EDISON

Pixium Vision

Progress on pipeline

Key advancements for Iris II and Prima in 2017

Healthcare equipment & services

Pixium Vision is developing two different retinal implants that provide vision by electrically stimulating the retina. Commercialisation efforts for Iris II are starting in Europe. Prima intends to target a larger population, and human trials could start in H117. Using a risk-adjusted NPV model, we obtain a pipeline rNPV of €131.4m, up from €125.5m, previously.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/15	3.3	(15.6)	(1.23)	0.0	N/A	N/A
12/16	2.5	(12.4)	(0.98)	0.0	N/A	N/A
12/17e	4.9	(10.8)	(0.85)	0.0	N/A	N/A
12/18e	14.9	(17.3)	(1.35)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

With CE Mark, Iris II gearing for initial EU sales

The Iris II epi-retinal implant received CE Mark clearance in 2016, and is designed to partially restore vision in profoundly blind retinitis pigmentosa (RP) patients. Pixium is building up a sales channel across Europe and the Middle East, and finished recruitment for a 10-patient study. It is seeking conditional reimbursement in Germany and France, and in February 2017 received a positive decision in Germany where it was granted NUB Status-1 (full approval). This allows selected hospitals to negotiate with insurance providers to obtain maximum Iris II coverage.

Prima ready to start human studies in Dry ARMD

Prima is a wireless miniaturized sub-retinal implant that could potentially offer better visual resolution than Iris II, while also requiring a less complex implantation procedure. This is being developed for late-stage, dry form of age-related macular degeneration (ARMD), which we believe affects c 10x more people than advanced RP. Having completed thermal and electrical safety studies in 2016, Pixium expects to start a five-patient EU feasibility study in H117. We anticipate commercialisation in 2020 and 2022 for the EU and US, respectively (from 2019 and 2021 previously).

Valuation: €11.31/sh including €12.9m YE16 net cash

We value Pixium using a risk-adjusted net present value (rNPV) approach, using a 12.5% cost of capital and applying a 70% probability of success for Iris II (given market acceptance and reimbursement risks) and a 12.5% success probability for Prima. After reducing our G&A expense and near-term R&D forecasts, pushing back Prima launch estimates, adjusting our FX assumptions and rolling forward our estimates, we now obtain a pipeline rNPV of €131.4m, up from €125.5m, previously. After including €12.9m Q416 net cash, we obtain an equity valuation of €144.3m, or €11.31 per share (up from €10.78, previously). We estimate that Pixium's net cash, with its €11m debt financing facility, if fully drawn, could fund operations into Q218. We assume 2017 and 2018 operating cash burn rates of €11.7m and €14.8m, respectively and that Pixium will raise an additional €10m in 2017 (to build a buffer), €15m in 2018 and €30m in 2019. For illustrative purposes only, our forecast funding requirements are added to long-term debt.

30 March 2017

Price	**€6.5**
Market cap	**€83m**
	€/US$1.07
Net cash (€m) at 31 December 2016	12.9
Shares in issue	12.8m
Free float	26%
Code	PIX
Primary exchange	Euronext Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(7.4)	3.7	(13.6)
Rel (local)	(11.4)	(1.3)	(25.5)
52-week high/low		€8.40	€5.30

Business description

Pixium Vision is a French medical device company developing retinal implants for patients with retinitis pigmentosa and macular degeneration. CE Mark clearance was received in 2016 on its initial product, Iris II. A sub-retinal implant, Prima, is also being developed simultaneously.

Next events

Start Prima human feasibility study	H117
Decision from French agency on conditional Iris II reimbursement	H117

Analysts

Pooya Hemami	+1 646 653 7026
Maxim Jacobs	+1 646 653 7027

healthcare@edisongroup.com

Edison profile page

Pixium VisionPixium Vision is a research client of Edison Investment Research Limited

Investment summary

Company description: Retinal implants for vision restoration

Pixium Vision was founded in France in 2011 and initially raised €24.3m in venture funding. It then raised €39.5m in its IPO in 2014. The company purchased the Iris epi-retinal implant assets from Intelligent Medical Implants in 2012 for €11m and is developing this device primarily for severely blind patients with retinitis pigmentosa (RP). Iris II received CE Mark approval in 2016 and commercialisation efforts in Europe and the Middle East are underway. The Prima sub-retinal implant was developed in conjunction with Stanford University and is awaiting first-in-human trials. Prima is theoretically capable of approaching facial recognition levels of visual acuity (VA).

Exhibit 1: Pixium Vision product pipeline

Product	Indication	Development status	Product highlights
Iris II epi-retinal implant	End-stage retinitis pigmentosa (RP)	CE Mark received in July 2016	Provides crude visual recovery, with patients capable of detecting lights and shapes. Implant is explantable and potentially upgradeable.
Prima sub-retinal implant	End-stage age-related macular degeneration (ARMD) and RP	Human feasibility study expected to start H117	Will potentially offer superior visual acuity than Iris II and surgical implantation procedure expected to be quicker. ARMD market is much larger than RP.

Source: Company reports

Valuation: Pipeline rNPV of €131.4m

We value Pixium using a risk-adjusted net present value (rNPV) approach, which applies a 70% probability of success for Iris II (given market acceptance and reimbursement risks) and a 12.5% probability for Prima. We have pushed back our start date for Prima pivotal studies into H118, which lowers our near-term R&D forecasts and delays our Prima launch estimate by about nine to 12 months in the EU and US. After also reducing our G&A expenses, applying a €/US$1.07 exchange rate forecast (vs €/US$1.11 previously) and rolling forward our estimates, we obtain a pipeline rNPV (enterprise value) of €131.4m, up from €125.5m, previously. After including €12.9m Q416 net cash, we obtain an equity valuation of €144.3m, or €11.31 per share (up from €10.78, previously).

