

## Healthcare Equipment &amp; Services



Source: Eikon Thomson Reuters

## Market data

EPIC/TKR	AVO
Price (p)	43.0
12m High (p)	209.0
12m Low (p)	44.0
Shares (m)	72.7
Mkt Cap (£m)	31.3
EV (£m)	21.8
Free Float*	58%
Market	AIM

\*As defined by AIM Rule 26

## Description

Developing next generation proton therapy systems for use in radiation therapy of cancers. The first system is expected to be installed in Harley Street, London during 2019; to be operated through a joint venture company with CircleHealth. Machine able to treat superficial tumour by 3Q 2018 and first patient treated expected in end of 2Q 2020.

## Company information

Exec. Chairman Michael Sinclair  
CEO Nicolas Serandour

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[www.advancedoncotherapy.com](http://www.advancedoncotherapy.com)

## Key shareholders

Board & Management	21.2%
Brahma AG	15.0%
MK Trust	6.7%
Banca Profilio	5.2%
AB Segulah	4.6%
Aviva Investors	4.4%

## Diary

31 <sup>st</sup> March	General Meeting
May-17	Finals
Jun-17	AGM

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## Advanced Oncotherapy

## Delivery of LIGHT

AVO is focused on delivering a more affordable, novel, proton-based radiotherapy system, based on technology originally developed at the world renowned CERN. The company is entering an exciting stage with construction work on its Harley Street site expected to commence this month following preliminary assessment work. Meanwhile, individual modules for the LIGHT system are being integrated and tested in Geneva. At the March 2017 investor presentations, AVO provided a revised timeline for completion of the London Proton Therapy Centre, first patient treatments, and an update on its commercial and financial strategies.

- **Strategy:** To develop a compact and modular proton therapy system at an affordable price for the payor, financially attractive to the operator, whilst generating superior patient outcomes. AVO benefits from the technology know-how developed by ADAM, Geneva and relies on a base of world-class suppliers.
- **Timeline:** A revised timeline has been provided showing a clear pathway for installation of the first LIGHT system at Harley Street. Excavation work will commence by April with construction expected to take 62-96 weeks, followed by fit-out.
- **Key milestone achieved:** Meanwhile, the technical aspect is progressing at ADAM with a key milestone announced at the Investor meeting on the 6<sup>th</sup> March 2017 – the proton beam has been successfully fired through the RFQ at 5MeV, which is the exact requirement of energy acceleration of this component.
- **Partnership:** The relationship with Thales is the key driver of success for full commercialisation of the LIGHT system. A facility for two production lines is being developed at Thonon, bringing a manufacturing capacity of eight machines per year when fully operational.
- **Commercial:** The Harley street project is independent of the commercial success of the LIGHT system, as it bears its own challenges. Independently of the timetable of the Harley Street site, AVO is in active discussions with multiple partners, potential customers and distributors across the world.
- **Risks:** Construction work in a listed area of London has some challenges. More validation work is needed on the LIGHT system, which is mitigated by the know-how of the ADAM team and the Thales partnership, and provides a strong base for commercialisation of the technology. The main risk is that of execution.
- **Investment summary:** Demand in Proton Therapy 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 already started. Attention is focused on the construction timetable for the flagship Harley Street site and installation of the first LIGHT system. Resolution of its financing requirement is an important milestone.

