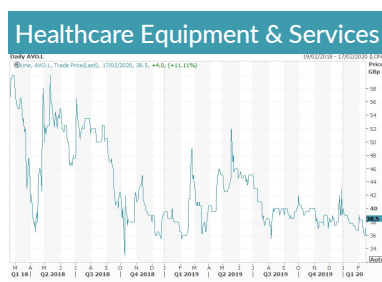


17 February 2020



Source: Refinitiv

### Market data

EPIC/TKR	AVO
Price (p)	36.0
12m High (p)	52.0
12m Low (p)	32.5
Shares (m)	237.6
Mkt Cap (£m)	87.8
EV (£m)	101.7
Free Float*	72%
Market	AIM

\*As defined by AIM Rule 26

### Description

AVO is developing next-generation proton therapy systems for use in cancer radiotherapy. The first system is expected to undergo CE marking during 2020. Standard radiation procedures have evolved over many years. PBT delivers radiation via a beam of proton particles rather than a beam of photons used in conventional radiotherapy (X-rays).

### Company information

Exec. Chairman Michael Sinclair  
 CEO Nicolas Serandour  
 +44 203 617 8728  
[www.avopl.com](http://www.avopl.com)

### Shareholders

Liquid Harmony (Board)	18.5%
Other Board	9.6%
P. Glatz	6.4%
DNCA Investments	4.9%
Lombard Odier	4.1%
Brahma AG	3.2%
Barrymore Inv.	3.2%

### Diary

May'20	Final results
July'20	AGM

### Analysts

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## ADVANCED ONCOTHERAPY

### Confidence in LIGHT gaining momentum

AVO's goal is to deliver an affordable and novel proton beam therapy (PBT) system, based on state-of-the-art technology developed originally at the world-renowned CERN. In the past 18 months, the project has been de-risked through important technical milestones. AVO is working on the verification and validation phase, prior to CE marking and LIGHT being used on the first patients. The company has made two important commercial announcements regarding the installation of LIGHT systems, which highlights the increasing confidence that is building in AVO's ability to deliver LIGHT in the near future.

- **Strategy:** AVO is developing a compact and modular PBT system, which is affordable for the payor, financially attractive to the operator, and generating superior patient outcomes. AVO benefits from technology know-how developed by ADAM (CERN spin-off) and relies on a world-class supplier base.
- **Harley Street:** Last week, AVO announced a new partnership with The London Clinic (TLC), which will run the day-to-day operational activities for the LIGHT machine at its Harley Street site. Although financial terms were not disclosed, it will have a profit share arrangement that highlights AVO's innovative business and financing strategy.
- **Mediterranean Hospital of Cyprus:** Today, AVO has also announced a purchase order, valued at €50m/£41.7m, for the installation of a LIGHT accelerator system, which will support three treatment rooms. AVO will also receive a share of the profit generated from this PBT service.
- **Risks:** Since 2018, the more complex technical challenges have been overcome, and progress towards a fully functional accelerator is under way in readiness for CE marking. Focus is now moving towards commercial execution and management's ability to have its innovative financing strategy adopted.
- **Investment summary:** AVO's market capitalisation of £88m equates only to the amount invested into LIGHT to date, which does not reflect either the enormous technical challenges that have been overcome, or the market potential. DCF analysis of LIGHT's prospects gives an NPV of at least 229p a share (fully-diluted). The disconnect between fundamental and market valuations offers an interesting investment opportunity at a time when commercial execution is showing through.

### Financial summary and valuation

Year-end Dec (£m)	2017	2018	2019E	2020E	2021E	2022E
Sales	0.0	0.0	0.0			
Gross profit	0.0	-1.9	0.0			
Administration costs	-12.9	-15.7	-15.0			
EBITDA	-14.1	-21.4	-18.9			
Underlying EBIT	-14.5	-21.8	-20.6			
Statutory EBIT	-14.5	-21.8	-20.6			
Underlying PTP	-16.5	-21.9	-21.7			
Statutory PTP	-16.5	-21.9	-21.7			
Underlying EPS (p)	-17.6	-14.0	-8.9			
Statutory EPS (p)	-18.9	-13.4	-8.9			
Net (debt)/cash	-9.2	-2.0	-13.9			
EV/EBITDA	-	-	-			