Financials: Funded into 2018, more capital needed for Prima

Pixium's year-end 2016 net cash position was €12.9m (€14.2m gross cash minus €1.3m in short-term advances). We assume a 2017 and 2018 operating cash burn rate (excluding net interest) of €11.7m and €14.8m, respectively. The firm entered an €11m debt financing facility in H216 which, if fully drawn, we estimate will fund operations into Q218. Beyond this facility, we assume Pixium will raise an additional €10m in 2017 (to build a buffer and extend its runway beyond Q218), €15m in 2018 and €30m in 2019, with much of it going towards Prima studies and Iris II commercialisation. For illustrative purposes only, we have added our forecast funding requirements to long-term debt.

Sensitivities: Regulatory, commercial and funding

Much development risk lies with the Prima implant as it has yet to be tested on humans. Further, the visual improvements offered by Prima and Iris II must be sufficient to persuade patients and insurers to cover the implant, and be competitive vs existing (Argus II) and emerging alternatives. Pixium will also depend on maintaining access to additional capital to fund Prima development and early Iris II sales. While our model accounts for these financings as long-term debt, the firm may have difficulties raising funds or need to issue equity instead, and there is a potential risk that pricing is not favourable for current shareholders, which would lead to significant dilution.

Company description: Restoring sight

Pixium Vision is a French medical device company, which is advancing retinal implants, or bionic vision systems (BVS), that aim to provide vision to those with profound vision loss attributable to retinal diseases. These diseases permanently damage photoreceptor cells and impair their ability to translate visual stimuli into electrical signals transmittable into the optic nerve. Pixium's BVS products intend to replace the signal processing functions of damaged photoreceptors by electrically stimulating other retinal cells. These cells would then transmit the information towards the brain via the optic nerve.

Iris II is the first commercial-stage epi-retinal implant competitor to the Argus II, from Second Sight (EYES: Nasdaq).[1] Like the Argus II, the Iris II is an epi-retinal[2] implant that transforms light into electrical pulses to stimulate the retinal ganglion cell (RGC) layers, providing the patient with crude vision. Pixium is also developing a wireless sub-retinal implant, Prima, which delivers the electrical impulses at a more upstream level in retinal signal processing, and could provide superior VA while requiring less electrical energy than Iris II, with a possibly less invasive surgical technique.

Overview of Iris II retinal implant

Pixium acquired the technologies and intellectual property surrounding the Iris implant via its 2012 acquisition of Germany-based Intelligent Medical Implants (IMI) for €11m. The first iteration of this device (Iris I) was implanted and studied in eight patients across five European sites between 2012 and 2016, with favourable safety data.

Pixium developed a second-generation version of this implant (Iris II), containing 150 electrodes rather than the 50 in the first model, and started a 10-patient human trial in early 2016 (interim data expected mid-2017, full data in H218).The higher electrode count and density of Iris II could improve the level of visual resolution perceived by the user. This could also help better differentiate this device compared to the Argus II, which has 60 electrodes. Another potential advantage of the Iris II vs Argus II is that it can be explanted more easily (ie to allow for the implantation of potentially improved later-generation BVS devices in the future). The Iris II is targeted at severely blind patients with RP or other retinal dystrophies. CE Mark approval was obtained in July 2016, clearing the device for sales in Europe.

ATIS video capturing algorithm

Both Iris and Prima use asynchronous time-based image sensor (ATIS) technology for the imaging camera and sensor (on patient-worn goggles), enabling real-time delivery of visual information with relatively lower bandwidth than a traditional frame-by-frame capture and delivery system. The ATIS method sends signals that respond to movement and changes in contrast and luminance, which is more similar to the way the human eye functions, as opposed to sending frame-by-frame images, which carries redundant information and encompasses higher power and processing requirements.

Iris II European study recruitment completed

The final patient in the 10-patient European Iris II study was implanted in early 2017. The 10 treated patients will receive post-operative visual rehabilitation training and will be assessed at predefined intervals (at up to 18 months post-implantation), and compared to pre-treatment levels on functional areas including VA, standardised picture recognition and image localisation.

[1] Second Sight's Argus II was the first retinal implant approved for human use, with CE Mark clearance in 2011 and FDA approval in 2013.

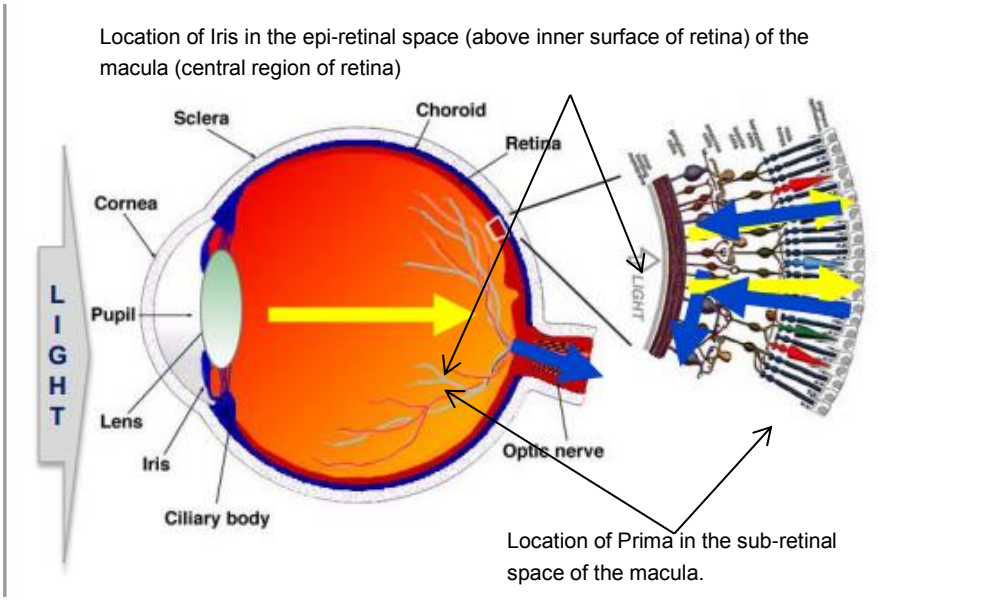
[2] Located at the surface of the retina.