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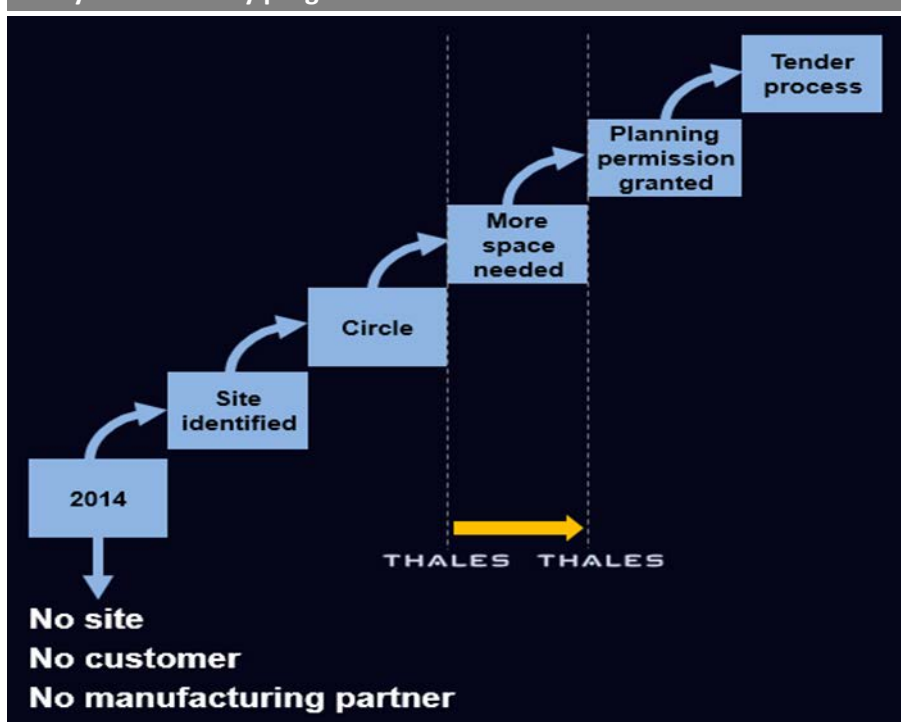
## Delivery of LIGHT

### Quick snapshot

#### Operational

- ▶ **Thales industrialisation agreement** – Good progress in the partnership with Thales, a global leader and well-established manufacturer of radio frequency energy equipment, to assemble and commission the LIGHT system
- ▶ **Production lines** – Engineering studies have been undertaken by Thales. Two production lines are being envisioned to provide the capacity to manufacture eight machines per year
- ▶ **Harley Street** – Planning Permission for the Harley street site has been granted and the contractor appointed. After concluding preliminary assessment and preparatory work, excavation work is scheduled to start at the end Q1' 2017
- ▶ **Edgbaston, Birmingham** – Discussions are ongoing surrounding an agreement to supply a LIGHT system alongside Circle Health's planned new-build hospital in Birmingham
- ▶ **LIGHT system** – The first proton beam has been fired through the Radio Frequency Quadrupole (RFQ) and accelerated to its initial energy target of 5MeV, which represents a key, and de-risking, technical milestone
- ▶ **Commercial** – The commercial priorities are the UK with the first LIGHT system to be installed at Harley Street site. Ongoing discussions are also progressing in continental Europe, the US, Asia/China and the Middle-East

#### Two years of steady progress



Source: Advanced Oncotherapy

Multiple partners working together

**Technical**

Over the last two years, AVO has made enormous technical progress. It has agreed partners who have each gone on to build and test their individual modules. These have been shipped to the ADAM site in Geneva, where key components are being validated, assembled and tested as a complete unit. Clearly, each module will not be run at full strength/capacity in the first instance, this will be built-up over time. Once all the modules have been tested, partly at Thales’ facilities (Velizy and/or Thonon, France), partly at Geneva (ADAM), they will be shipped to the UK and assembled at the Harley Street site when construction has been completed. The commercial production of the LIGHT system will then be done at the Thales manufacturing site in Thonon, France.

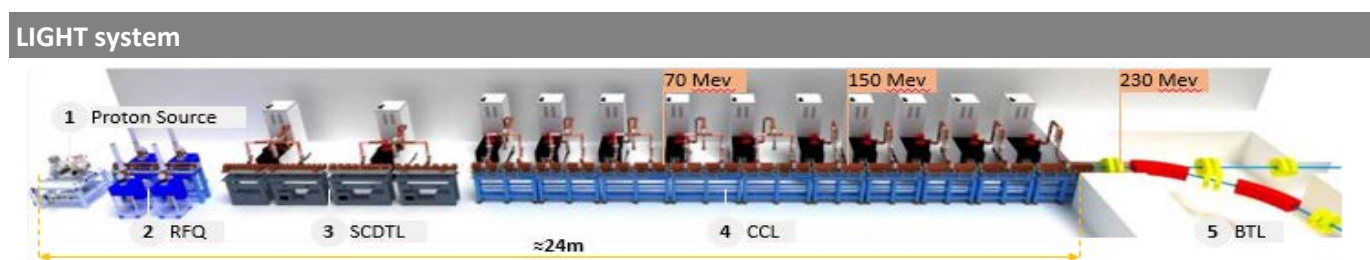
The advantageous properties of LIGHT proton therapy system over X ray systems were eloquently described by Professor Myers (Executive Chairman of Adam):

*“...a proton, being miniscule in size, can penetrate matter to a distance determined by its speed....and one with an energy of 230MeV (travelling at 0.6x speed of light) can penetrate water to a depth of 32cm...providing the potential to treat all radio-sensitive tumours...”*

With a number of key technical milestones...

