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Advanced Oncotherapy

Confidence greatly boosted

AVO is focused on delivering a more affordable, novel, proton-based radiotherapy system, based on technology developed originally at the world-renowned CERN. Major technical milestones were achieved in 2017 and the company remains on track with its development plan. Confidence has been enhanced significantly with integration of the first three structures and overcoming the technical challenge of accelerating the proton beam. Meanwhile, construction of the Harley Street site is on schedule for completion in 1H 2019, and new financing and distribution arrangements add further to confidence about the whole project.

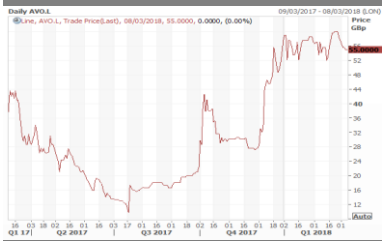
- **Strategy**: To develop a compact and modular proton therapy (PT) system at an affordable price for the payor, financially attractive to the operator, and generating superior patient outcomes. AVO benefits from the technology know-how developed by ADAM, Geneva, and relies on a base of world-class suppliers.
- **Technical milestones:** Two major milestones were delivered on time in 2017 and, with most of the modular components to complete the machine already on site in Geneva, further integration work is underway to accelerate the proton beam to its target energy level. The LIGHT project is being increasingly de-risked.
- **Commercialisation:** Strong manufacturing partners, and Thales' infrastructure and experience will allow mass production of a proton accelerator for the first time, in a multi-billion-dollar market. With construction progress at its Harley Street site, AVO is confident of having a LIGHT system fully tested in 2019.
- **Risks:** The funding risk has now reduced greatly, although release of cash from the People's Republic of China requires approval from the Government. The more complex technical challenges of the LIGHT project have been overcome, and integration of the different units follows known working prototypes.
- **Investment summary:** Demand for PT is increasing worldwide and the need for a small, flexible, affordable and close-to-patient machine is desirable. AVO has attracted strong partners and discussions with potential customers have started already. Attention is focused on the construction timetable for the flagship Harley Street site and installation of the first LIGHT system. Resolution of AVO's financing requirements brings further assurance.

Financial summary and valuation

Year end Dec (£m)	2014	2015	2016	2017E	2018E	2019E
Sales	0.1	0.0	0.0	0.0	0.0	0.0
Administration costs	-5.1	-6.6	-11.2	-12.5	-13.4	-13.6
Milestones/up-fronts	0.0	0.0	0.0	0.0	16.5	0.0
EBITDA	-5.1	-6.4	-10.8	-12.1	3.5	-13.1
Underlying EBIT	-5.2	-6.6	-11.2	-12.5	3.1	-13.6
Reported EBIT	-6.5	-8.5	-13.1	-14.5	0.7	-16.2
Underlying PBT	-5.1	-6.7	-11.3	-13.9	0.3	-16.6
Statutory PBT	-7.6	-8.6	-13.2	-15.9	-2.1	-19.2
Underlying EPS (p)	-14.9	-7.1	-13.9	-15.9	1.2	-8.5
Statutory EPS (p)	-22.3	-12.3	-14.4	-17.8	-0.4	-10.0
Net (debt)/cash	0.5	8.0	0.9	-10.5	2.8	-17.7
Capital increase	10.2	21.1	13.5	5.8	26.2	8.0

Source: Hardman & Co Life Sciences Research

Healthcare Equipment & Services



Source: Eikon Thomson Reuters

Market data

EPIC/TKR	**AVO**
Price (p)	56.5
12m High (p)	64.8
12m Low (p)	9.5
Shares (m)	150.5
Mkt Cap (£m)	85.0
EV (£m)	78.0
Free Float*	42%
Market	AIM

**As defined by AIM Rule 26*

Description

AVO is developing next generation proton therapy systems for use in radiation treatment of cancers. The first system is expected to be installed in Harley Street, London, during 2019; it will be operated through a JV with Circle Health.

Company information

Exec. Chairman	Michael Sinclair
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Key shareholders

Board & Management	16.0%
Yantai CIPU	29.9%
AB Segulah	12.6%
Brahma AG	6.0%
MK trust	3.3%
Others	32.3%

Diary

1Q'18	Beam through SCDTLs
Jun-18	Finals
3Q'18	Beam able to treat superficial tumours

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LIGHT – status update

Key features

AVO is developing the first compact linear accelerator for PT

Driven by the demand for compact, flexible, and affordable systems, PT equipment manufacturing represents a $1.0bn market. AVO, together with its research division ADAM, a spin-off from CERN, is developing a PT system that will fulfil, among many things, all the requests of the medical community and its patients. AVO will have the first proton system to use a compact linear accelerator – Linac Image-Guided Hadron Technology (LIGHT).

Key differentiators

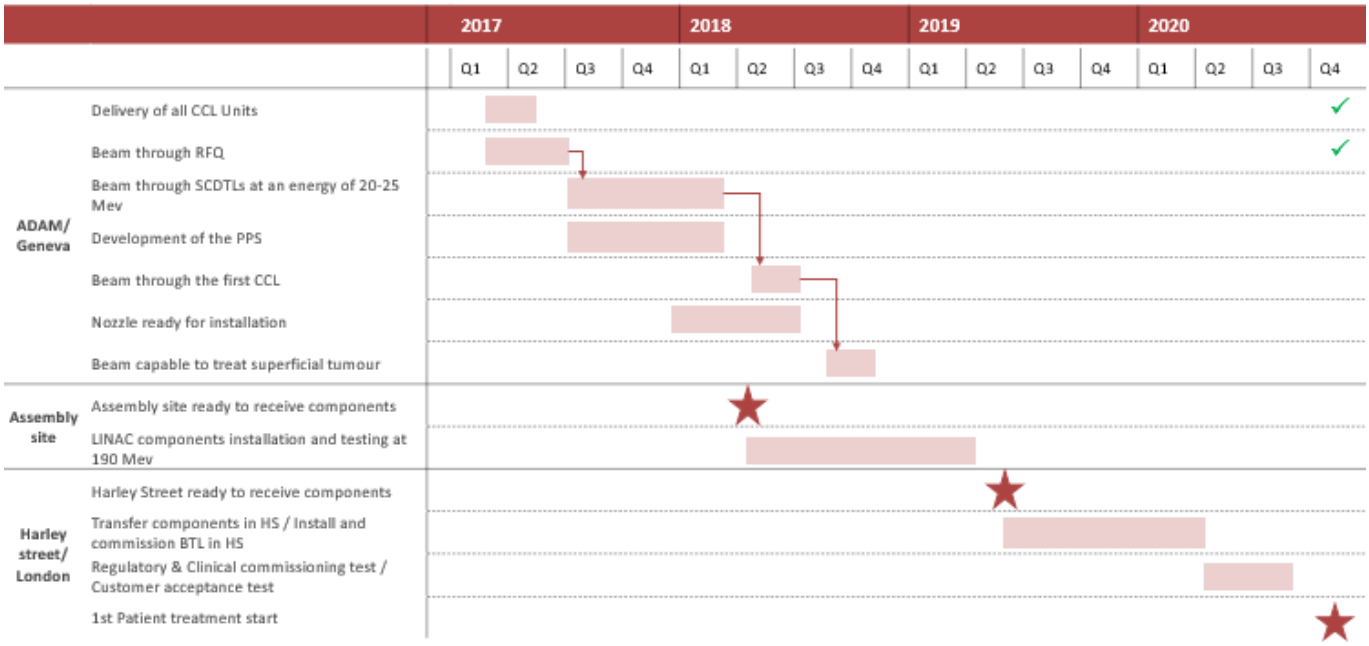
The LIGHT technology has been designed with the following characteristics:

- **Affordability:** LIGHT is positioned to represent an upfront cost in line with the most competitive PT systems currently on the market. This price positioning is possible thanks to the modularity of the system and the mass-production manufacturing.
- **Precision:** The level of accuracy is designed to become much higher compared with commercially available PT systems, enabling better targeting of moving tumours. For reference manufacturer Ion Beam Application (IBA) disclosed at its Capital Markets Day on 25th September 2017 that its system generates beam availability every 50-100ms. In contrast, we note that LIGHT is expected to generate a proton beam at least 10x more frequently than IBA machines, a key advantage, particularly for moving targets.
- **Integration:** The work-flow for delivering cost-effective proton beam therapy requires an integrated approach to all processes, achieved through the tight integration of software and hardware to ensure optimal interoperability to deliver the optimal treatment in each session. The software is tailored for the LIGHT system, and is designed to facilitate and enhance the user experience and operability.
- **Compact:** The entire LIGHT system is designed to be not only small, but also considerably lighter. Without the need for heavy cranes, this significantly reduces the size and construction cost of the facility required to house it. In addition, the footprint can be reduced further by doubling the beam back on itself, a feature achievable from the modularity of the system.
- **Close-to-patients:** Owing to its compact size and modularity, the LIGHT system can be made available in existing hospitals/clinics and in city centres (highlighted by the Harley Street site, in Central London).
- **Modular:** LIGHT will be modular in nature, providing healthcare operators with greater freedom to customise their service to particular treatments. An added benefit for operators is the possibility of lower-energy accelerators for eye, head or neck treatments, without precluding the possibility of extending this to higher energies by means of a simple installation of additional units and without dismantling, and then re-installing, a completely new system.
- **Lower shielding requirements:** LIGHT will have a low shielding requirement, thereby reducing the time and cost of installation and, eventually, the decommissioning cost.

First machine treating patients at the Harley Street site in 2020

At its investor forum in March 2017, AVO set out revised plans for delivering the first LIGHT system. The aim is to install, validate, and obtain regulatory approval (CE Mark) of the first LIGHT system at its site in Harley Street, London, ready for patient treatments to begin in 2020.