Next-generation Prima implant offers potential advantages

Pixium's next-generation BVS platform, Prima, is gearing for human feasibility studies. Prima is a miniaturized photovoltaic wireless sub-retinal implant that could potentially better visual resolution than Iris II, while also requiring a less complex surgical procedure for instillation. Prima is a sub-retinal device and is implanted underneath the retina. Instead of stimulating RGCs (more downstream in the visual signal processing) as Iris II does, Prima aims to stimulate bipolar cells (more mid-stream in physiological visual signal processing). In normal visual function, photoreceptor cells (located on the outer portion of the retina, or closer to the choroid) send information to bipolar cells (located within the retina), which then relay information into RGCs (which are on the inner portion of the retina). Because Prima functions more upstream, it allows for more physiological or natural image signal processing and requires less electrical energy than Iris II (since functioning inner retinal cells amplify the raw electrical signals before sending them to the optic nerve).

The reduced energy requirement allows Prima to operate through a wireless approach, through micro photodiodes. This eliminates the need for permanent trans-scleral wires (as needed by Iris II).

Exhibit 2: Schematic of eye displaying location of Iris and Prima implants



Source: Edison Investment Research, Pixium Vision presentation

Thus, the surgical procedure to install Prima can be easier, quicker and less invasive than for Iris II. Prima requires clear optical media to function effectively, so patients with significant corneal scarring may be contraindicated (and cataracts would need to be removed prior to implantation).

Improved resolution of Prima opens door to much larger Dry ARMD market

Pixium believes that Prima could allow for higher VA than Iris II. Animal studies suggest Prima could reach up to 20/250 in humans (reflecting 8% of the resolution seen by healthy individuals). This could be sufficient to provide meaningful improvements and justify implantations in patients in late stages of the dry form of ARMD, such as those with retinal scarring or geographic retinal atrophy reducing best-corrected VA in both eyes to below 20/200. This adds the possibility for wider clinical use than the RP markets targeted for Iris II, and supports the implantation of Prima in areas where there is less grave vision loss than advanced RP cases.

Preclinical studies clear way for human studies

Data studied on ex-vivo[3] blind primate retina confirmed that there are localised, pixel (location-specific) responses in the RGCs, following sub-retinal stimulation using a Prima prototype. Animal model thermal[4] and electrical safety studies were completed in 2016 and, according to management, successfully showed that the system meets the safety thresholds for thermal and electrical safety requirements for the eye. Pixium has also finished surgical procedure studies, and believes it has successfully completed all the required steps needed before first-in-human testing for ARMD patients in Europe.

Prima could start human studies in H117

Pixium submitted a proposed study protocol in H216 for a five-patient feasibility study in ARMD patients with French regulatory authorities (ANSM). While it originally planned clearance by year-end 2016, it now expects to receive this and perform the first implantation in H117, with potential completion of the feasibility trial by year-end 2017. If it is successful, Pixium plans to start a registration-enabling, pivotal EU Prima study for ARMD in H118. Since ARMD is a larger market than RP (late-stage ARMD's prevalence is over 6x higher than all-stage RP), we anticipate that before allowing commercial clearance, European regulators will require the pivotal study to cover about 30 implantations, with follow-up periods of six to 12 months. We now forecast this pivotal study to start in H118 (vs our prior expectation of H217) will cost about €10-14m and have pushed back our EU potential launch timelines to 2020, vs 2019 previously.

Pixium is in discussions with the FDA to potentially start Early Feasibility Studies (EFS) on Prima. EFS are small-size (n<15), proof-of-concept trials on devices in novel indications and/or for which there are significant unknowns on performance. EFS data may be required by the FDA before allowing the start of a traditional US feasibility (pilot) study, which is carried on a larger number of subjects and often precedes a pivotal study. However, data from the EU feasibility study could potentially fulfil the EFS requirements for Prima, which is what we assume in our forecasts. Beyond this, Pixium believes the FDA would require a pilot study of about 30 patients and a pivotal study thereafter.

To obtain US approval in RP, Argus II required 30 implantations and follow-up. Given the larger market size for late-stage ARMD, we estimate that, for approval, the FDA would likely require the pivotal study to involve approximately 60-80 implantations, with monitoring for up to 18-24 months. We estimate that the US Prima pivotal study would cost $30-45m.

Exhibit 3: Projected Prima clinical development pathways for EU and US

EU clinical pathway	US clinical pathway
Clinical studies needed	
1. Small-size (~5-pt) feasibility study	1. Medium-size (~30-pt) pilot study
2. Medium-size (~30-pt) pivotal trial	2. Larger (~60-80pt) pivotal trial
Projected characteristics and requirements for pivotal trial	
Start in H118	Start in H218
6-12 months of follow-up data needed	18-24 months of follow-up data needed
Study must show product safety	Study must show safety and efficacy
Projected commercial launch timeline	
2020	2022

Source: Edison Investment Research estimates

Under an ideal scenario, Pixium could combine data from sites participating in the EU pivotal trial into a US premarket approval (PMA) registration file. Our model assumes this will be the case, and that Pixium will start recruiting US sites as part of a US pivotal study staring in H218. We expect

[3] Living cells, but tested outside the host organism.