- ▶ The proton source, manufactured by Pantechnik at its facility in Bayeux (France), generates protons from a source of hydrogen gas
- ▶ The Radio Frequency Quadruple (RFQ) which accelerates the protons from zero to 5MeV has been integrated with the proton source
- ▶ The first proton beam has been fired successfully through the Radio Frequency Quadrupole (RFQ) and accelerated to achieve its crucial energy target of 5MeV
- ▶ The Side Coupled Drift Tube Linac (SCDTL) module has been tested at low power levels and is now ready for high power testing, which will accelerate the protons from 5MeV to 20-25MeV. Each of the four modules is different so that it matches the increasing velocity of the proton

...notably the achievement of the important 5MeV energy level



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

**Financial**

- ▶ **Subscription & Open offer** – Raised £13.4m of gross new capital in 4Q 2016, and attracted a new major shareholder, MK Trust, who has also become a senior advisor and will be active in business development in Asia
- ▶ **Bracknor** – Tranching financing agreement of up to £26m with this Dubai-based investment group. AVO will issue convertible loan notes, in tranches of £1.3m each, with a minimum of £13m and maximum of £26m over the next two years, giving AVO more flexibility in its discussions surrounding other future financing opportunities
- ▶ **Non-dilutive financing opportunities**– Management is also progressing the ‘non-dilutive’ financing package which was part of the re-negotiation of the Metric Capital loan facility. AVO has announced that discussions commenced in September 2016 with a potential strategic partner, and these are continuing, with the scope expanded

## Development of Harley Street site

141-143 Harley Street



Source: Advanced Oncotherapy

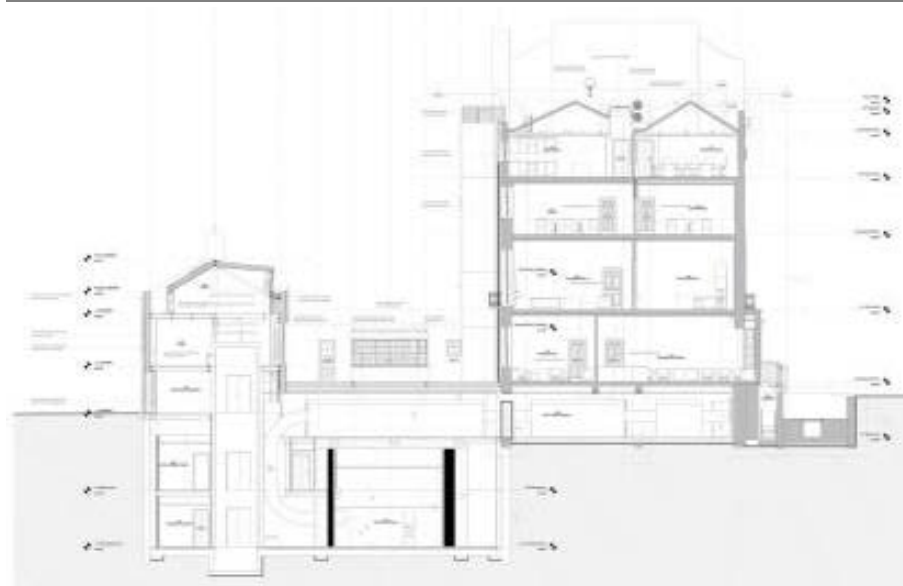
*Considerable achievements to date  
in a challenging setting*

The idea of having a proton therapy facility, usually synonymous with big cyclotron machines and heavy bunkers, in an upmarket and trendy street of Central London, is probably something that specialists in the art would not think realistic. But this is precisely what Advanced Oncotherapy is aiming to achieve with its flexible, smaller, and more cost effective proton therapy LIGHT system.