LIGHT development timeline



Source: Adapted from Advanced Oncotherapy investor presentation March 2017 by Hardman & Co Life Sciences Research

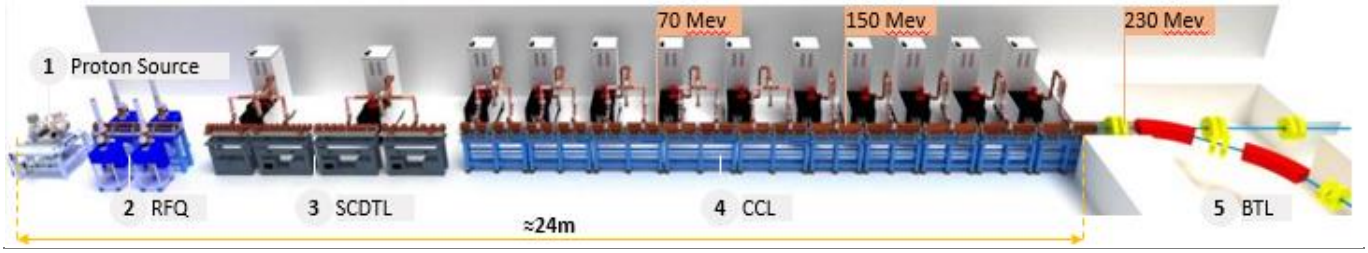
Planning forward, AVO is putting in place a network of manufacturing partners including a number of leading global outsourcing partners with particular expertise in specific areas, which will ultimately allow for mass-production of LIGHT. At present, preparations are underway to ramp up production to four LIGHT systems per annum and per production line.

The LIGHT system, module-by-module

The LIGHT proton beam accelerator unit is composed of four main structures, which are integrated with delivery and patient positioning systems:

- **Proton source:** The proton source generates a very high rate of up to 200 pulses of protons per second (a rate higher than any competitors) from a source of hydrogen gas. The protons are accelerated to an energy level of 40keV.
- **Radio Frequency Quadruple (RFQ):** This focuses the beam and accelerates the protons from 40keV to 5 MeV. The RFQ structure is composed of four units, each designed to match the proton velocity. The RFQ unit has been designed and built by CERN. It operates at the highest frequency in the world at 750MHz (compared with the closest RFQ at 400MHz), which allows the wavelength to be much shorter; this, in turn, allows the RFQ module to be shorter and more affordable.
- **Side Coupled Drift Tube Linac (SCDTL):** Manufactured by TSC and VDL, the SCDTLs, each with their own power unit, sit between the RFQ and the CCL. modules. The four low-speed accelerating units aim to accelerate the protons from 5MeV to 37.5MeV. Again, each unit is different so that it matches the increasing velocity of the protons.
- **Coupled Cavity Linac (CCL):** This structure is composed of up to 15 separate units to accelerate the proton beam from 37.5MeV to the clinically relevant energy of up to 230MeV (0.6x the speed of light).
- **Dose Delivery System (DDS, or 'nozzle')**: Once fully accelerated, the high-energy beam passes into the DDS, which ensures that the proton beam is both measured and targeted to maximise its effectiveness in cancer treatment.

LIGHT system



Source: Advanced Oncotherapy investor presentation

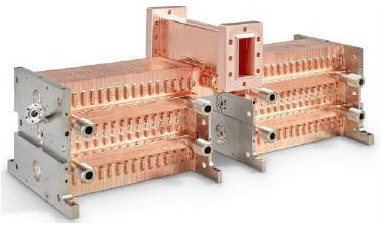
- **Patient Positioning System (PPS):** This represents the end-part of the machine, and comprises several components that allow the perfect positioning of the patient for both imaging and therapy.

Development update

Following successful integration of the first SCDTL with the RFQ and proton source, the biggest technical challenges for the proton accelerator have probably been overcome. During 2018, the next steps will include the further integration of the remaining three SCDTLs and then the CCLs.

Milestone 1 achieved: delivery of CCL units

CCL module



Source: Advanced Oncotherapy

The CCL units that are needed for the LIGHT system to accelerate protons to an energy capable of treating superficial tumours have been shipped to the Geneva testing facility. This represented the first of the milestones set out in March 2017. Although the timeline was modestly extended, this was insignificant in the overall picture and was not a rate limiting step.

The CCL units are each unique in respect of accelerating the proton beam. They will all go through further testing before integration with the SCDTLs. When integrated, the CCL units will accelerate the proton beam from 37.5MeV to 190-230MeV (the higher the speed, the more CCLs that are needed).

Milestone 2 achieved: beam accelerated through the RFQ to 5MeV

RFQ module

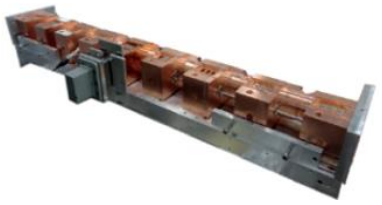
Source: Advanced Oncotherapy

In December 2016, AVO successfully integrated the proton source and the RFQ. Following further testing at full power, in February 2017, the energy of the proton beam was successfully increased from 40keV to the target 5MeV for this module. This represents one of the most difficult and significant steps required to make the LIGHT system a reality.

This milestone was reached in February 2017, and announced to investors the following month. At the Investor Forum in March 2017, the importance of the 5MeV energy level was compared with the first push a cyclist needs to action on the pedal in order to set the whole bicycle in motion. This crucial step of reaching the initial and predictable 5MeV target following a linear path is a significant differentiator in the approach taken by AVO with LIGHT, compared with existing cyclotron technology.

Since then, the focus has been on enhancing the proton source, further testing, and intensive usage and repeatability of beam firing through the accelerating structures.

SCDTL module



Source: Advanced Oncotherapy

Milestone 3 in progress: manufacture and integration of SCDTLs

In September 2017, AVO announced that the first of the four SCDTL units had been integrated within the scheduled timeline, with the predicted energy level of 7.5MeV being generated and recorded. This means that AVO has managed to integrate three (proton source + RFQ + SCDTL) of the four different structures and proven that the proton beam can achieve the target energy level when passed through them.

This represents another significant element in the de-risking of the whole project, validates the design and manufacture of the SCDTL, and provides confidence that the other three units can be integrated successfully. Professor Ugo Amaldi, President of the TERA Foundation and member of Company's Medical advisory board, commented:

> *"The most challenging part in building a new linear accelerator is the manufacturing and individual testing of the accelerating structures; their integration in a single linear accelerator is a simple process……An identical system is working up to 35MeV in the ENEA laboratory at Frascati, Italy".*

Each of the SCDTL units that have been manufactured successfully have also been tested individually. They are all different, so that they can provide an increasing acceleration of the proton beam. At the end of the fourth SCDTL unit, the proton beam is expected to reach an energy level of 37.5MeV.

Patient Positioning System

Source: Advanced Oncotherapy

Milestone 4 in progress: creation of Patient Positioning System (PPS)

Although all the focus has been largely on the back-end of the LIGHT system, significant progress has been made also on the PPS. Multiple components of the treatment room have been manufactured, inspected and tested by the company's partner, P-Cure Ltd. This encompasses the treatment chair and the robotic arm that moves and aligns the chair and patient to the proton beam. The connectivity between the PPS and the LIGHT system has also been validated.

As other sub-systems are completed, such as the imaging and treatment management software, they will be integrated to form the whole PPS.

The LIGHT system will be equipped with imagery modules such as:

- **Diagnostic Quality CT scanner:** This will image the patient in a seated position. It has been manufactured, integrated and tested successfully.
- **Orthogonal real-time X-ray imaging:** This will map 3D tumour motion in a continuous imaging process and has been developed already.
- **NDI Medical's optical cameras:** These track the 3D position and orientation of active or passive markers attached to surgical tools.
- **Vision RT's stereo-optical cameras:** These ensure that the patient is positioned in the same way during radiation treatment as he/she was during simulation/pre-planning.
- **Gating system:** This provides clean images for planning so that clinicians can more clearly visualise the target with fewer image artefacts associated with respiratory motion.

LIGHT technology has already been demonstrated by CERN with LIBO

Milestone 5 in progress: proton acceleration

It is worth mentioning that the technology involved in accelerating the proton with the CCL modules to high energy has been validated previously, in 2002, with the LIBO (LInac BOoster) machine. This has a similar linear structure to the structure that will be used in the LIGHT system, with integrated CCLs that have successfully accelerated a proton beam from 62MeV up to 73MeV. The idea behind LIBO was to upgrade current systems with a low-energy cyclotron machines to allow higher-energy PT programmes (e.g. eye proton therapy service at Clatterbridge NHS Foundation Trust, UK).

Energy vs range (body penetration)

Energy	Range in water
70 MeV	4.0 cm
100 MeV	7.6 cm
150 MeV	15.5 cm
200 MeV	25.6 cm
250 MeV	37.4 cm

Source: adapted from Education, Technology, Health & Medicine, 29th February 2012

The success of the LIBO prototype validates the whole concept of a full linear accelerator and is another element in de-risking the technical hurdle for the accelerator, again providing increased confidence.

Milestone 6: nozzle

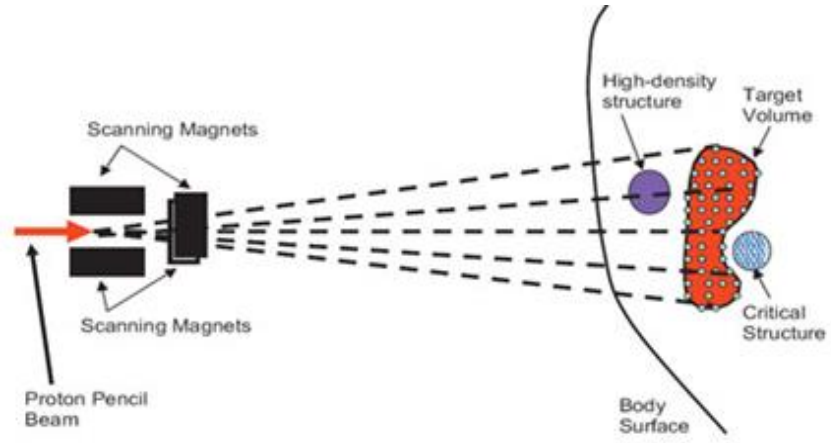
The nozzle monitors the beam position, size and dose level at the 'near patient' end of the system and delivers the proton beam. The nozzle has been designed to move the beam by active methods in all three dimensions. In the transverse plane, it will be achieved by bending magnets, while the longitudinal coordinate is changed by continuously and rapidly varying the energy of the beam electronically. This is different from existing systems where the beam is turned off while the scanning magnet is changed/moved to the next spot. Also, as each layer of the tumour is painted at one beam energy, the subsequent beam energy is reduced layer by layer.