[4] Lorach H, Wang J, Lee DY, et al. Biomed Opt Express. 2015 Dec 4;7(1):13-21. doi: 10.1364/BOE.7.000013.

that CE Mark clearance (and EU launch) would still occur 18-24 months earlier than US PMA approval and launch. We now model US approval and launch in 2022 (vs 2021 previously).

Exhibit 4: Pixium Vision SA upcoming catalysts

Event	Timing
Start human feasibility studies for Prima implant (Europe)	H117*
Initial Iris II sales in Europe	2017**
Start recruitment in EU for EU Prima pivotal study	H118**
Start US recruitment for US Prima pivotal study	H218**
CE Mark approval and EU launch for Prima	2020**
PMA Approval and US launch for Prima	2022**

Source: *Pixium Vision guidance, **Edison Investment Research estimates

Market size assumptions for RP and ARMD

Iris II can be indicated in patients with both severe central and peripheral vision loss; RP and other severe retinal dystrophies represent the target market. Prima has the potential to provide a higher level of central VA and target a wider range of patients, namely those with severe central vision loss (but intact peripheral vision). Late-stage ARMD is therefore a reasonable target for Prima. Both devices require the patient to have a functional RGC layer and optic nerve pathway.

Retinitis pigmentosa (RP)

RP is a progressive inherited retinal degeneration causing loss of peripheral vision that culminates in a loss of central vision. Prevalence is 0.025%,[5] making RP the most common inherited retinal degeneration or dystrophy. Only the most severe cases develop end-stage RP with near-total central and peripheral visual blindness. We estimate that roughly 10% of the RP population reach such a stage, and would represent the target Iris II market. We model that of this 10% of RP patients, 45% would meet the remaining inclusion criteria for a retinal implant (such as good overall health status, suitable age, etc.). We estimate that 5,700 RP patients in Europe and about 4,400 in the US would meet RP inclusion criteria for Iris II and reflect the potential target market.

Dry age-related macular degeneration (Dry ARMD)

ARMD is the leading cause of blindness in adults over age 55 in Western countries, and is characterised by damage to the macular[6] region of the retina, leading to central vision loss. Unlike RP, ARMD patients maintain their peripheral vision. While the exact pathophysiology is not fully understood, ARMD is believed to be caused by oxidative stress, mitochondrial dysfunction and/or inflammatory processes. There are two forms of ARMD: dry (non-exudative) and wet (exudative).

- The wet form is accompanied by exudative and neovascular changes, which can lead to macular scarring and more rapid vision loss. This form accounts for about 10-20% of ARMD cases, but prior to the usage of anti-VEGF (vascular endothelial factor) injection treatments, it accounted for over 80% of ARMD patients with legal blindness.[7]
- The dry form accounts for about 80-90% of cases and does not involve neovascular changes; cellular atrophy is the cause of photoreceptor damage. Prima is intended for Dry ARMD.

[5] Medscape. http://emedicine.medscape.com/article/1227488-overview#a6

[6] The macula is the central region of the retina and it contains the highest density of photoreceptors compared to other regions, thus accounting for the high level of resolution and colour perception associated with the central vision.

[7] Legal blindness refers to patients with a central VA of 20/200 (10%) or worse in the better eye when a patient is wearing their best-corrected prescription lenses, or those with a visual field of less than 20 degrees.

The prevalence of ARMD is adults above age 45 is estimated at 8.0%, and late-stage ARMD (with best-corrected vision acuity of 20/200, or 10% or worse) affects about 0.4% of this age group.[8] This represents about 815,000 people in Europe and 517,000 in the US. We believe that 30% of this late-stage subgroup would have sufficiently poor central vision to warrant potential consideration for Prima, and that 30% of these would meet all remaining inclusion criteria (including having the dry form of the disease) and/or be suitable as potential responders (ie this considers that many of the ARMD patients are in poor general health and/or have concomitant eye diseases such as glaucoma or poor optical media transparency, which would render them ineligible for Prima). Thus we view the target ARMD treatment population for Prima as about 73,200 in Europe and 46,500 in the US.

Competitive landscape

Pixium's BVS will need to compete with other implants on the market or in development.

Second Sight

Argus II uptake to date has been fairly limited, as in 2016 there have only been 12 Argus II implants in North America and 30 in Europe and the Middle East (EMEA), down from the 75 implantations worldwide in 2015. The limited level of vision provided by the 60-electrode device (patients may still require mobility assistance) could help explain the limited uptake to date.

Second Sight is also studying Argus II in ARMD and is developing a follow-on product (Orion I) that stimulates the visual cortex of the brain rather than the retina. By bypassing the optic nerve, Orion I could help patients with diseased optic nerves (eg glaucoma, optic neuropathy, etc). The firm intends to begin an Orion I human feasibility study in 2017, and potentially a pivotal study in 2018. Neurosurgery is more invasive than retinal surgery, so we estimate that unless Orion I can provide better VA than Iris II or Prima for retinal diseases, its potential use would likely be concentrated towards optic nerve diseases and thus may not directly compete with Iris II or Prima.