### Achievements to date

- ▶ **April 2014:** Commencement of discussions with Howard de Walden Estates about finding a suitable site to house LIGHT within the prestigious Harley St. area
- ▶ **28 January 2015:** AVO signed 50 year lease for the whole of 141 Harley Street and part of 143 Harley Street, which together represented about 8,000 sq ft of space for conversion into a proton therapy centre
- ▶ **28 July 2015:** Agreement to expand the original 8,000 sq ft floor space to approximately 15,000 sq ft in order to allow an additional treatment room and improved imaging facilities. While reconfiguration of the site required a revision of the plans, delaying the application for Planning Permission, and impacting the construction timeframe, the improved capacity and facilities would be in the best long-term interests of the company and the operator of the clinical facility
- ▶ **12 October 2015:** Joint venture operator agreement for the completed proton centre with CircleHealth
- ▶ **19 October 2016:** Key milestone with Planning Permission being granted by Westminster City Council
- ▶ **January 2017:** Following a tender process and the appointment of a principal contractor by Howard de Walden Estates, Deconstruct (UK) Ltd carried out preliminary assessment works
- ▶ **End March 2017:** Commencement of excavation work

### Plans for 141-143 Harley Street project



Source: Advanced Oncotherapy

## Future work

- ▶ **Construction:** Work is expected to take about 18 months (62-96 weeks, with demolition, excavation, rebuild, radiation shielding); subsequent fit-out work is expected to take place afterwards
- ▶ **First patient treatment:** Now expected at the end of 2Q 2020

### Computer-generated image of the Harley Street project



Source: Advanced Oncotherapy

*Construction costs of £7-10m...*

*...will be borne by Howard de Walden Estates*

*Patients likely to come from around the world*

*A better defined and more precise project timeline*

### *Howard de Walden Estates*

Howard de Walden Estates is responsible for the full re-development of the site into a Proton Therapy Centre that can house the first LIGHT machine to be constructed in the world that will support two treatment rooms and state-of-the-art imaging facilities, over which AVO will have a 50 year lease. Altering the original plan and extending the surface area at ground level increase the capacity from one to two treatment rooms and highlight the flexibility of the LIGHT system. The total cost of the development is being borne by Howard de Walden, and is estimated at £7-10m.

### *The operator: CircleHealth*

The new centre will be known as the London Proton Therapy Centre (LPTC) and will be run as a 49.9% : 50.1% joint venture between AVO and Circle Holdings. AVO will be responsible for all technical matters, whilst Circle will take responsibility for all operational and clinical matters related to LPTC, and provision of insurance. Circle expects to start operating this new 15,000 square foot facility from 3Q 2020. When fully operational, LPTC will have the capacity to treat approximately 500 patients per annum. LPTC will be looking to offer its services to UK hospitals, including the NHS, that want access to this first class facility. However, patients are likely to come from across the globe.

### *Project timeline*

At investor presentations on March 6<sup>th</sup> (London) and 7<sup>th</sup> (Zurich), AVO provided a revised timeline for completing the Harley Street project and validating the LIGHT system. From the first beam testing through the RFQ to first patient treatment, the project is now expected to take just over three years. Updates are expected from AVO on the achievement of significant milestones against this improved timetable.



## Thales partnership

*Thales adds considerable credibility to AVO's execution capabilities both short- and long-term*

*AVO will fund initial Thales costs and then recover them when LIGHT goes into full commercialisation*

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

*...and to identify opportunities to reduce costs*

### Planning for commercial scale-up

In order to gear up and enter into the commercialisation stage of the LIGHT system, AVO secured a manufacturing agreement with Thales, one of the leading global players in the manufacture and supply of RF energy equipment, including Klystrons, electron tubes, amplifiers and X-ray detectors, as well as synchrotrons, accelerators and advanced medical imaging equipment. As such, Thales offers AVO access to its specialised execution and engineering skills to manage the transition from a prototype machine to full production manufacturing, as well as evaluating cost reduction initiatives. In addition, the partnership provides Advanced Oncotherapy with a reach and ability to maintain and service equipment.

### Customised production line

Thales is currently performing engineering studies and testing the facilities commissioning required for construction of a custom-designed series production line. The anticipated cost of this manpower and engineering process will be borne initially by AVO. When the machine enters full production, AVO will recover these costs through the retention of 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 around 40%.