- **The ionisation chamber**: In September 2017, the ionisation chamber was delivered by Pyramid Technical Consultants to the Geneva testing facility. It will be positioned at the delivery end of the LIGHT accelerator after the beam has been fully accelerated by the CCLs. The ionisation chamber has been designed specifically for use within the LIGHT system, enabling the precise measurement of the position of the proton beam (both horizontal and vertical axes) on a pulse-by-pulse basis (up to every five milliseconds), and monitoring the dose/intensity delivered to the target – beam energy, intensity and point size.
- **The scanning magnets:** In December 2017, the scanning magnets were produced. This component will enable the use of the Multi-Painting Spot Scanning technique, due to its ability to rapidly move the proton beam and to deliver a very short energy pulse. Unlike traditional techniques, which deposit the dose of radiation in the whole tumour volume in one go, this technique employs a focused proton pencil beam approach, which uses multiple successive dose applications to small elements called voxels[1]. This method allows delivery of the maximum dose, spread precisely over the whole tumour, while reducing the dose received by the surrounding healthy tissues.

Dynamic spot scanning should be more cost-effective than passive beam systems (which include single and dual scattering using a combination of custom-made collimators and compensators that conform the dose to the target volume) or first-generation active scanning beam systems – for example, Pencil Beam Scanning, which is offered by the majority of its competitors (IBA, Varian, Hitachi). AVO's key competitive advantage is the repetition rate (up to every five milliseconds), with which it can "paint" the tumour, thereby potentially increasing throughput.

[1] Basic unit of computed tomography reconstruction – used in 3D modelling; smallest distinguishable box-shaped part of a 3D space, represented as a pixel in a CT image display

Principle of spot scanning – schematic diagram



Source: Advanced Oncotherapy

Dynamic and fast energy-changing spot scanning should allow for greater hypo-fractionation of tumours, resulting in fewer patient visits to treatment centres. Typically, radiation therapy is spread out over time, referred to as fractionation. This is done to allow:

- time to recover for normal healthy cells exposed to radiation (while tumour cells are generally less efficient in repairing themselves between fractions);
- tumour cells that were in a relatively resistant phase of the cell cycle to move into a sensitive phase of the cycle before the next fraction is given;
- and tumour cells that were chronically or acutely hypoxic (radio-resistant) to potentially re-oxygenate between fractions, thus improving the tumour cell kill.

First installation of LIGHT

Based in Central London and in a world-renowned medical location, the Harley Street facility best defines the needs that LIGHT can fulfil. At present, from the outside, it is not possible to see what is happening behind the scaffolding at 141/143 Harley Street, but AVO provides on-site video updates.

Harley Street showcase

Success of the LIGHT system is independent of the success of the Harley Street site

Installation of the LIGHT system in the Harley Street facility will unlock regulatory approval. AVO's intention has always been to have the first LIGHT system up and running in a central location, close to the patients. The LIGHT system at the Harley Street site will be a showcase for the system, and an experience for clinicians and patients. It will provide a working example of the modularity and flexibility of the system, applicable in a logistically complex location found in a large city and being close to the patient. Already the provenance, flexibility, modularity and cost of LIGHT are attracting attention.

Progress to date

Deconstruct is the principal contractor company appointed by The Howard de Walden Estate. It specialises in complex deconstruction and construction structures and sub-structures in Central London, especially in preserving the integrity of Grade 2 listed buildings. According to Mick Durie, the project director at Deconstruct, enabling the 141/143 Harley Street site, progress is "going apace". Demolition and piling works have been completed. Further excavation works are in progress but there is no comparison with the size of the site needed for the installation of the UCLH proton facility currently being undertaken nearby.

CE Mark regulatory approval will be done in parallel with the aim of the first patient being treated in 2H 2020

Initiated in 1Q 2017, work is expected to take about 18 months (62-96 weeks, for demolition, excavation, rebuild, and radiation shielding); subsequent fit-out work is expected to take place afterwards. The timeline suggests that the Harley Street site will be ready to receive the first LIGHT module in 2Q 2019, and it will take an additional year to have the system up and running. It is expected that the regulatory approval for CE Mark will be done in parallel, and commissioning and certification will be done on site and be ready for the first patient in 2H 2020.

Construction at Harley Street

Source: Advanced Oncotherapy

Regulatory requirement

AVO is engaged with partners that follow the 'best practices' manufacturing capabilities. They are certified by both European and US regulatory bodies. This will enable AVO to fast-track the certification process through the governing regulatory agencies. Regulatory submission for CE Mark will be done in parallel with the installation of LIGHT at the Harley Street development, with the commissioning and certification being obtained at the end of the project.

Michael Baelen, Head of Regulatory Affairs for AVO, is experienced in dealing with regulatory authorities in the US and China, having spent 19 years in various positions including Health Policy Compliance Director and Head of Regulatory Affairs and Quality Assurance at IBA.

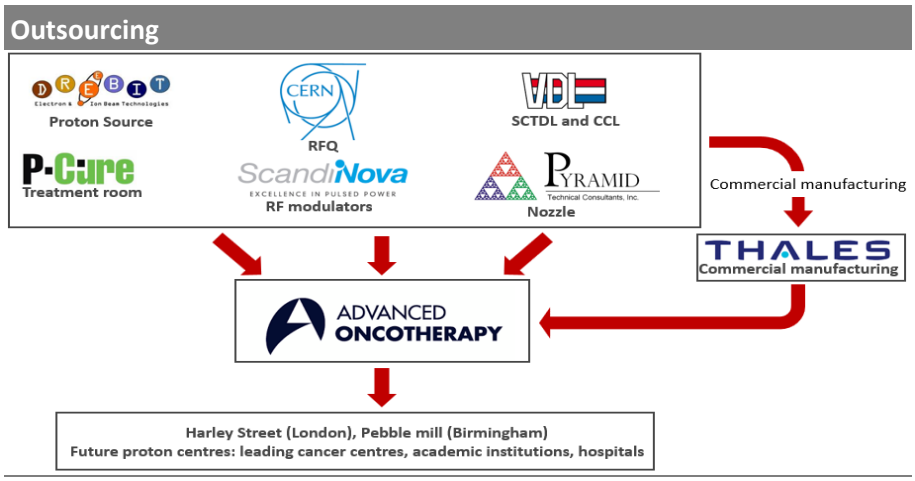
Paving the way to mass production

Production and manufacturing

A key advantage of the LIGHT system is its modular design. This allows the various complex components to be manufactured and tested independently by different specialist global suppliers. Each validated module can then be shipped for integration with, and construction of, the entire system. This provides enormous flexibility to the whole process, differentiating LIGHT from all other commercially available systems.

Current partnerships

AVO has laid the foundations for an efficient supply chain focused on modularity. Currently, all the modules are outsourced to key world-class technology providers, from the proton source to the treatment room with specialised software. Thales will be responsible for the latter stages of development, and will focus on mass-production and cost-saving opportunities once the anticipated demand is better understood.



Source: Hardman and Co Life Sciences Research

In the long term, AVO will be responsible mainly for the commercial side of the business, building up relationships, completing commercial deals with PT centres, and being in the forefront for innovation.

Thales partnership

Thales is adding considerable credibility to AVO's execution capabilities in both the short and long term

In October 2016, AVO secured a renowned manufacturer through its industrialisation agreement with Thales, a global technology leader for the aerospace, transport, defence and security industries. What attracted Thales to AVO, rather than to other PT providers, was the ability for the linear proton system to be manufactured using a mass-production process, a feature that is not currently possible with existing machines (cyclotrons and synchro-cyclotrons).

This partnership is an important step in ensuring the successful commercial roll-out of LIGHT after the first system has been installed and validated at Harley Street. While AVO is already expecting to provide a system at a lower cost compared with first-generation PT machines (cyclotrons), the cost-reduction skills of Thales and its ability to reduce lead times through process optimisation will ensure that this next-generation PT system is affordable and, therefore, more widely and quickly available for cancer patients around the world. The ability to deliver new machines in a timely manner is becoming increasingly important.

Manufacturing

Being able to provide manufacturing lines for the LIGHT system will be a real advantage compared with competitors that usually deliver their machines on a case-by-case basis. A manufacturing line will provide cost savings and speed capabilities that will be key to AVO providing an affordable machine in a desired timeframe. While the market is currently focusing on cost, this will provide more flexibility in the price of the machine – hence increasing the attractiveness of the LIGHT machine, and providing cutting-edge technology.

Thales has the capability to deliver the commercial roll-out...

...and to identify opportunities to reduce costs

The anticipated cost of engineering studies is being borne initially by AVO. When the machine enters full production, AVO will recover these costs through the retention of a 100% gross margin on the first few LIGHT machines produced, following which Thales will start to be paid a fee per machine. By organising the series production in a way that will drive down costs under an appropriate quality framework, management expects the longer-term gross margin to stabilise at around 40%.