Retina Implant

Retina Implant is a private German company developing a sub-retinal implant. Alpha IMS earned CE Mark in 2013 and a follow-on product, Alpha AMS, received CE Mark clearance in 2016, but neither product appears to be generally available for commercial use. The Alpha IMS implant appears to safely restore VA to the light perceptions and hand movements level.[9]

Nano Retina

Nano Retina is an Israel-based firm that is developing a miniature chip retinal implant, NR600, which is currently in preclinical development. The company claims that the product can be implanted using a minimally invasive surgical procedure in under one hour. Like Prima, the product would have its own internal power supply, powered by photovoltaic elements generating operating voltage from infrared laser light delivered by the Nano Retina eyeglasses worn by the patient.

iBionics

Based in Ottawa and founded in 2015, iBionics is designing an epi-retinal implant that stimulates the retina via diamond electrodes. The current iteration has 256 electrodes, with the possibility of increasing up to 1,024. The firm believes that a 1,024-pixel version could enable patients to recognize faces, read and navigate freely. Human trials are planned to start within 30 months.

[8] Wong WL, Su X, Li X et al. Lancet Glob Health. 2014 Feb;2(2):e106-16.

[9] Stingl K, Bartz-Schmidt KU, Besch D et al. Vision Res. 2015 Jun;111(Pt B):149-60. doi: 10.1016/j.visres.2015.03.001. Epub 2015 Mar 23.

Other competing technologies

Alternate therapies (beyond electronic implants) are being developed to restore sight to patients with retinal diseases which, if successful, could compete with Iris II or Prima. These include:

- **Retinal transplantation** (ie transplantation of retinal cells or of immature retinal stem cells). This line of development is very premature and speculative with limited human data to date, but there have been reports of vision loss in some experimental treatments on ARMD patients.[10]
- **Implantable telescope.** VisionCare Ophthalmic Technologies offers an FDA-approved implantable miniature telescope for ARMD, providing 2.2-2.7 times magnification, but it does not improve the ability of the damaged retina to resolve details.
- **Alternate sensory reproduction**. Wicab's BrainPort V100 projects an image recorded by a video camera mounted on a pair of sunglasses onto a tongue array containing 400 electrodes. This device can offer functionality in patients with damaged optic nerve transmission.

Commercial strategy for Iris II

Pixium is building up a sales channel across Europe, and has started to recruit market developers in Spain and Germany. It is also working on securing insurance reimbursement. Given the expected high cost of the implant (we model net revenue of €78,000 per implant), we believe that payer/insurer coverage will be the primary channel for Iris II purchases, so obtaining coverage across different countries is key to optimising penetration. The reimbursement processes vary between each EU member country. The ongoing Iris II clinical study should provide efficacy data that can support long-term reimbursement applications in various European countries. Interim data (eg six months post-implantation), expected in mid-2017, could support these processes in some countries, although complete data (12-18 months post-implantation) will likely be needed for permanent reimbursement in most territories.

Before obtaining the data needed to support permanent coverage, Pixium is seeking temporary (or conditional) reimbursement applications in parts of Europe where innovative/breakthrough technologies can be funded as supportive clinical efficacy data are being gathered. Examples of such programmes include the Forfait Innovation in France, the NUB in Germany and the Commissioning through Evaluation (CtE) programme in the UK. Argus II has received coverage through the NUB, Forfait Innovation and CtE programmes (CtE in place since late 2016).

Provisional reimbursement strategies underway

In February 2017, Pixium received a positive decision from the German Institute for the Hospital Remuneration System (InEK), whereby it was granted NUB (Neue Untersuchungs- und Behandlungsmethoden) Status-1 (full approval) for Iris II as an epi-retinal device. The NUB Status-1 decision, renewable annually, allows for selected hospitals in Germany (five hospitals were covered under Pixium's application) to negotiate with insurance providers to obtain maximum coverage for Iris II implantations (including both the implant cost and for the medical procedures and rehabilitation) in patients with RP or other severe retinal dystrophies (other NUB status tiers provide limits to possible coverage). The five participating hospitals are in the process of negotiating with insurers; Pixium expects this process to be completed in H117.

In France, Pixium has applied for a Forfait Innovation programme to cover potentially up to 40 implantations over a five-year period at up to 10 hospitals. It expects such coverage would be contingent on the monitoring of approximately half of these patients over a two-year period, to build

[10] Kuriyan AE, Albini TA, Townsend JH, et al. N Engl J Med. 2017 Mar 16;376(11):1047-1053. doi: 10.1056/NEJMoa1609583.

data supporting the efficacy of the implant. This request is similar to a funding structure in place for Argus II, where up to 36 patients are being covered by this programme for Argus II. Because vision rehabilitation and training is required to ensure proper adaptation to the Iris II so that maximal benefit could be realized, Pixium is also requesting coverage across a wide network of vision rehabilitation centres as well. The company expects to receive a decision in Q217.

Pixium will apply for the coverage of a small number of UK Iris II implantations through the CtE programme, but does not expect to receive a CtE decision before H217. In late 2016, the NHS announced it would cover 10 Argus implantations as part of a CtE programme. Most of the remaining European and Middle Eastern countries targeted for Iris II sales do not have a national insurance framework and private payment is expected to drive the majority of potential sales in such regions.

Sensitivities

Development and regulatory risk. Much development risk lies with Prima as it has yet to be tested on humans. While there are favourable preclinical data, it is unknown whether Prima can provide superior central vision to epi-retinal implants and/or do so without additional safety risk. Compared to Iris II (implanted in patients with poor central and peripheral vision), Prima is being advanced in patients with intact peripheral vision and it is uncertain how well the visual system in Prima-implanted patients will interpret natural intact peripheral vision with artificial central vision. Further, degradation of the inner retina over time can reduce the VA offered by a retinal implant.

