EDISON

Pixium Vision

Pixium seeks to address short Iris II lifespan

Iris II commercial suspension

Healthcare equipment & services

Pixium Vision recently reported data from its 10-patient Iris II study showing that it improves visual performance, but stops operating as intended at approximately nine to 12 months post-implantation. Pixium has halted new implantations as it plans to study a potential remedy to improve longevity. We have lowered our success probability estimates and delayed our launch dates for both Iris II and Prima. Our rNPV is reduced to €63.0m, from €129.3m 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	2.8	(13.3)	(1.01)	0.0	N/A	N/A
12/18e	3.0	(18.8)	(1.39)	0.0	N/A	N/A

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

Six-month data and possible cause of short lifespan

Six-month data shows that Iris II can improve square localisation and direction of motion performance among implanted patients. Pixium believes that mechanical forces (from eye movement) led to microfractures (or breaks) of the wiring emanating from the 150 electrodes embedded on the Iris II device, in the studied patients. There may also be moisture accumulation that caused electrical shorts.

Iris II relaunch likely delayed to at least 2019

Pixium proposes, for all of the 10 participants in the Iris II study and who consent to this proposal, to explant the existing Iris II implantations and to then re-implant the device with an additional application of a biocompatible seal at the most sensitive point of insertion, with the view that this should reduce mechanical load on the device and extend its lifespan. The firm is petitioning with European regulatory agencies to proceed with this strategy, and expects to monitor the participating patients for approximately another year or longer. We do not expect commercial sales to resume until 2019 at the very earliest.

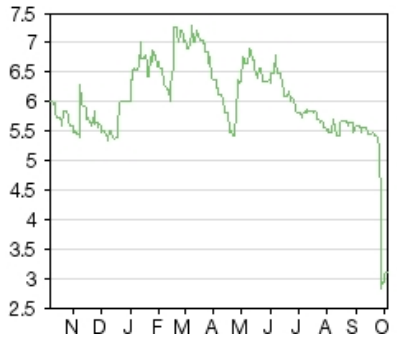
Valuation: Risked-NPV down to €63m

With the uncertainty on when and whether the issue surrounding premature Iris II operational failure will be resolved, we are lowering our Iris II probability of success estimate to 40% (from 70%, previously). We have pushed back our launch timing estimates for Prima by about six months (to 2021 in Europe; H222 in the US). We believe the Iris II product longevity issues highlight the possibilities for unanticipated operational disruptions to Prima as well, and we reduce our probability of success estimate for Prima to 10% (from 12.5% previously). We now obtain a pipeline rNPV (enterprise value) of €63.0m, down from €129.3m, previously. After including €5.4m in net cash at H117, we obtain an equity valuation of €68.5m, or €5.12 per share (compared to €10.08, previously). We estimate Pixium will raise €98m in funding through 2020, which would fund Prima through US and EU pivotal trials, before reaching positive cash flows in 2021 (after Prima is launched).

5 October 2017

Price	**€3.09**
Market cap	**€41m**
	US$1.18/€
Net cash (€m) at H117	5.4
Shares in issue	13.4m
Free float	18%
Code	PIX
Primary exchange	Euronext Paris
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(44.8)	(46.1)	(48.8)
Rel (local)	(47.5)	(48.1)	(57.2)
52-week high/low		€7.3	€2.8

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	Q417
Start Prima EU pivotal study	H119

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Iris II launch halted as short product lifespan identified

Pixium recently reported interim six-month follow-up results on the 10-patient European Iris II clinical trial. The first patient was implanted in early 2016 and the final patient was implanted in early 2017. While the preliminary data showed that patients had moderately improved visual function when the device was in operation (compared to when it was off), the company found that for the first five implanted patients, the device stopped operating correctly at approximately nine to 12 months post-implantation. At this time point, the implant stopped communicating with the companion patient-worn goggles and sensor. This cessation of function occurred much earlier than was originally anticipated (the CE Mark was provided assuming a lifespan of three years). It expects that the remaining patients who have been implanted with the device would eventually reach the same conclusion (product operational failure within a year of implantation). The company has decided to suspend future commercial Iris-II implantations until the issue is resolved.