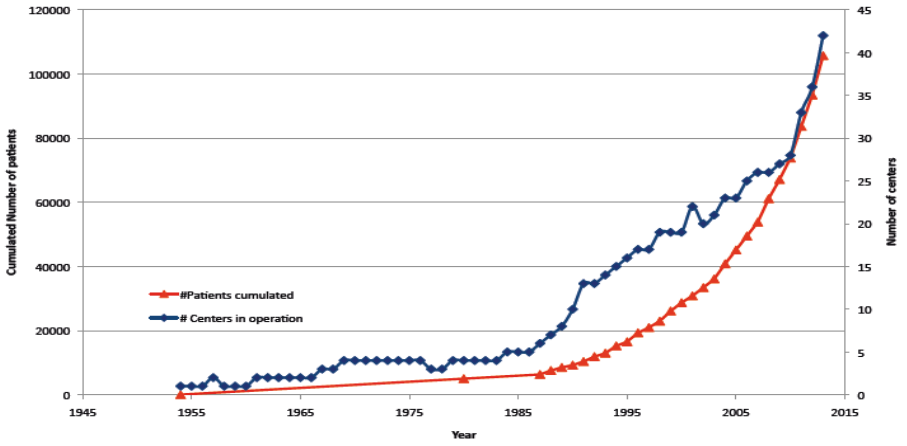
This agreement also opens up big opportunities for a fast and efficient production ramp-up in a market characterised by high demand. Thales will rely on its extensive experience in scientific accelerator integration to manage the transition from the first machine to series production of LIGHT, putting the concept on the cusp of a steepening adoption curve with tremendous growth potential. The target number of eight machines per year via two production lines is simply an initial target. Given the size of the global opportunity, the aspirations and ambitions of AVO are significantly larger, therefore, additional manufacturing sites are anticipated as demand increases.

Commercial opportunity

A snapshot of proton therapy

In July 2017, there were 68 active centres (more than 180 rooms) operating, with ca.150,000 cumulative patients having been treated with PT[2]. Since the early nineties, there has been a sharp increase in the number of PT centres and patients treated. This outcome is due to a better understanding of the benefits and clinical efficacy of PT compared with conventional therapies.

Patients treated vs. number of centres



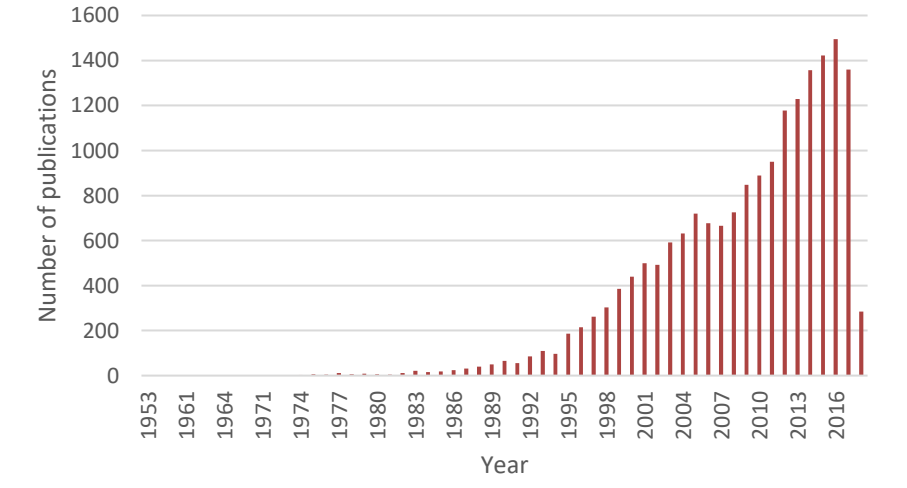
Source: Particle Therapy Co-Operative Group website

Clinical evidence

Clinical evidence of PT in cancer is growing with increasingly more cancer indications treated

The increased use of PT correlates well with the number of clinical studies and publication of scientific papers that gather more and more evidence and validation regarding the benefits of therapy.

Publications on proton therapy



Source: PubMed website, 1st March 2018

[2] PTCOG web site

Currently, with around 270 clinical trials registered (www.clinicaltrials.gov, recruiting, not yet recruiting, active, enrolling by invitation), the use of PT is being extended continually, in addition to establishing it as both a first- and second-line treatment.

In 2013, an NHS commissioning document[3] suggested that more than 50% of the 360,000 new cancer cases in the UK each year should receive radiotherapy as part of their treatment, whereas it was estimated that only 37% of cancer patients had actually accessed this treatment in England. In addition, another NHS document[4] highlighted the fact that 10% of cancer patients should receive more accurate PT to treat tumours. The reasons included:

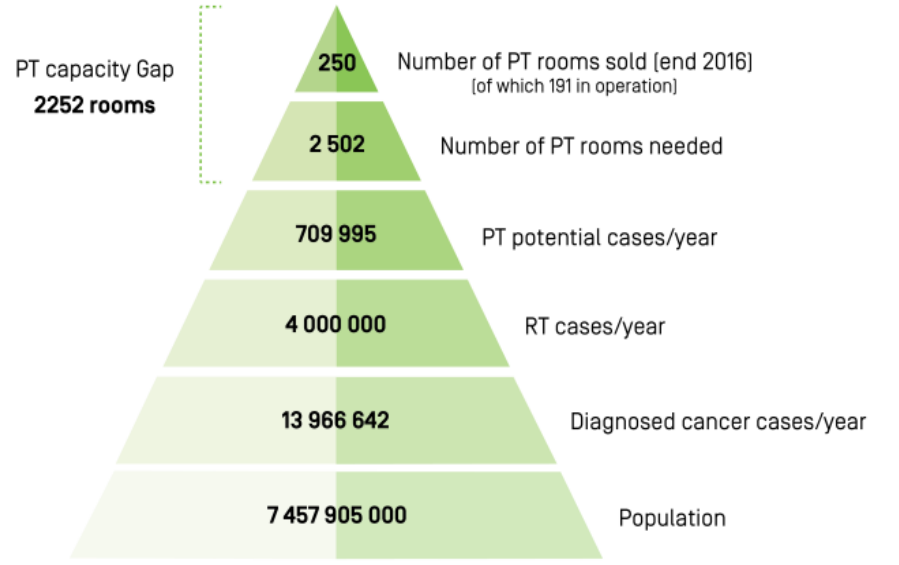
- Cancers in locations near tissues which are radiosensitive.
- Treatment of children at risk of developing significant side effects to radiation therapy.
- A combination of safety, tolerability and cancer recurrence issues.

As the cost of PT reduces, the demand, and hence the proportion, receiving more accurate PT is expected to increase.

In the US, nearly 1.7 million people were diagnosed with cancer in 2016. Of these, the NIH National Cancer Institute estimates that nearly 60% will receive, or have received, radiation therapy. The 27 PT centres open in the US today are equipped with 82 treatment rooms, which is equivalent to only 2% of the number of X-ray treatment rooms[5]. Based on the assumption that 10% of patients would be eligible for PT, representing a population of >100,000, more than 400 rooms would be required, in the US alone.

Globally, the need is even greater, as highlighted by IBA's estimates which are depicted in the following graphic:

Global estimate for PT treatment rooms



Source: IBA

[3] https://www.england.nhs.uk/wp-content/uploads/2013/06/b01-radiotherapy.pdf
[4] http://www.nhsconfed.org/regions-and-eu/welsh-nhs-confederation/events/proton-beam-therapy
[5] www.floridaproton.org

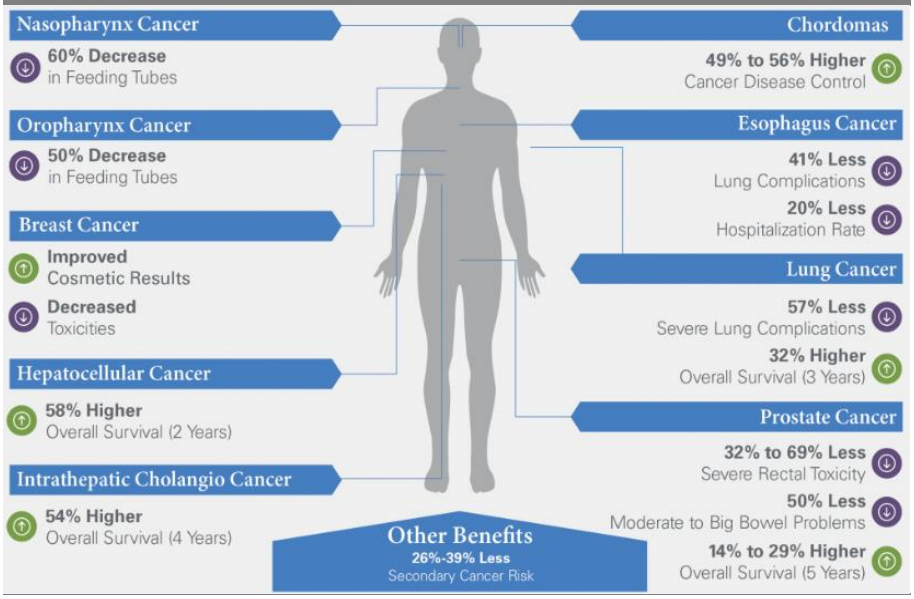
Globally, the number of new cancer cases is estimated at 14.1million per annum. In developed countries, between 40% and 60% of those patients are treated with radiotherapy, depending on the country in which the treatment is given. Considering that the lifetime cost of PT is already proven to be favourable in 10% to 15% of cancer cases traditionally treated with radiotherapy, this means that more than 700,000 patients need protons therapy every year, representing more than 2,800 treatment rooms. These numbers are also likely to increase as the cost of PT decreases.

Benefits

The benefits of PT are multiple compared with traditional radiotherapy, and evidence of its cost effectiveness is continuing to grow as increasingly more cancers are treated with PT. In addition, improvements in the imaging technology enable a more accurate targeting and dosing of the tumours and motion management.

- Reduced risk of damage to healthy tissue and organs.
- Shown to be effective in adults and children.
- Can be used to treat recurrent tumours, even in patients who have already received traditional forms of radiation.
- Fewer short- and long-term side effects.
- Lower incidence of secondary tumours.

Clinical benefits of proton therapy



Source: ProtonPals Patient support group website

Current estimates show proton beam therapy to be cost-effective if appropriate risk groups are chosen as targets. Furthermore, an investment in a proton facility may be cost-effective compared with conventional radiation when the associated reduction in adverse events and the improvement in life quality are taken into account. The three main inhibitory factors for a greater uptake of proton beam therapy are:

- More proof of efficacy for additional cancers.
- Getting adequate reimbursement.
- Better funding options for PT centres.