Commercial and competition risk. The visual improvements offered by Prima and Iris II must be sufficient to persuade patients and insurers to cover the implant and be competitive vs alternatives (for now the Argus II is the primary competitor in RP). Particular risk lies in the need for patients to properly undergo vision rehabilitation training to make full use of the Prima or Iris device; if patients do not fully engage in this process, the level of vision improvement possible could be restrained, affecting the commercial value proposition for the device.

Financing risk. Pixium's year-end 2016 net cash of €12.9m, plus up to €11m available through a debt facility, should support its runway into Q218. We assume Pixium will raise an additional €55m by year-end 2019 to sustain its operations, as we do not expect Iris II sales to cover the firm's operating and R&D costs (for Prima) over this period. While our model accounts for these financings as long-term debt, the firm may need to issue equity instead, and there is the risk that pricing is not favourable for current shareholders and leads to significant dilution. We do not expect Pixium to start generating sustainable, positive, recurring operating cash flows until 2020, once Prima reaches EU commercialisation in our model.

Financial forecasts and valuation

The company reported FY16 results in February 2017, with €2.5m in revenue (essentially from subsidies and research tax credits), €12.5m in operating loss and €12.4m net loss (€0.98 per share). This compares favourably to operating and net losses of €15.6-15.7m in 2015; the variance is largely due to lower R&D costs in 2016 (€10.9m) vs 2015 (€15.2m), which is explained by a reduction in Iris-related development costs (the final development of the Iris II prototype was completed in 2015).

We have lowered our G&A expense forecasts and short-term R&D spending forecasts. We now expect G&A costs of €3.7m and €6.4m in 2017 and 2018, respectively, versus our prior estimates of €4.5m and €7.1m, respectively. We have also reduced our 2017 R&D cost forecast to €9.0m, versus our prior forecast of €12.0m, due to a later than previously anticipated start to the EU Prima

pivotal study. We have also pushed back our launch timelines for Prima in Europe and the US to 2020 and 2022, respectively, from 2019 and 2021, respectively. We assume the company will allocate its US clinical trial resources to bringing Prima to market, and we do not include potential US Iris II sales in our forecasts. We have also reduced our near-term Iris II sales forecasts to reflect a more conservative initial uptake in European regions; we now expect Iris II sales of €1.9m and €11.9m in 2017 and 2018, respectively, down from €2.5m and €19.6m, respectively. Our peak market share forecasts are unchanged and our complete Iris II and Prima forecasts are below.

Exhibit 5: Financial forecasts for Iris II and Prima

	2017	2018	2019	2020	2021	2022	2023	2024
Iris in Retinitis pigmentosa (RP)								
EU population (m)	512	513	514	516	517	518	520	521
Retinitis pigmentosa prevalence	0.025%	0.025%	0.025%	0.025%	0.025%	0.025%	0.025%	0.025%
Total EU RP population (000)	127.9	128.3	128.6	128.9	129.3	129.6	129.9	130.3
Unit sales in EU	24	151	390	750	872	601	427	329
Average revenue per treatment (€)	78,000	78,722	80,265	81,813	83,393	85,011	86,723	88,468
Total EU revenue (€000) for IRIS-RP	1,852	11,920	31,330	61,359	72,694	51,074	37,041	29,141
Prima in Retinitis pigmentosa								
Unit sales in EU	-	-	-	152	436	776	876	878
Average revenue per treatment (€)	N/A	N/A	N/A	81,900	81,900	82,971	84,580	86,272
Total EU revenue (€000) for PRIMA-RP	-	-	-	12,465	35,702	64,359	74,108	75,784
US population (m)	330	332	335	337	340	342	345	347
Retinitis pigmentosa prevalence	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%
Total US RP proportion (000)	98.9	99.7	100.4	101.2	101.9	102.7	103.4	104.2
Unit sales in US	-	-	-	-	-	138	373	600
Average revenue per treatment ($)	N/A	N/A	N/A	N/A	N/A	151,529	153,971	157,031
Total US revenue ($000) for PRIMA-RP	-	-	-	-	-	20,970	57,376	94,213
Prima in Macular degeneration								
Prevalence of Late ARMD in >45 age group	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%
Estimated EU treatment population (000)	818.9	821.0	823.1	825.2	827.3	829.4	831.5	833.7
Unit sales in EU	-	-	-	464	1,367	2,797	3,738	3,748
Total EU revenue (€000) for PRIMA-ARMD	-	-	-	37,991	111,958	232,115	316,192	323,343
Estimated US treatment population (000)	527.5	531.5	535.5	539.5	543.5	547.6	551.7	555.9
Unit sales in US	-	-	-	-	-	615	1,517	2,252
Total US revenue ($000) for PRIMA-ARMD	-	-	-	-	-	93,160	233,546	353,483
Assumed $/€ rate	1.07	1.07	1.07	1.07	1.07	1.07	1.07	1.07
Worldwide total revenue (€000)	1,852	11,920	31,330	111,815	220,354	454,211	699,231	846,676

Source: Edison Investment Research

Our 70% probability of success estimate for Iris II includes risk adjustment factors for commercialisation (market acceptance, reimbursement). We continue to attribute a 12.5% success probability for this product. Given the above changes and after rolling forward our forecasts and applying a $1.07/€ exchange rate forecast (vs $1.11/€ previously), we now obtain a pipeline rNPV (enterprise value) of €131.4m, up from €125.5m, previously. After including €12.9m estimated Q416 net cash, we obtain an equity valuation of €144.3m, or €11.31 per share (up from €10.78, previously).