Source: Hardman &amp; Co Life Sciences Research

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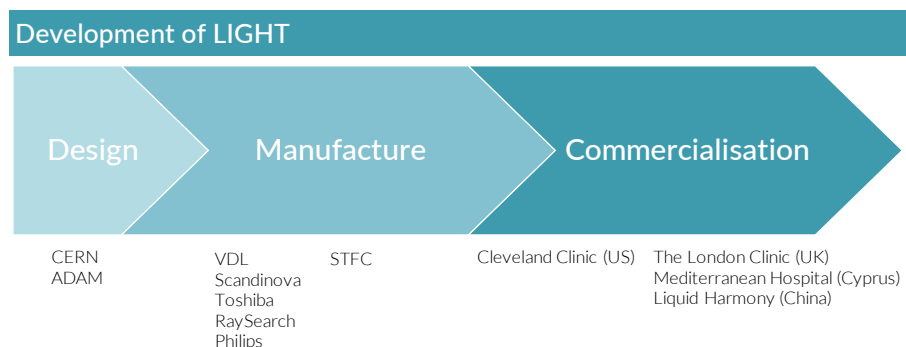
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## Commercial progress

Until now, with respect to AVO, most of the focus has been on the technical aspects, the manufacturing, and the validation of LIGHT, a next generation PBT system, aimed at satisfying strong demand for a compact and affordable machine that delivers highly targeted radiotherapy to generate superior patient outcomes. As the company approaches the final stages of this project, attention is turning to the commercialisation of LIGHT. Today's announcement, taken together with the announcement last week of the collaboration with The London Clinic (TLC), mark another important step in the transformation of the company.



Source: Hardman & Co Life Sciences Research

## Harley Street

AVO has announced a partnership with the prestigious TLC for all the operating activities at its first London-based PBT site at 141-143 Harley Street.

### Background

The challenging development of the Harley Street site moved on to its final stage in 3Q'19 when the freeholder, the Howard de Walden Estate, handed over the site to AVO following completion of all the structural work. Since then, AVO has commenced the fitting-out stage of the site in readiness for installation of its LIGHT accelerator.

Phase three, the fit-out, has started at the flagship Harley Street site

Development of 141-143 Harley Street		
Stage	Description	Status
#1	Excavation, piling, and wall and roof reconstruction	✓ Completed
#2	Landlord fitting, including lifts, air extractors, etc	✓ Completed
#3	Tenant design and fitting	In progress

Source: Hardman & Co Life Sciences Research

### Operations

In October 2015, AVO announced a joint venture (JV) agreement with CircleHealth to run the daily operational activities at the Harley Street site. Changes to both the business strategy of the Circle hospital group and to the development schedule for LIGHT, coupled with the passing of the long-stop date included in their JV agreement, has resulted in a natural evolution of this relationship, which has been superseded by the new partnership announced with TLC. Under this initial 10-year new agreement, AVO will supply the LIGHT proton accelerator and treatment room equipment and TLC will manage the clinical operation of the facility.

## Advanced Oncotherapy

PBT is a natural addition to TLC's core oncology activities

TLC is one of the UK's largest private hospital groups, dedicated to providing the best available, personalised healthcare through a breadth of surgical and medical expertise, at a number of sites in Harley Street and also in Devonshire Place. It has a particular strength in oncology, providing state-of-the-art radiotherapy and chemotherapy. Consequently, the provision of PBT is a natural extension of its core activities. Furthermore, the proton therapy centre adjoins the main site of TLC on Harley Street; this unique location provides the opportunity for both parties to extend the site and operate a second treatment room, which will have a clear impact on the revenue and profit of the centre.

Profit share arrangement...

TLC will be responsible for the sourcing and management of staff, governance and other services necessary for the everyday running of AVO's Harley Street facility. Although the financial terms of the partnership were undisclosed, both AVO and TLC will receive a share of the profits generated by the centre. While AVO's core business model remains that of manufacturing and selling LIGHT systems, management believes that it is important to have a vested interest in the operational success of its Harley Street facility because of: 1) the cachet of being associated with a PBT centre in one of the world's most pre-eminent medical addresses; 2) the necessity to align interests between the provider of the technology and the operator; and 3) the opportunity to generate more sustainable cash-flows in the long term.

...and kudos of Harley Street

## Cyprus

€50m/£41.7m order for LIGHT with three treatment rooms from Mediterranean Hospital...

In a separate statement, AVO announced that it is selling a LIGHT system to the Mediterranean Hospital of Cyprus for a consideration of €50m/£41.7m. In addition to this, the company will also be receiving a share of the profits generated by the new proton therapy facility, although the financial terms were not disclosed.