All of these factors could be solved by the introduction of cheaper centres, which, in turn, could be solved only by the introduction of smaller ('compact') machines that would not compromise the quality of the proton beam. Several manufacturers are talking about reducing costs via cut-down versions of existing PT systems, but these are likely to result in diminished quality, which would defeat the object of the exercise. In addition, their initiatives to reduce costs (upfront, operating and de-commissioning) and manufacturing lead times have had limited success to date, which we believe is due largely to the limitation of using legacy circular accelerators.

Cost-effectiveness

In the past, the use of PT has been limited mainly to patients with certain types of cancer (base of the skull, eyes, children etc) for which the long-term benefits are considered to be greatest. With products currently on the market (cyclotrons and synchrotrons), hosting a machine with two to three treatment rooms and relevant shielding requires an independent large multi-storey building that can cost up to $150m.

For example, in the UK, where there is no high-energy PT centre yet, patients are being sent overseas in order to receive treatment. To overcome this, the government has invested at least £250m to equip two hospitals (University College Hospital London, and Christie Hospital, Manchester), each with a three-room proton beam accelerator. Such expenditure invariably affects the cost of the treatment itself, and its wider availability – hence the need for a cheaper option that will be more cost effective.

Nowadays health economic data provide evidence on the cost-effectiveness of treating certain types of cancer and the relevance of the position of the cancer in the body – proximity to a vital organ for example. In addition, some professional healthcare bodies such as the American Society for Therapeutic Radiation Oncology (ASTRO), are setting up lists of conditions where the cost-effectiveness of PT has been proven; and this list of conditions is growing constantly.

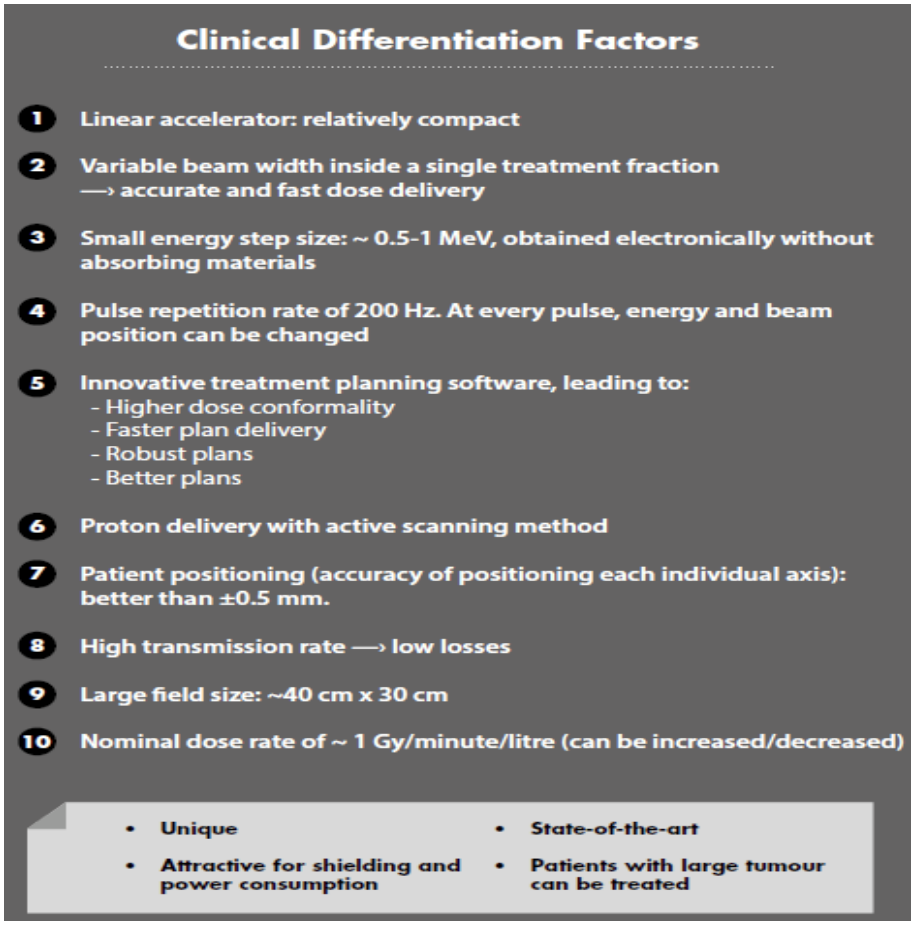
LIGHT's unique selling points

AVO will introduce the first linear and modular system for PT, LIGHT. Its main objective is to provide a technology which makes PT affordable and available to all those who need it. This means offering a system at a price in line with, or below, the most competitive technology available on the market today. In this context, the modularity of LIGHT offers strong perspectives of cost savings in coming years.

In addition, as detailed above, the less onerous building work required to house and install the machine make the LIGHT system even more affordable. Being modular in design, installation is much easier, as it can be done in an existing building – hence avoiding the need to build new and large facilities, as is the case with circular accelerators. These features are all the consequence of the modular design and the light weight of the accelerator. The initial investment is also positively affected by the lower shielding requirements of LIGHT.

Most importantly, this compact design does not compromise on the quality of the beam. In fact, the beam size from a LIGHT machine is small which enables a rapid change of position, energy and dose during therapy, allowing the beam to more accurately target cancer cells and spare healthy tissues, while limiting the need for large and expensive magnets.

Advantageous features of the LIGHT system



Source: Advanced Oncotherapy 2016 Annual Report

Pipeline

Independent of the timetable for the Harley Street project, AVO is in active discussions with multiple partners, potential customers and distributors.

- **UK:** Two sites being constructed in London (Harley Street) and Birmingham (Pebble Mill).
- **US:** Ongoing discussions with three centres, two of which are:
  - **Syracuse** – Initially a one-room system, with the potential for expansion to two treatment rooms.
  - **Unnamed** – Two-room treatment systems.
- **Spain:** One project.
- **Italy:** One new project.
- **China and Asia:** Strategic distribution agreement with Yantai CIPU in China and Hong Kong, Macau, Taiwan and South Korea. Yantai CIPU will make an up-front payment of £16.5m – subject to approval from the Government of the People's Republic of China – in exchange for an exclusive right to market and sell LIGHT in the stated territories. A number of prospective customers have already been identified by Yantai CIPU.
- **Middle-East and Australia:** Potential for use at leading academic and clinical centres.

Yantai CIPU distribution agreement

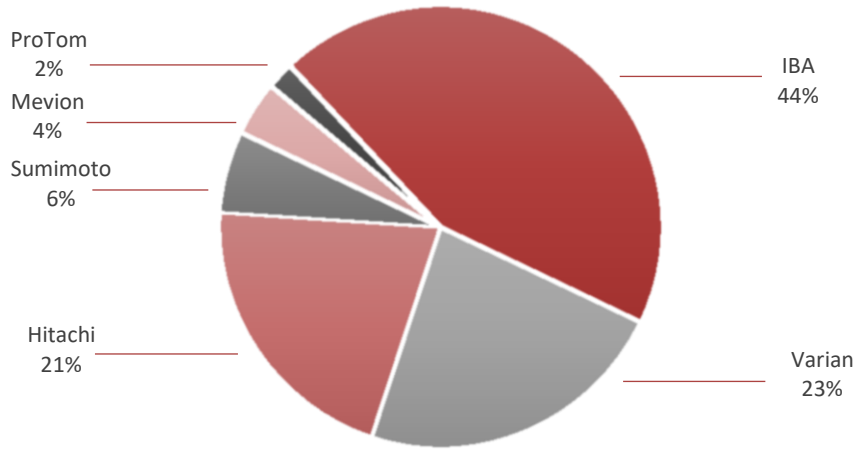
Yantai Medical Technology Co.Ltd. (Yantai CIPU) will make an up-front payment of £16.5m – subject to approval from the Government of the People's Republic of China – in exchange for the exclusive right to market and sell LIGHT in the stated territories.

From the outset of its strategy to deliver an affordable PT system that addresses the needs of the patient, the operator and the payor, AVO has recognised that the People's Republic of China represents a significant opportunity with the need for at least 100 PT centres. The appointment of Yantai CIPU, an experienced health industry investor, particularly in high-end medical equipment companies, as the exclusive distributor of LIGHT in China, Hong Kong, Macau, Taiwan and South Korea is an important step for AVO to take advantage of this opportunity.

Competitive landscape

The PT market is controlled largely by IBA and Varian, with specialist companies like AVO as challengers. IBA is the market leader with a 44% share of the installed treatment room base, followed by Varian (23%) and Hitachi + Mitsubishi (21%). The barrier to entry is high due to the technical expertise involved as well as the high capital cost.

Market share – June 2017



** Hitachi + Mitsubishi*
Source: adapted from IBA 1H'17 presentation

IBA is leading the number of facilities under construction and in the planning stage, with 21 sites in total, followed by Varian with 18 sites.