Exhibit 1: Six-month visual function in Iris II study

Parameter	Proportion of patients with improved function when device ON (vs OFF)
Square localisation	77% (7/9)
Direction of motion	88% (8/9)
Visual field	56% (5/9)

Source: Company reports

The firm believes it has identified a cause for the earlier than expected cessation of functionality. Fortunately, Iris II was designed to be explantable (and potentially exchangeable, replaceable or upgradeable) and hence, after explanting the first patient for which this issue was identified in or around May 2017, investigators localised a “kink” or fold in the foil at the edge of the device. It is hypothesized that during the operation of device (after implantation), mechanical forces (from eye movement) can lead to microfractures (or breaks) of the wiring emanating from the 150 electrodes embedded on the device. In addition, there may be moisture accumulation that can lead to electrical shorts and a disruption in communication.

There were some adverse events (AEs) reported in the 10-patient clinical study. One patient had a vitreo-retinal traction occur (was resolved), one had a refixation of the device (was resolved), and two had hypotony (low intraocular pressure; one was resolved at six months and one is ongoing). These AEs (frequency of 0.4/implantation) were largely manageable and generally do not affect the long-term safety or biocompatibility of the device.

Potential solution – apply a biocompatible relief

Pixium proposes, for all of the 10 participants in the Iris II study and who consent to this new proposal (it is currently unknown how many participants have already provided such consent), to explant the existing Iris II implantations and to then re-implant the device with an additional application of a biocompatible seal (similar to a bandage of sorts) at the most sensitive (or potentially fragile) point of insertion, with the view that this should reduce mechanical load on the device and extend its lifespan. The company is petitioning with French and European regulatory agencies to proceed with this strategy, and expects to monitor the participating patients for approximately another year or longer, to determine whether product lifespan improves. While the company may contemplate resuming Iris II commercialisation prior to obtaining data on the re-implantations of this cohort, we believe it is not likely to be successful in re-launching Iris II until a definitive solution to this problem can be confirmed. And hence we do not expect commercial sales to resume until 2019 at the very earliest. Further, there remains a definite risk that the company’s proposed remedy to address the premature product failure may not succeed in extending the product’s operational lifespan. If the issue cannot be resolved, we are doubtful that an Iris II implant

that would only function for nine to 12 months at a time (and thus require re-implantation at such intervals) would be commercially viable.

Revisions to Iris II commercial forecasts

As stated above, we are pushing back our forecast for the resumption of Iris II sales, to 2019. We also believe that the presently identified issue with Iris II may diminish the commercial appeal of the product for the intended target population, those patients with retinitis pigmentosa (RP) or other severe retinal dystrophies. We have lowered our peak market share assumption from 15% to 10% within this group, and have pushed back our year of peak sales forecast from 2021 to 2022.

Exhibit 2: Financial forecasts for Iris and Prima

	2019	2020	2021	2022	2023	2024
Iris in retinitis pigmentosa (RP)						
EU population (m)	514	516	517	518	520	521
Retinitis pigmentosa prevalence	0.025%	0.025%	0.025%	0.025%	0.025%	0.025%
Total EU RP population (000)	128.6	128.9	129.3	129.6	129.9	130.3
Unit sales in EU	45	177	436	583	285	220
Average revenue per treatment (€)	78,000	79,123	80,652	82,163	83,769	85,455
Total EU revenue (€000) for IRIS-RP	3,496	13,992	35,158	47,871	23,853	18,766
Prima in retinitis pigmentosa						
Unit sales in EU	-	-	185	524	832	878
Average revenue per treatment (€)	N/A	N/A	81,900	83,007	84,607	86,272
Total EU revenue (€000) for PRIMA-RP	-	-	15,176	43,532	70,428	75,784
US population (m)	335	337	340	342	345	347
Retinitis pigmentosa prevalence	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%
Total US RP proportion (000)	100.4	101.2	101.9	102.7	103.4	104.2
Unit sales in US	-	-	-	35	279	584
Average revenue per treatment ($)	N/A	N/A	N/A	151,763	154,085	157,060
Total US revenue ($000) for PRIMA-RP	-	-	-	5,257	42,942	91,758
Prima in macular degeneration						
Prevalence of late ARMD in >45 age group	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%
Estimated EU treatment population (000)	823.1	825.2	827.3	829.4	831.5	833.7
Unit sales in EU	-	-	744	2,238	3,552	3,748
Total EU revenue (€000) for PRIMA-ARMD	-	-	60,946	185,736	300,493	323,343
Estimated US treatment population (000)	535.5	539.5	543.5	547.6	551.7	555.9
Unit sales in US	-	-	-	142	1,084	2,208
Total US revenue ($000) for PRIMA-ARMD	-	-	-	21,480	167,079	346,690
Assumed $/€ rate	1.18	1.18	1.18	1.18	1.18	1.18
Worldwide total revenue (€000)	3,496	13,992	111,280	299,796	572,757	789,458