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. Whilst AVO is already expecting to provide a system at a fraction of the cost of first generation proton therapy machines (cyclotrons), the cost reduction skills of Thales and its ability to reduce lead times through process optimisation will ensure that this next generation proton therapy system is affordable and, therefore, more widely and quickly available for cancer patients around the world.

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 first machine to series production of LIGHT, putting the concept on the cusp of a steepening adoption curve with tremendous growth potential.

### Manufacturing site

The dedicated LIGHT manufacturing site will be based at Thonon, France, near Geneva and is expected to be fully operational in 12-18 months. The site will receive components in 1Q 2018 and be fully installed and testing at 230MeV by 1Q 2019. The site will occupy a surface of 2,400m<sup>2</sup> and will be composed of two production lines, bringing a manufacturing capacity of eight machines per year when fully operational.

- ▶ Effective floor area of 2,400m<sup>2</sup> – approximately 45m x 62m
- ▶ Two production lines
- ▶ Development area for the treatment room
- ▶ Lead time of 12-18 months

Thales Thonon site



Source: Thales/Advanced Oncotherapy

Plans for Thales Thonon site



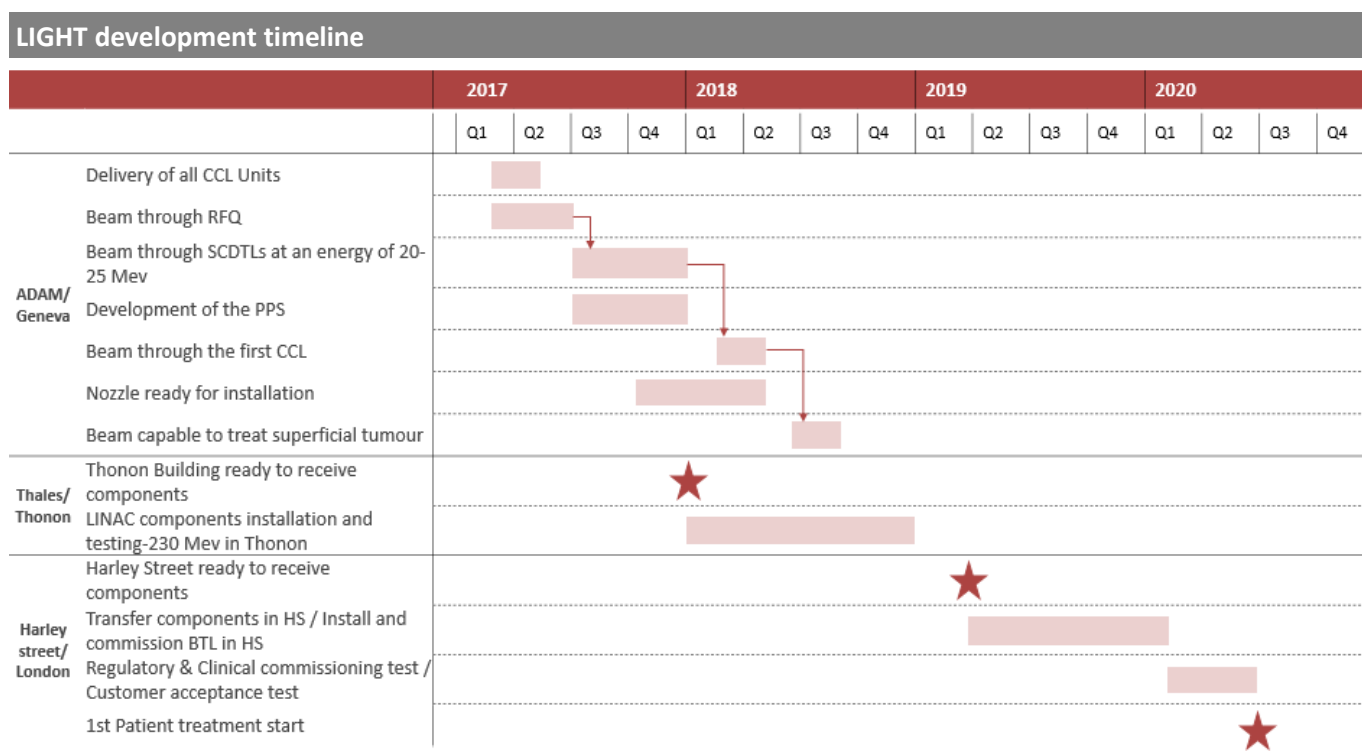
Source: Advanced Oncotherapy



## Key milestones

Over the next two years, AVO will be reporting on a number of key technology milestones, which will validate the LIGHT system, for example the successful integration of the modules in the testing facilities at Geneva and Thonon. The first proton beam fired successfully through the Radio Frequency Quadrupole (RFQ) and accelerated to achieve its crucial energy target of 5MeV, is another breakthrough milestone. The ability of the company to meet these objectives could be considered as an indication of the increased commercial interest and an indication of the likely future sales ramp-up.