New PT facilities – planned and under construction

Company	Facilities at planning stage		Facilities under construction	
	Sites	Rooms	Sites	Rooms
IBA	5	8	16	35
Varian	5	10	13	41
Hitachi + Mitsubishi*	3	3+?	2	9
Mevion	2	4	3	3
Sumimoto	1	4	2	2
ProNova	1	2	1	3
ProTom	1	3	1	1
Toshiba	-	-	1	2
Advanced Oncotherapy	-	-	2	4
Other	4	10	7	20
Total	**22**	**44+**	**48**	**120**

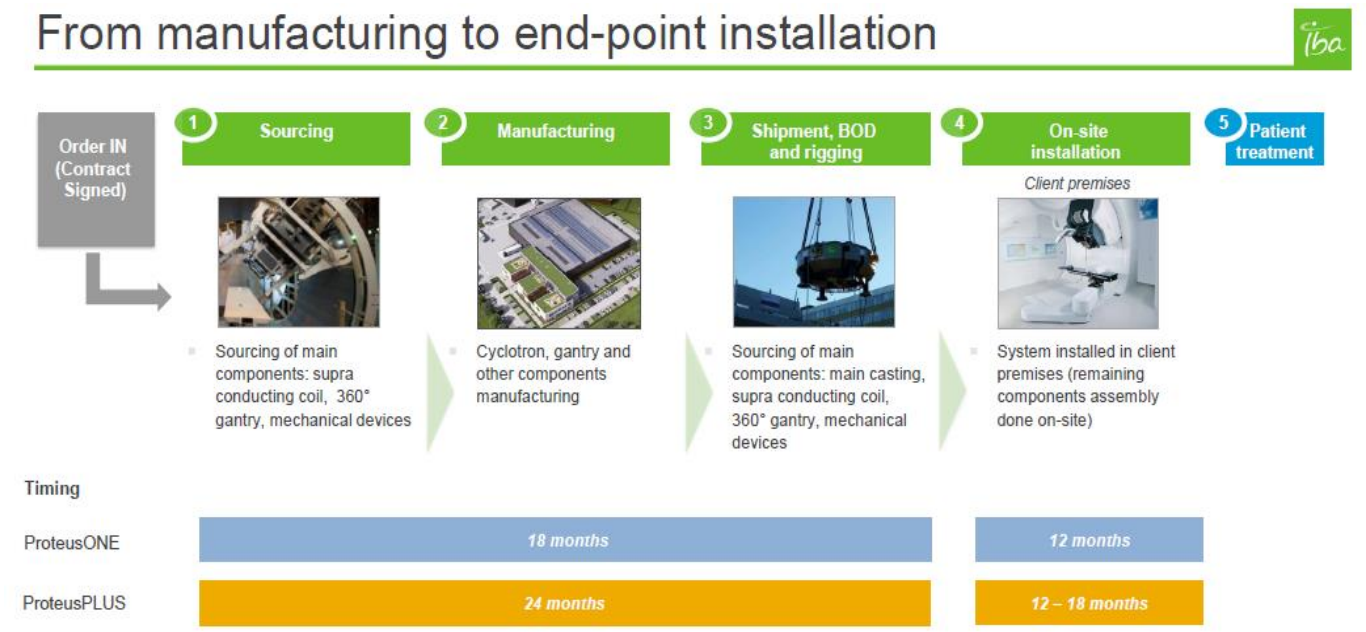
**Merger of PT into single entity announced 7th November 2017*
Source: PTCOG website, Hardman & Co Life Sciences Research

Market trends

Recently, several of the leading players have shifted their offering to compact systems, adopting shrunk versions of their first-generation cyclotrons and synchrotrons.

The rapidly increasing demand over the last five years has highlighted the need for all manufacturers to revisit their manufacturing processes. For example, during 2017, IBA reported significant delays in the delivery of nearly half of its PT solutions currently under construction. It is not clear where the problems lie, but an extra six months has been added to the schedule for construction purposes at customer sites. IBA usually quotes 30-42 months from the contract signature to the first patient treatment for its PT machines, ProteusONE and ProteusPLUS.

IBA's Proton solutions timeline



Source: IBA 1H'17 results presentation

Mass-production is not currently possible with cyclotrons and synchro-cyclotrons for technical reasons: these accelerators require significant quantities of steel, which has impurities, and this requires the magnetic field to be adjusted for each machine. The use of laminated steel that enables a reduction in the size and weight of such accelerators (from ca.200 tons to ca.40 tons of steel) brings another technical issue in terms of accurately controlling the temperature during the manufacturing process.

Market consolidation

Hitachi (TSE:6501) and Mitsubishi Electric (TSE:6503) have announced their intention to combine their respective PT offerings into a single entity, to generate efficiencies in the design, manufacture and commercialisation of their systems and to offer a better post-installation service. This consolidation is not really a surprise. As for IBA, it is clear that to obtain the final signature at the end of the contract takes more time and effort than before. This might be due to the situation at existing sites, which have financial difficulties, with some sites closing down, added to the difficulty in recruiting patients to make PT centres self-efficient. We highlight the following possible needs:

- A new, disruptive and cheaper solution –with the LIGHT machine, AVO could play the strong outsider.
- Additional cancer conditions eligible for PT – which is already happening with the new guidelines from the American Society for Radiation Oncology (ASTRO)[6] and the National Comprehensive Cancer Network (NCCN)[7] endorsing PT in new cancer indications.

Market drivers

The need for cost-effective treatments and more potent technologies coupled with increasing evidence of clinical efficacy and improved patient reimbursement, is increasing both the use and demand for PT around the world. There is strong evidence of demand in China, with six sites/24 rooms under construction. There is also evidence of fresh demand from territories where there are currently no existing PT clinics (MENA territories). With regard to the US, we note that it is at the replacement stage and is also expanding the offering with nine sites/24 rooms under construction and four sites/10 rooms at the planning stage. In addition, new technologies and improvements in software and imaging systems, which allow accurate, real-time tracking and dosing of mobile tumours, bring a health-economic rationale for PT, which is associated with less damage to healthy tissue. AVO is very well positioned to take a considerable part of the market with its flexible, modular LIGHT system.

Proton therapy – drivers and obstacles

Drivers	Obstacles
Growing cancer prevalence	Installation costs
Growing use of radiation therapy	Competitive technologies
Emerging markets under-penetrated	Clinical benefit yet to be fully elucidated
Technological innovation (imaging solutions, dose delivery, robotic positioning systems)	Reimbursement rates

Source: Hardman & Co Life Sciences Research

[6] www.astro.org
[7] www.nccn.org

LIGHT forecasts

A model has been constructed to estimate the opportunity for LIGHT and potential returns for shareholders. In order to achieve this, we have made a number of key assumptions:

- The first LIGHT system machine will be ready for patient treatments in 2020.
- The first system will be installed in Harley Street, and payment for the machine only will be spread over a five-year time frame.
- Forecasts assume that a complete LIGHT system will cost $40m, and customers will be invoiced according to the following schedule: 25% deposit on signature; 25% on commencement of installation; and 50% on completion of installation.
- Systems will come with a one-year warranty, after which an annual service contract, equivalent to 10% of the cost of the machine, will start in the second year following installation.
- Gross margins on the LIGHT system will start low and build to about 40% over a five-year period, as more systems are manufactured and installed.
- The margin on the servicing side of the business will remain consistent at ca.60%.
- No allowance has been made for software upgrades.
- Much of the sales and marketing cost will be borne by AVO's distribution partners.
- This assumes that there are two production lines each capable of producing four machines per year.
- These forecasts are for the LIGHT system only and do not take account of the corporate overheads and financing costs that appear in the group financial forecasts (see page 24).

Financial model for LIGHT

$m	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9
Systems sold	1	2	5	7	8	8	8	8	8
Cumulative system sold	1	3	8	15	23	31	39	47	55
LIGHT sales	8.0	28.0	78.0	168.0	258.0	300.0	320.0	320.0	320.0
Services sales	0.0	2.0	4.0	12.0	32.0	60.0	92.0	124.0	156.0
Group sales	**8.0**	**30.0**	**82.0**	**180.0**	**290.0**	**360.0**	**412.0**	**444.0**	**476.0**
COGS LIGHT	-7.2	-22.4	-58.5	-117.6	-167.7	-180.0	-192.0	-192.0	-192.0
COGS services	0.0	-0.8	-1.6	-4.8	-12.8	-24.0	-36.8	-49.6	-62.4
Group COGS	**-7.2**	**-23.2**	**-60.1**	**-122.4**	**-180.5**	**-204.0**	**-228.8**	**-241.6**	**-254.4**
LIGHT gross profit	0.8	5.6	19.5	50.4	90.3	120.0	128.0	128.0	128.0
Services profit	0.0	1.2	2.4	7.2	19.2	36.0	55.2	74.4	93.6
Group gross profit	**0.8**	**6.8**	**21.9**	**57.6**	**109.5**	**156.0**	**183.2**	**202.4**	**221.6**
Gross margin LIGHT	10%	20%	25%	30%	35%	40%	40%	40%	40%
Gross margin services	-	60%	60%	60%	60%	60%	60%	60%	60%
Group gross margin	**10%**	**23%**	**27%**	**32%**	**38%**	**43%**	**44%**	**46%**	**47%**
Marketing costs	-0.8	-2.5	-5.1	-7.6	-10.3	-10.5	-11.8	-12.5	-13.1
Marketing as % sales	10%	9%	7%	5%	4%	4%	4%	4%	4%
LIGHT EBIT*	**0.0**	**4.3**	**16.8**	**50.0**	**99.2**	**145.5**	**171.4**	**189.9**	**208.5**
LIGHT EBIT margin	0%	14%	21%	28%	34%	40%	42%	43%	44%

** Before R&D expenses*

Source: Hardman & Co Life Sciences Research

Financing update

As expected with R&D projects in the accelerator field, a lot of energy is spent on raising funding. To date, ca.£60m has been invested into the project, in addition to an estimated £14m invested previously by Brahma into the technology. However, hitting the technology milestones during 2017 considerably altered the risk profile of the project and increased confidence in achieving a successful outcome. In 2H'17, a shareholder loan, coupled with receipt of an R&D tax credit from HMRC, provided the working capital requirements for AVO. This was followed by the announcement, in December 2017, of a funding and distribution agreement, which was approved by shareholders at a General Meeting on 23rd January 2018.

Distribution agreement and capital increase

As described in our previous note published on 11th December 2017 "*Distribution agreement and capital increase*"[8], AVO announced a significant capital increase to resolve the company's funding requirements together with a distribution agreement covering the important market opportunities for PT in China and Southeast Asia. An overall headline total of £37m is being raised. Yantai CIPU Medical Technology Co. Ltd (Yantai CIPU) has signed a distribution agreement with AVO for the exclusive right to commercialise LIGHT in China and Macau, Taiwan, Hong Kong and South Korea, and has also made a direct investment in AVO.