Source: Edison Investment Research

For Prima, the company continues to expect to approval from EU regulators to start the five-patient European feasibility study for Prima in Q417 and to have the first human implantation occur before YE17. After obtaining six-month data from study participants, the company plans to start an EU pivotal study (we assume a US pivotal study will commence in parallel). We previously assumed both pivotal studies would start in H218, but Pixium now expects the earliest time for a pivotal study to start will be in early 2019. This pushes back our EU and US Prima launch timeline estimates to 2021 (from H220, previously) and H222 (from 2022, previously). Hence, we estimate that Prima will start generating revenue (in Europe) in 2021.

Valuation

With the suspension of Iris II sales and the uncertainty as to whether the present issue surrounding premature device operational failure will be resolved before 2019, we are lowering our Iris II probability of success estimate to 40% (from 70%, previously). For Prima, as stated above, we have pushed back our launch timing estimates by about six months. We note there are significant differences in device design and functionality between Prima and Iris II (subretinal layer

implantation location for Prima vs epiretinal layer for Iris II), and most notably, the signal communications approach applied between the devices and their accompanying goggles headset (Prima uses a wireless photovoltaic approach, versus the wiring and cabling employed on Iris II). Despite these differences, the product longevity issues raised on the Iris II highlight the possibilities for unanticipated or premature operational disruptions to any delicate bionic vision system (BVS) device (that interacts with human tissue), due to mechanical or other unexpected stresses or factors. Further, Prima has not yet received authorisation from European regulators to commence a feasibility study; recall that the company had guided in H216 that this milestone would have been likely to occur by YE16. Accordingly, we believe it is appropriate to reduce our probability of success estimate for Prima to 10% (from 12.5% previously).

Exhibit 3: 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 but sales suspended	17.3	1.30	40.0%	Relaunch in 2019	48 in 2022
Prima	Retinitis Pigmentosa	Preclinical	24.8	1.86	10.0%	2021 (EU) and H222 (US)	185 in 2025
Prima	Age-related macular degeneration	Preclinical	100.4	7.51	10.0%	2021 (EU) and H222 (US)	722 in 2025
Corporate costs & expenses							
G&A expenses			(28.4)	(2.12)			
Net capex, NWC & taxes			(51.1)	(3.82)			
Total rNPV			**63.0**	**4.72**			
Net cash (debt) (H117)			5.4	0.41			
Total equity value			**68.5**	**5.12**			
FD shares outstanding (000) (H117)			13,365				

Source: Edison Investment Research

Given the above changes, we now obtain a pipeline rNPV (enterprise value) of €63.0m, down from €129.3m, previously. After including €5.4m in net cash at H117 (€14.9m gross cash minus €1.4m in conditional advances and €8.1m in long-term debt), we obtain an equity valuation of €68.5m, or €5.12 per share (compared to €10.08, previously).

We reiterate that Prima remains the dominant value driver for Pixium, as the age-related macular degeneration (ARMD) market is much broader and more potentially lucrative than the far more narrow RP market that Iris II is targeting. For instance, if we were to remove future Iris II sales from our forecasts and valuation, our pipeline rNPV would decrease by only €5.9m (to €57.1m). While the firm's announcements and issues on Iris II do not explicitly or specifically affect the Prima programme, as stated earlier, we believe that they do justify an increase in the risk factor discount applied to Prima.

Financials

We continue to assume a 2017 operating cash burn rate (excluding net interest) of €13.4m and we now estimate a 2018 burn rate of €13.6m (versus €15.1m, previously). Lower projected marketing (since Iris II sales are suspended) and R&D (since the anticipated start of Prima pivotal studies is being pushed into 2019) costs drive the lower 2018 burn rate assumption.

While we believe Pixium has enough gross cash to maintain operations into H118, we expect it will draw the last remaining €3m tranche from the €11m Kreos financing facility in H217 to strengthen its runway and augment financial flexibility. For the same reason, we also continue to assume that Pixium will raise an additional €10m in H217 and €15m in 2018. Our model assumes that, strictly speaking, Pixium would only require €10m in funding to maintain a positive cash balance at YE18, but to maintain operational flexibility and avoid the need to pursue funding methods of last resort, we assume, as is the case for most of our coverage universe, that the firm will seek to always maintain at least six months of financial runway in terms of cash and equivalents on-hand. Hence,

our model assumes the firm will raise €25m in total, through YE18, in funding beyond the Kreos financing facility.