The Mediterranean Hospital of Cyprus, situated in Limassol, is one of the largest private hospitals in Cyprus. It is the first health centre integrated with the newly created National Health System (NHS) of Cyprus, the ambition of which is to modernise and upgrade the health sector into a more streamlined and cost effective system and bring Cyprus on par with its European peers in terms of efficient and affordable public healthcare. In 2018, the President of Cyprus commented that the Mediterranean Hospital would contribute to the greater goal of making Cyprus a regional hub for medical services, offering high-quality medical services to citizens of Cyprus but also to tourists seeking medical treatment.

...due to be installed and validated by the end of 2023

The installation is due to be completed before the end of 2023, to coincide with the completion of construction works being carried out at the hospital. The timings and the full execution of the partnership remain subject to other agreements, which are related to operational management.

## Cleveland clinic

These commercial arrangements follow on from the research collaboration announced in December 2019 with the Ohio-based Cleveland Clinic, which provides clinical and hospital care, and is a leader in research, education and health information. As part of the collaboration, both companies will work jointly to demonstrate the benefits of using minibeam, which is particularly relevant for delivering a more conformal treatment to patients. This is a key technical differentiating feature of LIGHT, which – together with the potential use of ultra-efficient hypofractionation (FLASH technology) at any energies – bodes well on the positioning of LIGHT and the ability of the company to capture significant market shares going forward.

Commercial execution is gathering momentum

## Conclusion

After several years focusing on the technological and manufacturing challenges of LIGHT, the focus is rapidly changing over to the commercial execution. These three partnerships represent a step-change for the company and provide an insight into how the company is building its business model.

# Commercial model

## Commercial momentum for LIGHT

Aiming to make PBT more affordable and more widely available

As indicated in our report dated 13 May 2019<sup>1</sup>, “*Commercialising a breakthrough technology*”, there is a significant unmet medical need. It is believed, conservatively, that at least 18% of the patients treated with radiotherapy could have benefited from PBT, whereas less than 1% are currently doing so. This implies the need for new treatment rooms is roughly 10 times what is available today. When considering the increasing incidence of cancer, the ageing of the population and the opportunity to treat patients at a price much closer to conventional radiotherapy, then more demand can be foreseen.

Meeting this unmet need is part of AVO’s mission to democratise PBT and make the treatment both more affordable and more widely available. We are, therefore, very encouraged to see that the company is reaping the rewards of its strategy.

## Flexible business model

Supply and maintenance contracts is a successful business model...

There are many examples of companies which have established a successful business model whereby most of the value is created through long-term maintenance contracts, as opposed to the sale of products, Schindler being a good example. This well-respected Swiss firm has been able to create an attractive, fast-growing and sustainable source of cashflows by installing and servicing the lifts that it produces. AVO is well-positioned to replicate this success.

...which, coupled with profit share, increases long-term cashflows

However, reliance on long-term maintenance contracts, while important, is not enough. This appears to have been anticipated by AVO’s management team, as evidenced by the company taking a share of customers’ profit, which inflates the long-term base of cashflows generated by AVO, further diversifying its revenue base.

AVO can capture this pool of profit in its offering if the company is able to reduce the upfront investment required by customers and act as project sponsor. This is precisely what has transpired from these recent announcements. Customers expect to provide staffing and other operational support on the clinical site with part of the profit being shared with AVO. This gives an additional long-term source of revenues and cash for the company in addition to the installation and maintenance fees.

## Overcoming pricing erosion

Pricing is reaching a plateau, so the optimisation of all the other project costs for setting up a PBT centre needs to occur

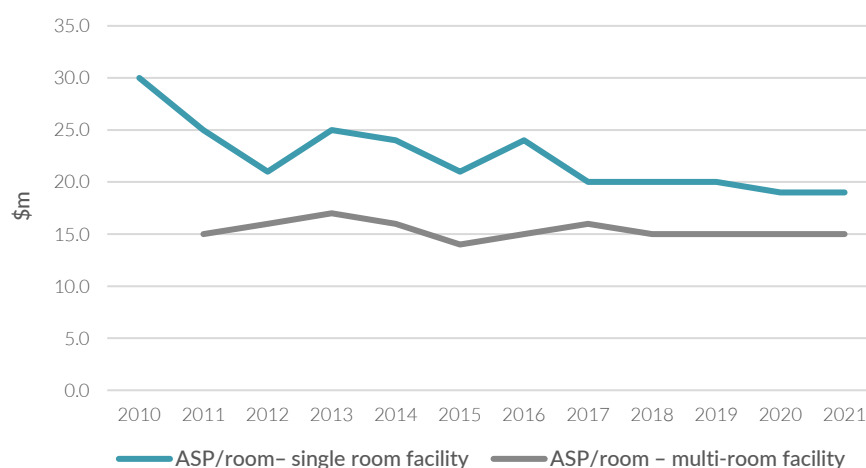
The PBT market is characterised by a lack of technical differentiation. All manufacturers on the market – with the exception of AVO – produce circular proton accelerators. Beyond the challenges of tackling technical and cost constraints associated with such accelerators, existing market players have adopted an aggressive pricing strategy, which has now reached its limits. As illustrated below, the selling price of proton therapy equipment is plateauing.