- **Distribution agreement:** Yantai CIPU has agreed to make an up-front payment of £16.5m to AVO in return for an exclusive distribution agreement to commercialise LIGHT in specified territories in South-East Asia. This payment is awaiting approval from the Government of the People's Republic of China for the transfer of cash overseas.
- **Equity raise:** AVO has issued 56.0m new Ordinary shares at 30p per share to raise £16.76m gross funds. Yantai CIPU subscribed for 45.0m (ca.80%) of these new shares, with the remainder being taken up by the directors. This was completed on 22nd February 2018 following receipt of approval for the transfer of cash out of China from the Government of the People's Republic of China and the admission for trading of the new shares on AIM. Yantai CIPU now owns 29.9% of the enlarged share capital.
- **Loan conversion:** Concomitantly with the equity raise, the consortium of investors led by AB Segulah which made a loan facility of £3.9m available to AVO in July 2017, has converted the loan and related interest into 13.70m new Ordinary shares, equivalent to £4.11m. This was also completed on 22nd February 2018.

Shareholder loan facility

The convertible loan facility has proved highly dilutive for the share price. Therefore, AVO renegotiated with Bracknor to waive the obligation to draw down at least 10 tranches of Convertible loan notes. It was replaced by the financing facility provided by a consortium of investors led by long-term investor, Segulah.

Blackfinch loans

In 2017, AVO and Blackfinch Investment entered into three loan agreements totalling £6.5m:

- **27th March 2017:** £3m loan at 11% interest rate secured on the Harley Street lease and certain equipment – buy-back secured by the Chairman, Michael Sinclair.

[8] http://www.hardmanandco.com/docs/default-source/company-docs/advanced-oncotherapy-documents/11.12.17-distribution-agreement-and-capital-increase.pdf

- **25th April 2017:** £2m loan at 11% interest rate secured on the Harley Street lease and certain equipment – buy-back secured by four shareholders and directors.
- **13th June 2017:** £1.5m loan at 12% interest secured against anticipated cash receivables.

Metric capital

In May 2016, AVO announced that it had secured financing for its Harley Street project. Metric Capital Partners, a Pan-European private capital fund manager, agreed to a five-year £24.0m loan to be drawn in two tranches to support the development and installation of LIGHT in Harley Street. The agreement was subject to the customary representations, and to an additional £25m cash or capital injection to fund the development of a manufacturing base.

Now that AVO has secured sufficient funding to satisfy some of the original Terms & Conditions for the potential drawdown of this facility, AVO has re-entered negotiations with Metric Capital. AVO and Metric are seeking to update the Terms & Conditions to reflect the advancements made in the development of Harley Street since the original agreement was signed, which would allow this £24.0m facility to be drawn down.

Warrants

AVO currently has 29.6m warrants outstanding, the majority of which are currently exercisable. Our cashflow forecasts assume that most of those exercisable today will be converted during 2018, raising ca.£6.4m, with the remainder being exercised during 2019 and 2020, raising up to a further ca.£8.4m, as detailed below.

Potential exercise of warrants

Fiscal year	Holder	# exercisable	Price	Raise
2018	Bracknor	7.0m	25p	£1.75m
	Bracknor	1.8m	42p	£0.76m
	Segulah	15.6m	25p	£3.90m
2019	Blackfinch	0.5m	100p	£0.5m
	Blackfinch	1.0m	150p	£1.5m
	Other	0.7m	150p	£1.0m
2020	Other	1.8m	177.5p	£3.3m
	Other (averages)	1.2m	181p	£2.1m
	Total	**29.6m**	**50.0p**	**£14.8m**

Source: Corporate announcements, Hardman & Co Life Sciences Research

Conclusion

At its period end (31st December 2017), our forecasts suggest that AVO had very little cash and had run-up short-term trade creditors in the knowledge that the new funding would be completed shortly after receipt of shareholder approval and Chinese government approval. The cash position will be further boosted in the near future, as soon as the up-front payment in respect of the distribution agreement is approved by the Chinese government, together with the potential exercise of warrants. This will provide AVO with sufficient working capital through 2019.

Based on our cashflow forecasts, we have included a 'top-up' capital increase (estimated £5m at 100p per share) in late 2019, when market confidence is high with respect to the installation and validation of the first LIGHT system in Harley Street, and the whole project is largely de-risked, upon reaching the energy sufficient to treat superficial tumours.

Financial forecasts

Profit & Loss

- **Administration:** We have assumed that the acceleration in investment in personnel seen in 1H'17 has continued through to the full year with 2018 and 2019 remaining largely flat.
- **R&D tax credit:** Forecasts are based on a 20% recovery in R&D investment, which is received in cash in the following fiscal year.
- **Yantai CIPU:** Receipt of the £16.5m up-front payment from the exclusive distribution agreement with Yantai CIPU has been recorded under 'other income' in 2019, assuming that Chinese government approval is received.
- **Harley Street:** Consistent with our model of LIGHT forecasts (page 21), no sales or costs have been recorded for Harley Street over the forecast period. These, together with the JV costs/profits will be included from 2020.
- **Purchase orders:** To remain conservative, forecasts do not include other purchase orders beyond that from Circle Health in Harley Street.

Profit & Loss account						
Year-end Dec (£m)	**2014**	**2015**	**2016**	**2017E**	**2018E**	**2019E**
Sales	0.11	0.00	0.00	0.00	0.00	0.00
Cost of goods	-0.20	0.00	0.00	0.00	0.00	0.00
Gross profit	**-0.10**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Administrative costs	-5.09	-6.59	-11.18	-12.50	-13.40	-13.60
Underlying EBITDA	**-5.06**	**-6.41**	**-10.83**	**-12.14**	**3.52**	**-13.12**
Depreciation	-0.12	-0.18	-0.35	-0.36	-0.42	-0.48
Amortisation	0.00	0.00	0.00	0.00	0.00	0.00
Other income	0.00	0.00	0.00	0.00	16.50	0.00
Underlying EBIT	**-5.18**	**-6.59**	**-11.18**	**-12.50**	**3.10**	**-13.60**
Share-based costs	-0.47	-1.03	-1.91	-2.00	-2.40	-2.60
Exceptional items	-0.80	-0.89	0.00	0.00	0.00	0.00
Statutory EBIT	**-6.45**	**-8.51**	**-13.09**	**-14.50**	**0.70**	**-16.20**
Net interest	0.12	-0.12	-0.10	-1.42	-2.76	-3.04
Underlying pre-tax profit	**-5.06**	**-6.72**	**-11.27**	**-13.92**	**0.34**	**-16.64**
Extraordinary items	-1.23	0.00	0.00	0.00	0.00	0.00
Reported pre-tax profit	**-7.56**	**-8.63**	**-13.18**	**-15.92**	**-2.06**	**-19.24**
Tax payable/credit	0.00	2.78	2.82	1.36	1.47	1.56
Underlying net income	**-5.06**	**-3.65**	**-8.46**	**-12.56**	**1.81**	**-15.07**
Discontinued operations	0.00	-0.71	0.02	0.00	0.00	0.00
Forex	0.00	0.29	1.61	0.50	0.00	0.00
Statutory net income	**-7.56**	**-6.27**	**-8.74**	**-14.06**	**-0.59**	**-17.67**
Ordinary 25p shares:						
Period-end (m)	41.1	56.7	72.5	80.9	174.9	185.4
Weighted average (m)	33.9	51.2	60.8	78.8	153.5	177.5
Fully-diluted (m)	48.1	67.4	74.4	118.3	168.6	187.1
Underlying basic EPS (p)	**-14.91**	**-7.13**	**-13.91**	**-15.94**	**1.18**	**-8.49**
Statutory basic EPS (p)	-22.29	-12.25	-14.37	-17.84	-0.38	-9.96
U/l fully-diluted EPS (p)	**-10.53**	**-5.41**	**-11.37**	**-10.62**	**1.07**	**-8.06**
Stat. fully-diluted EPS (p)	-15.73	-9.31	-11.75	-11.89	-0.35	-9.45
DPS (p)	0.00	0.00	0.00	0.00	0.00	0.00

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Net debt:** Our forecasts are based on the assumption that AVO ended 2017 with very little cash, and debt of -£10.7m.
- **Short-term debt:** The reduction in short-term debt in 2018 is the result of the conversion of the 'Segulah' and Blackfinch loan into shares in February 2018 and during fiscal 2018, respectively.
- **Long-term debt:** The increase in 2018 is based on the assumption that AVO concludes negotiations for the £24m Metric Capital loan in the next few months.
- **Intangible assets:** Forecasts assume that there will be a further ca.£22.0m R&D investment in LIGHT, spread over three years, and capitalised.
- **Inventories:** Purchase of the various modules that comprise LIGHT from its manufacturing partners results in a build-up of 'inventory'.
- **Trade creditors:** In order to preserve cash, and in the knowledge that funding was in the final stages of completion, we have assumed that AVO had a build-up of trade creditors at the end of 2017, which will be paid in 2018.
- **Warrants:** Consistent with the assumptions detailed in the table on page 23, AVO's balance sheet will benefit from the exercise of warrants, raising ca.£6.4m and £3.0m in fiscal years 2018 and 2019, respectively.

