by the shareholders in general meeting. The Directors' general authority to allot shares was granted at the General Meeting held on 30 July 2021 which will expire at the conclusion of this AGM. Resolution 13 seeks a new general authority from shareholders for the Directors to allot Ordinary Shares or to grant rights to subscribe for and/or to convert any securities into Ordinary Shares up to an aggregate nominal value of 37,292,063. The Directors consider it desirable that the specified number of Ordinary Shares and/or rights to subscribe for and/or to convert any securities into Ordinary Shares be increased by 30% so that they can satisfy existing warrants and options and allow headroom to more readily take advantage of possible equity raising opportunities. Unless renewed, revoked, varied or extended, this authority will expire at the conclusion of the next AGM of the Company to be held in 2023 or fifteen months from the date of the passing of the resolution, whichever is the earlier.

SPECIAL RESOLUTION

Resolution 14: Disapplication of pre-emption rights

If the Directors wish to allot any Ordinary Shares for cash in accordance with the authority proposed in Resolution 13, the Companies Act 2006 requires that new Ordinary Shares must generally be offered first to shareholders in proportion to their existing holdings. These are the pre-emption rights of shareholders. In certain circumstances, it may be in the interest of the Company for the Directors to be able to allot some shares for cash without having to offer them first to existing shareholders. In line with common practice, Resolution 14 therefore seeks authority to empower the Directors to allot equity securities for cash other than in accordance with the statutory pre-emption rights, in connection with a rights issue and other pre-emptive offers and otherwise up to a maximum nominal amount of 37,292,063. In addition, there are legal, regulatory and practical reasons why it may not always be possible to issue new shares under a rights issue to some shareholders, particularly those resident overseas. To cater for this, this Resolution also permits the Directors to make appropriate exclusions or arrangements to deal with such difficulties. Unless renewed, revoked, varied or extended, this authority will expire at the conclusion of the next Annual General Meeting of the Company to be held in 2023 or fifteen months from the date of the passing of the resolution, whichever is the earlier.

COMPANY INFORMATION

DIRECTORS

Mr. Michael Bradfield * †	*Non-Executive Director*
Mr. Hans von Celsing * † §	*Non-Executive Director*
Ms. Lori Cross §	*Non-Executive Director*
Prof. Steve Myers	*Executive Chairman of ADAM*
Dr. Nick Plowman	*Non-Executive Director*
Mr. Nicolas Serandour	*Chief Executive Officer*
Dr. Michael Sinclair	*Executive Chairman*
Dr. Enrico Vanni * † §	*Non-Executive Director*
Mrs. Renhua Zhang	*Non-Executive Director*

* Member of the Audit Committee
† Member of the Remuneration Committee
§ Member of the Strategic Committee

COMPANY SECRETARY
Henry Clarke

REGISTERED OFFICE
Level 17, Dashwood House
69 Old Broad Street
London, EC2M 1QS

TRADING AND CORRESPONDENCE ADDRESS
Third Floor, 4 Tenterden Street
London, W1S 1TE

REGISTERED NUMBER
05564418 (England and Wales)

WEBSITE
This annual report and other information about Advanced Oncotherapy plc, including share price information and details of results announcements, are available at www.avoplc.com

AUDITORS
RPG Crouch Chapman LLP
5th Floor, 14-16 Dowgate Hill
London, EC4R 2SU

NOMINATED ADVISER AND JOINT BROKER
Allenby Capital Limited
5th Floor, 5 St Helen's Place
London, EC3A 6AB

JOINT BROKER
SI Capital Limited
46 Bridge Street
Godalming, GU7 1HL

SOLICITORS TO THE COMPANY
Faegre Baker Daniels LLP
7 Pilgrim Street
London, EC4V 6LB

David Conway and Co
1 Great Cumberland Place
London, W1H 7AL

Dechert LLP
160 Queen Victoria St
London, EC4V 4QQ

PUBLIC RELATIONS
FTI Consulting
200 Aldersgate, Aldersgate Street
London, EC1A 4HD

REGISTRARS
Link Group
10th Floor Central Square
29 Wellington Street
Leeds, LS1 4DL

Annual report 2021

Powerful technology to treat cancer
with pinpoint precision

ADVANCED
ONCOTHERAPY