Technology milestones and successes in the development of the LIGHT system are completely independent of the unique challenges that are being faced with the construction of Harley Street site, which is out of AVO's hands.



Source: Adapted from Advanced Oncotherapy by Hardman & Co Life Sciences Research

## Commercialisation & financing

### Commercial strategy

*Small, flexible, affordable and close to patient proton therapy system, resulting in better clinical outcomes*

Medical advisors to AVO and clinicians are acutely aware that the best approach is to treat patients as close to where they live as possible. Consequently, the aim has been to produce a flexible and affordable system that can be deployed in several specialist centres that addresses the needs of the patient, the operator, and the payor, ultimately resulting in better clinical outcomes. The LIGHT system satisfies these requirements and, additionally, is expected to be at a price which allows several centres to be established in each country.

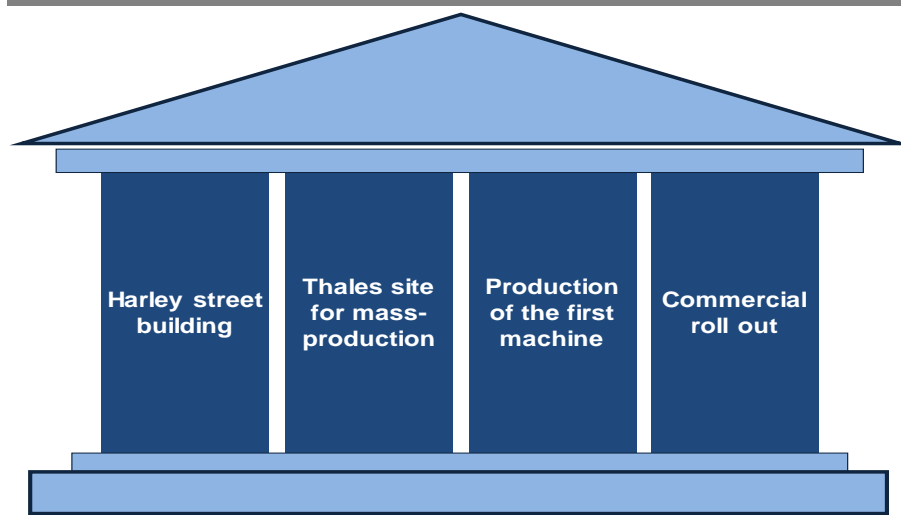
*The London Proton Therapy Centre at Harley Street is a key component of the commercialisation strategy*

It is also worth highlighting that the LIGHT system represents the new generation of proton therapy that would allow greater clinical effectiveness based on technological advances coming directly from the Conseil Européen Pour la Recherche Nucléaire (CERN) that brought the World Wide Web and the world's largest and more powerful particle collider beneath the France-Switzerland border near Geneva: the Large Hadron Collider (LHC). Its flexibility allows the LIGHT system to be installed in existing hospitals and clinics, as exemplified by the Harley Street site.

### Harley Street showcase

The intention of AVO has always been to have the first LIGHT system up and running in an important medical centre in the UK, and the focus on Harley Street will achieve this goal. The LPTC will be a showcase both for the system and the experience for clinicians and patients. Already the provenance, flexibility, modularity and cost of LIGHT is attracting attention.

#### Roadmap for commercialisation



*Four pillars of success*

*Source: Advanced Oncotherapy*

### Current status

*Generating worldwide interest*

Independently of the timetable of the Harley Street project, AVO is in active discussion with multiple partners, potential customers and distributors.