However, the price of the proton therapy equipment is only a fraction of the entire project cost for setting up and running a PBT centre. Other costs such as building and installation costs have a much greater impact on the hospital. Our previous reports have shown how the building costs of two projects can differ: the setting-up of a PBT facility at University College London Hospital (UCLH) compared with the PBT facility at Harley Street using LIGHT.

<sup>1</sup> <https://www.hardmanandco.com/research/corporate-research/commercialising-a-breakthrough-technology/>

The analysis shows that the building and installation costs are expected to be significantly lower when using LIGHT versus any other competing systems. As an illustration, the building work in Harley Street (LIGHT project) in the heart of London was carried out for £10m, whereas that for the UCLH project has been estimated at £190m.

**Average equipment price per room**



Source: MedRaysIntell

For this reason, it is essential to assess the viability of a business plan for a PBT centre by looking at the implied cost to treat patients. A focus on the treatment cost per patient allows to take into account all the project costs of setting up and running a proton therapy centre.

**AVO is adopting a business model that can exploit likely market trends**

Consequently, the business model being adopted by AVO has another important benefit. The overall medical equipment industry tends to see pricing erosion over time, with innovation not always being fully reflected in the price received. However, the commercial business model being pursued by AVO allows it to fully exploit the innovative features of LIGHT and the market trends. Our previous report<sup>2</sup>, "*FLASH benefits from new US reimbursement*" (dated 11 November 2019), highlighted the excitement in the clinical community around FLASH and the opportunity to treat patients in fewer than five fractions. We have commented also on the evolution of the reimbursement policy in the same report, which is evolving towards a payment per course as opposed to a payment per patient visit or fraction. Put simply, all of these market trends and release of new technical features are expected to result in a greater profit for the clinical centre, hence directly benefiting AVO thanks to the business model being pursued.

Of course, the company needs to implement the right financing plan to fund its growing pipeline, which can be done through working capital facilities. Management has indicated that it is in discussions with various financing providers, which will be another important piece of the jigsaw that the company is building.

<sup>2</sup> <https://www.hardmanandco.com/research/corporate-research/flash-benefits-from-new-us-reimbursement/>

## Forecast summary

Given the importance of these commercial announcements, the financial forecasts and valuation targets have been placed “under review”.



## Company matters

### Board of Directors

Board of Directors	
Name	Position
Dr Michael Sinclair	Executive Chairman
Nicolas Serandour	Chief Executive Officer
Prof. Steve Myers	Executive Director, ADAM executive Chairman
Michael Bradfield	Non-executive Director
Hans von Celsing	Non-executive Director
Chunlin Han	Non-executive Director
Dr Yuelong Huang	Non-executive Director
Dr Nick Plowman	Non-executive Director, Chairman Medical Advisory
Peter Sjostrand	Non-executive Director
Gabriel Urwitz	Non-executive Director
Dr Enrico Vanni	Non-executive Director
RenHua Zhang	Non-executive Director