For illustrative purposes only, we have added our forecast funding requirements to long-term debt. However, it is possible that Pixium may be required to raise equity instead of debt, to meet its funding needs. Given the recent correction in Pixium's share price following the announcement of premature Iris II implantation failure, we note that at the current share price, a €10m equity raise would dilute current shareholders by about 20%, and a €25m equity raise would dilute shareholders by about 39%.

Beyond this, we continue to estimate that Pixium will raise €30m in 2019, and €40m in 2020. As above, we have added these forecast funding requirements to long-term debt. We forecast that this funding should enable the completion of registration-enabling Prima clinical studies in both the EU and the US, to meet our estimated launch timelines. This timing for these projected funding requirements can be delayed to a certain extent, should the firm plan to complete US Prima pivotal studies over a longer time horizon than we currently anticipate (ie leading to a potential US launch in or after 2023). Our financial and valuation models do not include the potential dilutive impacts of future equity offerings. We assume that Pixium will only start to become cash flow positive on a sustainable basis once Prima is launched (in 2021).

Exhibit 4: Financial summary

€000s	2015	2016	2017e	2018e	2019e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	3,296	2,516	2,755	3,000	3,496
Cost of Sales	0	(141)	(562)	0	(2,439)
General & Administrative	(2,680)	(2,953)	(4,213)	(3,578)	(8,168)
Research & Development	(15,169)	(10,869)	(9,491)	(14,000)	(18,000)
EBITDA	(14,552)	(11,448)	(11,510)	(14,578)	(25,110)
Depreciation	(1,144)	(1,051)	(1,006)	(1,133)	(2,712)
Amortisation	0	0	0	0	0
Operating Profit (before exceptionals)	(15,697)	(12,499)	(12,516)	(15,711)	(27,822)
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(15,697)	(12,499)	(12,516)	(15,711)	(27,822)
Net Interest	52	58	(813)	(3,099)	(5,720)
Profit Before Tax (norm)	(15,644)	(12,441)	(13,329)	(18,810)	(33,541)
Profit Before Tax (FRS 3)	(15,644)	(12,441)	(13,329)	(18,810)	(33,541)
Tax	0	0	0	0	0
Profit After Tax and minority interests (norm)	(15,644)	(12,441)	(13,329)	(18,810)	(33,541)
Profit After Tax and minority interests (FRS 3)	(15,644)	(12,441)	(13,329)	(18,810)	(33,541)
Average Number of Shares Outstanding (m)	12.7	12.7	13.2	13.6	13.8
EPS - normalised (€)	(1.23)	(0.98)	(1.01)	(1.39)	(2.42)
EPS - normalised and fully diluted (€)	(1.23)	(0.98)	(1.01)	(1.39)	(2.42)
EPS - (IFRS) (€)	(1.23)	(0.98)	(1.01)	(1.39)	(2.42)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	11,087	10,184	9,563	12,430	16,718
Intangible Assets	8,822	8,205	7,942	7,942	7,942
Tangible Assets	2,265	1,979	1,621	4,488	8,776
Current Assets	27,682	17,405	24,671	18,803	11,992
Short-term investments	0	0	0	0	0
Cash	24,354	14,244	20,740	14,995	7,332
Other	3,328	3,161	3,931	3,808	4,659
Current Liabilities	(3,498)	(2,836)	(880)	(880)	(1,074)
Creditors	(3,498)	(2,836)	(880)	(880)	(1,074)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(315)	(1,505)	(22,678)	(37,678)	(67,678)
Long term borrowings	(164)	(1,333)	(22,490)	(37,490)	(67,490)
Other long term liabilities	(151)	(172)	(187)	(187)	(187)
Net Assets	34,956	23,248	10,676	(7,325)	(40,041)
CASH FLOW					
Operating Cash Flow	(15,584)	(11,188)	(13,425)	(13,646)	(24,943)
Net Interest	52	58	(813)	(3,099)	(5,720)
Tax	0	0	0	0	0
Capex	(2,106)	(148)	(176)	(4,000)	(7,000)
Acquisitions/disposals	0	0	0	0	0
Financing	56	(0)	(38)	0	0
Net Cash Flow	(17,582)	(11,279)	(14,452)	(20,745)	(37,662)
Opening net debt/(cash)	(41,965)	(24,190)	(12,911)	1,751	22,495
HP finance leases initiated	0	0	0	0	0
Other	(193)	(0)	(209)	0	0
Closing net debt/(cash)	(24,190)	(12,911)	1,751	22,495	60,158

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.

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