- ▶ **UK:** Two sites being established in London (Harley Street) and Birmingham
- ▶ **US:** Ongoing discussion with three centres:
  - **Syracuse** – Initially one-room system with potential for expansion to two treatment rooms
  - **Unnamed** – Two-treatment room systems

- ▶ **Spain:** One project
- ▶ **Italy:** One new project
- ▶ **Asia/China:** The Sinophi agreement has been terminated. Full distribution rights in China and South East Asia have returned to AVO, and discussions with potential customers (hospitals/clinics) and distributors have already started
- ▶ **Middle-East:** Big potential

## Financing LIGHT

### *Subscription and Open offer*

During 4Q 2016, AVO raised gross funds of £13.4m via a Subscription and Open Offer of new Ordinary shares at 100p per share, with the Management team and directors taking a significant part of the Subscription. The Subscription also attracted a new major shareholder, MK Trust, with (currently) 6.7% of the enlarged share capital.

*MK trust is a key shareholder and advisor of the vibrant Asian market*

MK Trust is a financial institution that is focused on Asian-related investments. It is owned by Ms Miky Kambara, who has become an advisor to AVO responsible for developing business opportunities for LIGHT in Asia. This decision is in line with AVO's strategy to expand in the Asian markets, particularly China, and has become more important since the termination of the distributor agreement with Sinophi.

*Tranched financing arrangement to raise up to £26m ...*

### *Bracknor financing arrangement*

In February, AVO entered into a financing arrangement with Bracknor, a Dubai-based investment company, to raise up to £26m of unsecured convertible notes issued in 20 tranches over two years. A minimum of ten tranches of £1.3m of convertible loan will be drawn down with a possible ten additional tranches at AVO's discretion, over the two year period, enabling to limit dilution compared with full immediate drawdown. The agreement can be summarised as follows:

*... With high flexibility allowing the company to pursue alternative financing opportunities*

- ▶ Each tranche to be converted into new Ordinary Shares
- ▶ Upon issuance of a tranche, Bracknor will receive warrants to purchase shares with an aggregate value equivalent to 20% of the nominal value of each tranche. Warrants will be exercisable at 130% of the volume weighted average price (VWAP)
- ▶ Bracknor is prevented from acquiring more than 29.9% of the company
- ▶ AVO controls the timing and total number of tranches
- ▶ AVO has the option to raise an additional £26m on the same terms
- ▶ Possibility to redeem tranches for cash
- ▶ Commitment (3%), conversion (3%) and legal (maximum: £40,000) fees to be paid to Bracknor
- ▶ AVO receiving 95% par value per tranche

*Active discussion with an additional non-dilutive financing arrangement*

### *Non-dilutive financing*

Management is also progressing the 'non-dilutive' financing deal which was part of the re-negotiation of the Metric Capital loan facility. AVO announced that discussions commenced in September 2016 with a potential strategic partner. These are continuing, and the scope has been expanded. Once this is concluded, AVO will then be able to drawdown the Metric Capital loan should it choose to do so.

## Glossary

CCL (Couple Cavity Linac)	The CCL accelerating structures are an essential part of the LIGHT proton therapy system. They consist of a series of cells which accelerate the protons from energies of 37.5 Mega-electron Volts ("MeV") to 230 MeV (energies required to treat radiosensitive tumours in a clinical setting).
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
HF-RFQ	High Frequency Radio Frequency Quadrupole is a linear accelerator which focuses, bunches and accelerates a continuous beam of charged particles with high efficiency whilst preserving the emittance up to 5 MeV. It is the only accelerator unit that can accept a low energy continuous beam of particles.
Klystron	A high-power pulsed RF amplifier, in a linear beam vacuum tube, used to generate and drive the power for particle accelerators. This can be bought off the shelf from Toshiba.
LIGHT	Linac Image-Guided Hadron Technology
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.
LPTC	London Proton Therapy Centre
MeV	1 million 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.
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.
Proton Source	A commercial device composed of several elements. It can produce any ion coming from hydrogen gas source. System will end with Einzel lens and a water-cooled collimator to fix the maximum beam intensity entering the system.
RFQ (Radio Frequency Quadruple)	First part of the LIGHT system that accelerates protons up to 5MeV. The 750MHz RFQ is currently being built at CERN for ADAM. It is 2 meters long and composed of 4 parts.
SCDTL (Side Couple Drift Tube Linac)	There are 4 SCDTL modules, each with its own power unit. These accelerate protons from 5 MeV to 37.5 MeV.

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