Exhibit 6: Pixium Vision rNPV assumptions

Product contributions (net of R&D and Marketing costs)	Indication	Status	rNPV (€m)	rNPV/share (€)	Probability of success	Launch year	Peak WW sales (€m)
Iris-II	Retinitis Pigmentosa	CE mark approval	71.9	5.63	70.0%	2017	73 in 2021
Prima	Retinitis Pigmentosa	Preclinical	34.1	2.67	12.5%	2020 (EU) and 2022 (US)	185 in 2025
Prima	Age-related Macular degeneration	Preclinical	134.4	10.53	12.5%	2020 (EU) and 2022 (US)	707 in 2025
Corporate costs & expenses							
G&A expenses			(21.6)	(1.69)			
Net capex, NWC & taxes			(87.4)	(6.85)			
Total rNPV			131.4	10.30			
Net cash (debt) (Q416)			12.9	1.01			
Total equity value			144.3	11.31			
FD shares outstanding (000)*			12,764				

Source: Edison Investment Research. Note: *At Q416.

Financials

Pixium's year-end 2016 net cash position was €12.9m (€14.2m gross cash minus €1.3m in short-term advances). Given the pushback in our expected timing for the start of the EU Prima pivotal study into 2018, our 2017 cash burn rate forecast has decreased. We now assume a 2017 and 2018 operating cash burn rate (excluding net interest) of €11.7m and €14.8m, respectively compared to our prior estimates of €15.2m and €13.3m, respectively. Beyond the announced €11m Kreos financing (which we estimate will be fully drawn in H217 and fund operations into Q218), we assume Pixium will raise an additional €10m in 2017, €15m in 2018 and €30m in 2019. Much of the funding should go towards Prima clinical studies and Iris II commercialisation. For illustrative purposes only, we have added our forecast funding requirements to long-term debt. Our financial and valuation models do not include the potential dilutive impacts of future equity offerings.

Exhibit 7: Financial summary

€'000s	2015	2016	2017e	2018e	2019e
31-December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	3,296	2,516	4,852	14,920	31,330
Cost of Sales	0	(141)	(1,389)	(6,488)	(12,072)
General & Administrative	(2,680)	(2,953)	(3,700)	(6,384)	(14,456)
Research & Development	(15,169)	(10,869)	(9,000)	(15,000)	(16,000)
EBITDA	(14,552)	(11,448)	(9,237)	(12,953)	(11,198)
Depreciation	(1,144)	(1,051)	(1,166)	(1,230)	(2,866)
Amortization	0	0	0	0	0
Operating Profit (before exceptionals)	(15,697)	(12,499)	(10,404)	(14,183)	(14,064)
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(15,697)	(12,499)	(10,404)	(14,183)	(14,064)
Net Interest	52	58	(394)	(3,077)	(5,663)
Profit Before Tax (norm)	(15,644)	(12,441)	(10,797)	(17,260)	(19,727)
Profit Before Tax (FRS 3)	(15,644)	(12,441)	(10,797)	(17,260)	(19,727)
Tax	0	0	0	0	0
Profit After Tax and minority interests (norm)	(15,644)	(12,441)	(10,797)	(17,260)	(19,727)
Profit After Tax and minority interests (FRS 3)	(15,644)	(12,441)	(10,797)	(17,260)	(19,727)
Average Number of Shares Outstanding (m)	12.7	12.7	12.8	12.8	12.8
EPS - normalised (€)	(1.23)	(0.98)	(0.85)	(1.35)	(1.55)
EPS - normalised and fully diluted (€)	(1.23)	(0.98)	(0.85)	(1.35)	(1.55)
EPS - (IFRS) (€)	(1.23)	(0.98)	(0.85)	(1.35)	(1.55)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	11,087	10,184	10,473	13,243	17,376
Intangible Assets	8,822	8,205	8,205	8,205	8,205
Tangible Assets	2,265	1,979	2,267	5,037	9,171
Current Assets	27,682	17,405	26,213	21,524	27,926
Short-term investments	0	0	0	0	0
Cash	24,354	14,244	21,659	14,744	19,268
Other	3,328	3,161	4,554	6,780	8,658
Current Liabilities	(3,498)	(2,836)	(1,730)	(2,070)	(2,334)
Creditors	(3,498)	(2,836)	(1,730)	(2,070)	(2,334)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(315)	(1,505)	(22,505)	(37,505)	(67,505)
Long term borrowings	(164)	(1,333)	(22,333)	(37,333)	(67,333)
Other long term liabilities	(151)	(172)	(172)	(172)	(172)
Net Assets	34,956	23,248	12,451	(4,809)	(24,536)
CASH FLOW					
Operating Cash Flow	(15,584)	(11,188)	(11,736)	(14,838)	(12,813)
Net Interest	52	58	(394)	(3,077)	(5,663)
Tax	0	0	0	0	0
Capex	(2,106)	(148)	(1,455)	(4,000)	(7,000)
Acquisitions/disposals	0	0	0	0	0
Financing	56	(0)	0	0	0
Net Cash Flow	(17,582)	(11,279)	(13,585)	(21,915)	(25,476)
Opening net debt/(cash)	(41,965)	(24,190)	(12,911)	674	22,589
HP finance leases initiated	0	0	0	0	0
Other	(193)	0	0	0	0
Closing net debt/(cash)	(24,190)	(12,911)	674	22,589	48,065

Source: Edison Investment Research, Pixium Vision accounts. Note: 2015 and 2016 revenues include tax credits and subsidies, which are forecast at approximately $3m per year through 2018.