Balance sheet

@31st Dec (£m)	2014	2015	2016	2017E	2018E	2019E
Shareholders' funds	11.13	27.28	33.99	25.73	51.29	41.62
Cumulated goodwill	0.00	0.00	0.00	0.00	0.00	0.00
Total equity	11.13	27.28	33.99	25.73	51.29	41.62
Share capital	10.28	14.18	18.12	20.23	43.73	46.35
Reserves	0.85	13.10	15.88	5.50	7.57	-4.73
Provisions/liabilities	0.00	0.00	0.00	0.00	0.00	0.00
Long-term loans	0.00	0.00	0.00	0.00	24.00	24.00
Short-term debt	0.99	1.00	0.54	10.70	0.00	0.00
less: Cash	1.47	8.96	1.45	0.20	26.80	5.27
Invested capital	**10.65**	**19.32**	**33.09**	**36.23**	**48.50**	**60.35**
Fixed assets	0.88	1.00	1.46	1.35	1.21	1.03
Intangible assets	9.22	12.74	23.36	30.15	37.50	45.32
Investments	1.20	0.31	0.31	0.31	0.31	0.31
JV investment	0.00	0.00	0.00	0.00	0.00	0.50
Inventories	1.11	4.42	7.44	11.00	16.51	24.76
Trade debtors	*0.07*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
Other debtors	*0.52*	*0.52*	*0.51*	*0.50*	*0.50*	*0.50*
Tax liability/credit	*-0.22*	*2.78*	*3.15*	*1.36*	*1.47*	*1.56*
Trade creditors	*-1.14*	*-0.34*	*-1.58*	*-4.40*	*-0.70*	*-0.70*
Other creditors	*-0.98*	*-2.12*	*-1.56*	*-4.05*	*-8.30*	*-12.94*
Debtors less creditors	-1.75	0.85	0.52	-6.59	-7.03	-11.57
Invested capital	**10.65**	**19.32**	**33.09**	**36.23**	**48.50**	**60.35**
Net cash/(debt)	**0.48**	**7.96**	**0.91**	**-10.50**	**2.80**	**-18.73**

Source: Hardman & Co Life Sciences Research

Cashflow

- **Distribution up-front:** £16.5m included in 'other income' in the P&L account in 2018, which drops through to the cashflow statement via the underlying EBIT, assuming that Chinese government approval is forthcoming.
- **Working capital:** The key feature is the forecast build-up of trade creditors at the end of 2017, which will probably be paid following completion of the capital increase (22nd February).
- **Interest payable:** The cash element of the interest charge is not the same as the interest charge shown in the P&L account, because it excludes the PIK element being accrued and payable on reversion/conversion.
- **Capitalised R&D:** Further investment in LIGHT R&D of ca.£22.0m, spread over three years, is forecast. This will be amortised when the first LIGHT system is installed in Harley Street.
- **Harley Street:** AVO remains on course for the first LIGHT system to be delivered and installed in Harley Street in 2019, but forecasts assume that it will not be fully validated and operational until 2020.
- **Capital increase:** Based on forecasts for cashflow, we have included a 'top-up' capital increase (est. £5m at 100p per share) in late fiscal 2019, at a point in time when the first LIGHT system will be mostly de-risked.

Cashflow

Year-end Dec (£m)	2014	2015	2016	2017E	2018E	2019E
Underlying EBIT	-5.18	-6.59	-11.18	-12.50	3.10	-13.60
Depreciation	0.12	0.18	0.35	0.36	0.42	0.48
Amortisation	0.00	0.00	0.00	0.00	0.00	0.00
Inventories	*-1.07*	*-3.11*	*-3.02*	*-3.57*	*-5.50*	*-8.25*
Receivables	*0.60*	*0.04*	*0.01*	*0.00*	*0.00*	*0.00*
Payables	*0.31*	*0.14*	*0.68*	*2.82*	*-3.70*	*0.00*
Change in working capital	-0.16	-2.92	-2.33	-0.74	-9.20	-8.25
Exceptionals/provisions	-0.80	0.00	0.00	0.00	0.00	0.00
Other	-0.20	-0.28	0.02	0.00	0.00	0.00
Net cash from ops.	**-6.22**	**-9.62**	**-13.14**	**-12.88**	**-5.69**	**-21.37**
Net interest	-0.18	-0.15	-0.25	-0.42	-0.91	-1.00
Tax paid/received	0.00	0.00	2.45	3.15	1.36	1.47
Operational cashflow	**-6.40**	**-9.77**	**-10.93**	**-10.16**	**-5.24**	**-20.91**
Capital expenditure	-0.33	-0.76	-0.77	-0.25	-0.27	-0.30
Capitalised intangibles	-0.98	-3.53	-8.91	-6.80	-7.35	-7.82
Free cashflow	**-7.71**	**-14.05**	**-20.61**	**-17.20**	**-12.86**	**-29.02**
Disposals	6.02	0.56	0.00	0.00	0.00	0.00
Cashflow after invests.	**-1.69**	**-13.49**	**-20.59**	**-17.20**	**-12.86**	**-29.52**
Share issues	10.16	21.06	13.54	5.80	26.15	8.00
Currency effect	0.00	0.00	0.00	0.00	0.00	0.00
Cash/(loans) acquired	1.23	-0.09	0.00	0.00	0.00	0.00
Change in net debt	**9.69**	**7.48**	**-7.05**	**-11.40**	**13.30**	**-21.52**
Hardman FCF/share (p)	-18.86	-19.09	-17.98	-12.88	-3.41	-11.78
Opening net cash	-3.04	0.48	7.96	0.91	-10.50	2.80
Closing net cash	**0.48**	**7.96**	**0.91**	**-10.50**	**2.80**	**-18.73**

Source: Hardman & Co Life Sciences Research

Company matters

Registration

Incorporated in the UK with company registration number: 05564418

Registered office:

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London
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www.advancedoncotherapy.com

Board of Directors

Board of Directors

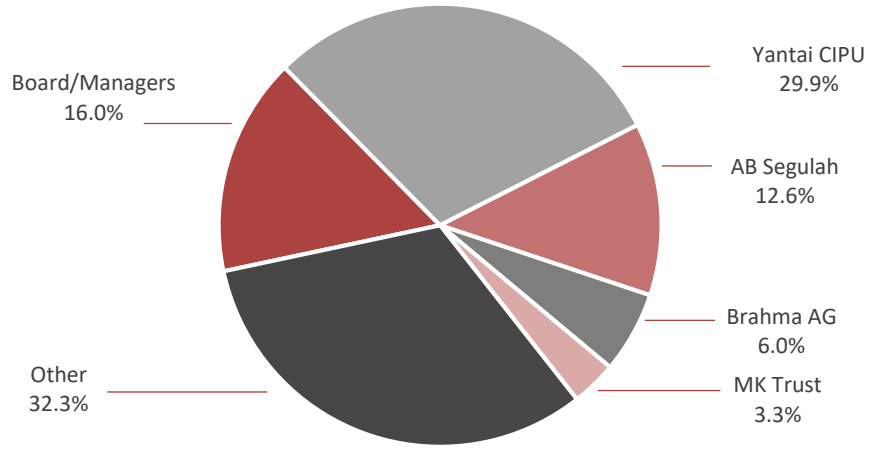
Position	Name	Remuneration	Audit
Executive Chairman	Dr Michael Sinclair		
Chief Executive Officer	Nicolas Serandour		
EVP Global Business Devt.	Dr Sanjeev Pandya		
Non-executive Director	Michael Bradfield	M	M
Non-executive Director	Hans von Celsing	C	C
Non-executive Director	Prof. Steve Myers		
Non-executive Director	Prof. Chris Nutting		
Non-executive Director	Dr Nick Plowman		
Non-executive Director	Dr Euan Thomson		
Non-executive Director	Dr Enrico Vanni	M	M

C = Chairman; M = member
Source: Company reports

Share capital

AVO has 150,501,673 Ordinary shares in issue. There are currently 9.60m options, and 29.6m warrants outstanding.

Key shareholders



Source: Company reports, Hardman & Co Life Sciences Research

Glossary

ADAM	Established on 20th December 2007, ADAM SA was founded to promote scientific know-how and innovations in medical technology for cancer therapy. ADAM research activity is focused mainly on the construction and testing of linear accelerators (LINACs) for medical purposes.
CERN	Conseil Européen pour la Recherche Nucléaire, or European Council for Nuclear Research. Established in 1954 and based near Geneva, it is a European research organisation that operates the largest particle physics laboratory in the world. CERN's main function is to provide the particle accelerators and other infrastructure needed for high-energy physics research.
Cyclotron	One of earliest particle accelerators, in which particles are accelerated in a circular spiral fashion (from the centre to the outer edge of the structure) using a magnetic field at a constant radiofrequency (RF). Cyclotrons were replaced by synchrotrons. Variants of the cyclotron include the Synchrocyclotron, in which RF frequency is varied and the Isochronous cyclotron, in which the magnetic field increases with radius.
Gantry	A rotating steel structure that moves around the patient to guide the proton beam from the beam transport line to the beam delivery nozzle, thereby treating the tumour from different angles. In most cases, gantries are 30m in diameter and can weigh up to 630 tons.
LINAC	Linear particle accelerator, in which particles are accelerated in a straight line with a target of interest at one end. They are often used to provide an initial low-energy start to particles before they are injected into circular accelerators. Medical grade LINACs accelerate electrons using a klystron and a complex bending magnet arrangement which produces a beam of 6-30 MeV of energy.
MeV	Mega electron volts. An electron volt is a unit of energy. For clinical applications particles are accelerated to between 70 and 250 MeV (protons) and up to 400 MeV in the case of carbon ions.
Photon	An energy packet of electromagnetic radiation – the elementary particle of photon radiation therapy (RT). X-rays and gamma rays are photon radiation.
Proton	A positively charged particle of an atom. The charge and relatively large mass (1,800 times that of an electron) of protons account for the Bragg Peak effect.
Synchrocyclotron	Particle accelerators in which the frequency of the RF field is varied unlike the cyclotron, where the frequency is constant and in which a super-conducting magnetic field enables the construction of a more compact system than the cyclotron or synchrotron.
Synchrotron	Particle accelerator, descended from the cyclotron, in which particles are bent into a closed orbit, using a magnetic field, which is synchronised to a particle beam of increasing kinetic energy, thereby keeping the orbit radius constant (unlike a cyclotron).
Voxel	Basic unit of computed tomography reconstruction – used in 3D modelling – smallest distinguishable box-shaped part of a 3D space, represented as a pixel in a CT image display.

Abbreviations

ASTRO	American Society for Therapeutic Radiation Oncology
CCL	Coupled Cavity Linac
DDS	Dose Delivery System
IBA	Ion Beam Application
LIBO	Linac Booster
LIGHT	Linac Image-Guided Hadron Technology
Linac	Linear Accelerator
MENA	Middle-east North Africa
NCCN	National Comprehensive Cancer Network
NIH	National Institutes of Health
NHS	National Health Service
PPS	Patient Positioning System
PT	Proton Therapy
RFQ	Radio Frequency Quadruple
SCDTL	Side Coupled Drift Tube Linac

Notes

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The fact that we are commissioned to write the research is disclosed in the disclaimer, and the research is widely available.

The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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