Source: Company reports

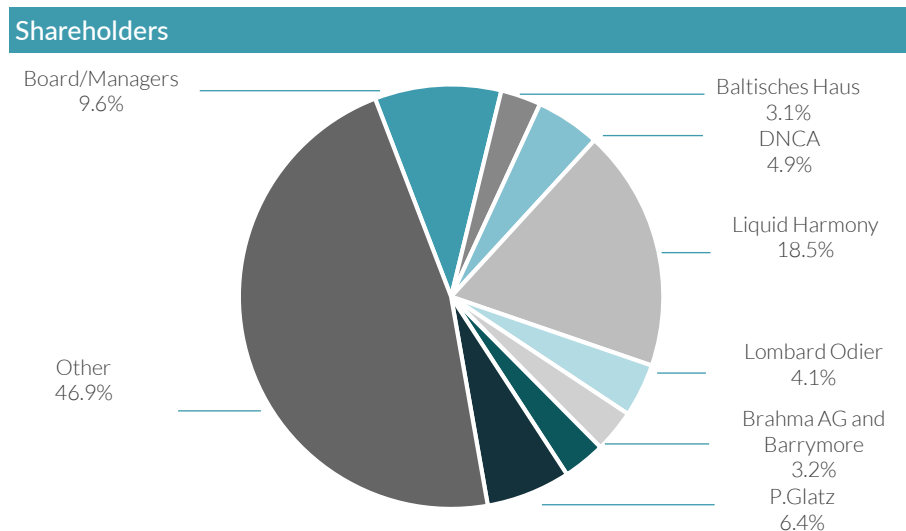
### Medical Advisory Board

Medical Advisory Board	
Name	Affiliation
Prof. Ugo Amaldi	Founder and President of the TERA Foundation
Dr Hanne Kooy	Associate Director of Medical Physics at Harvard Medical School
Dr Jay S Loeffler	Professor of Radiation Oncology at Harvard Medical School and Chair of Radiation Oncology at the Massachusetts General Hospital
Prof. Chris Nutting	Clinical oncologist & chair at The Royal Marsden and ICR London
Dr Margaret Spittle OBE	Clinical oncologist at University College Hospital London
Dr Euan Thomson	Operating partner at Khosla Ventures, CEO of AliveCor and Director of the Hospice of the Valley

Source: Company reports

## Share capital

There are 243,842,656 Ordinary shares in issue. In addition, there are currently 7.7m options and 34.3m warrants outstanding.



Source: Company announcements, Hardman & Co Life Sciences Research

## Appendix

### LIGHT is nearing reality

In May 2018, AVO signed a lease with the UK Government's Science and Technology Facilities Council (STFC) to establish a UK testing and assembly site in Daresbury (Cheshire). The first completed LIGHT machine will be assembled, verified, and validated on this site, prior to patient treatment.

At its 2019 AGM in July, management set out a schedule for the delivery of LIGHT components to Daresbury, which was updated in the 2019 interim results announcement in September, and is now further updated.

All the key modules and components that comprise LIGHT have all been manufactured, and most have been delivered to Daresbury. AVO is currently verifying and validating LIGHT in preparation for CE marking.

Delivery schedule for Daresbury					
Component	#	Manufactured	As of 25 Jul 2019	As of 31 Dec 2019	Status
Proton source	1	✓	By end of September 2019	✓ Delivered	✓
RFQ	1	✓	✓ Delivered	-	✓
SCDTL	4	✓	By end of September 2019	✓ All delivered	✓
CCL	13	✓	6 delivered, 7 during 4Q'19	✓ Delivered/stored	✓
Patient positioning	1	✓	By end of 2019	✓ Ready and in storage	✓
On-site validation		N/A	Throughout 2019 and 2020	No change	In progress
First patient treatment		N/A	By end of 2020	No change	In progress

Source: Advanced Oncotherapy; Hardman & Co Life Sciences Research

### What's next?

The next stage of AVO's execution plan focuses on the verification and validation process. Verification and validation processes are used for checking that a product meets requirements and specifications and that it fulfils its intended purpose. These are critical steps of a quality management system, such as ISO 13485, which the company obtained in January 2019. The verification and validation phase allows for completion of the documentation required for the CE marking and, as such, is an important step forward, prior to LIGHT being used on the first patients.

## Glossary

AAPM	American Association of Physicists in Medicine
CCL	Coupled Cavity Linac – accelerate the proton beam to the clinically relevant energy
CERN	Conseil Européen pour la Recherche Nucléaire
CMS	US Centers for Medicare & Medicaid Services
CBSA	Core-Based Statistical Area
FLASH	Delivery of ultra-high radiation dose of an entire therapy session in a single flash lasting less than a second
HOPD	Hospital Outpatient Department
Hypo-fractionation	Delivery of higher doses of radiation in fewer fractions than are used in conventional radiation therapy.
Linac	Linear accelerator
MeV	Mega-electron Volts
PBT	Proton Beam Therapy
PTCOG	Particle Therapy Co-Operative Group
RFQ	Radio Frequency Quadruple – focuses the proton beam and accelerates the protons up to 5MeV
RT	Radiotherapy
SCDTL	Side Coupled Drift Tube Linac – low-speed accelerating units that accelerate the protons from 5MeV to 37.5MeV
STFC	Science and Technology Facilities Council

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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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