Contact details	Revenue by geography
74 rue du Faubourg Saint-Antoin 75012 Paris, France +33 1 76 21 47 30 www.pixium-vision.com	N/A

Management team

Chairman: Bernard Gilly	Chief executive officer: Khalid Ishaque
Bernard Gilly has over 20 years' experience in the financial and pharmaceutical sectors and as an entrepreneur. He was VP of R&D for five years at Pasteur Mérieux Connaught (now Sanofi Pasteur). He subsequently served as CEO of Transgene from 1992 to 2000. He later joined Sofinnova Partners in Paris (2000-05). In 2005, he founded and became the CEO of Fovea Pharmaceuticals. After Fovea was acquired by Sanofi in 2009, he became executive VP of the Ophthalmology division of Sanofi. He founded Pixium Vision in 2011.	Khalid Ishaque has over 20 years' experience in the medical technology sector. He joined Pixium Vision in 2014, having spent 17 years with Boston Scientific in various commercial and business development roles, and most recently as general manager of the International Neuromodulation division commercialising Spinal Cord and Deep Brain Stimulation systems for chronic pain and movement disorders. Before joining Boston Scientific in 1997, he worked for Becton Dickinson. He received a Master's degree in engineering from Cranfield Institute of Technology in the UK and his Master's in international economics and management from SDA Bocconi University in Italy.
Chief operating officer: Robert Hill	**Chief Financial Officer: Didier Laurens**
Robert Hill is a specialist in industrial production and quality assurance systems. He has been leading the development and manufacturing of retinal implants for four years, in particular with IMI. Previously, he spent 14 years with InterVascular/Datascope where he was R&D director, and quality and regulatory affairs director. During his experience with InterVascular, Mr Hill also occupied several positions in which he was in charge of clinical affairs, OEM and major projects in the company. He also brings over 10 years' experience working with pharmaceutical and chemical companies.	Prior to joining Pixium Vision, Didier served as director of IR, financing and treasury at Korian, where he also served as interim CFO. Previously, he was a financial analyst with Société Générale, covering various sectors including healthcare, where he was involved with numerous IPOs. He also served as marketing manager in the pharmaceutical industry. Didier holds a post-graduate degree in pharmacy and is a graduate of SFAF/CIIA.

Principal shareholders	(%)
Sofinnova Ventures	22.67
Abingworth LLP	15.94
Innobio	12.22
Omnes Capital	11.21
Groupe BPI	7.87

Companies named in this report

Second Sight, Retina Implant, Nano Retina, iBionics

Edison is an investment research and advisory company, with offices in North America, Europe, the Middle East and AsiaPac. The heart of Edison is our world-renowned equity research platform and deep multi-sector expertise. At Edison Investment Research, our research is widely read by international investors, advisers and stakeholders. Edison Advisors leverages our core research platform to provide differentiated services including investor relations and strategic consulting. Edison is authorised and regulated by the Financial Conduct Authority. Edison Investment Research (NZ) Limited (Edison NZ) is the New Zealand subsidiary of Edison. Edison NZ is registered on the New Zealand Financial Service Providers Register (FSP number 247505) and is registered to provide wholesale and/or generic financial adviser services only. Edison Investment Research Inc (Edison US) is the US subsidiary of Edison and is regulated by the Securities and Exchange Commission. Edison Investment Research Limited (Edison Aus) [46085869] is the Australian subsidiary of Edison and is not regulated by the Australian Securities and Investment Commission. Edison Germany is a branch entity of Edison Investment Research Limited [4794244]. www.edisongroup.com

DISCLAIMER

Copyright 2017 Edison Investment Research Limited. All rights reserved. This report has been commissioned by Pixium Vision and prepared and issued by Edison for publication globally. All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report. Opinions contained in this report represent those of the research department of Edison at the time of publication. The securities described in the Investment Research may not be eligible for sale in all jurisdictions or to certain categories of investors. This research is issued in Australia by Edison Aus and any access to it, is intended only for "wholesale clients" within the meaning of the Australian Corporations Act. The Investment Research is distributed in the United States by Edison US to major US institutional investors only. Edison US is registered as an investment adviser with the Securities and Exchange Commission. Edison US relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a)(11) of the Investment Advisers Act of 1940 and corresponding state securities laws. As such, Edison does not offer or provide personalised advice. We publish information about companies in which we believe our readers may be interested and this information reflects our sincere opinions. The information that we provide or that is derived from our website is not intended to be, and should not be construed in any manner whatsoever as, personalised advice. Also, our website and the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. This document is provided for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research. Edison has a restrictive policy relating to personal dealing. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report. Edison or its affiliates may perform services or solicit business from any of the companies mentioned in this report. The value of securities mentioned in this report can fall as well as rise and are subject to large and sudden swings. In addition it may be difficult or not possible to buy, sell or obtain accurate information about the value of securities mentioned in this report. Past performance is not necessarily a guide to future performance. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (ie without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision. To the maximum extent permitted by law, Edison, its affiliates and contractors, and their respective directors, officers and employees will not be liable for any loss or damage arising as a result of reliance being placed on any of the information contained in this report and do not guarantee the returns on investments in the products discussed in this publication. FTSE International Limited ("FTSE") © FTSE 2017. "FTSE®" is a trade mark of the London Stock Exchange Group companies and is used by FTSE International Limited under license. All rights in the FTSE indices and/or FTSE ratings vest in FTSE and/or its licensors. Neither FTSE nor its licensors accept any liability for any errors or omissions in the FTSE indices and/or FTSE ratings or underlying data. No further distribution of FTSE Data is permitted without FTSE's express written consent.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney+61 (0)2 8249 8342
Level 12, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia