EDISON

Pixium Vision

Update - clinical trials

Iris II and Prima continue to advance

Healthcare equipment & services

Pixium Vision implanted its first Iris II epi-retinal implant in January 2016 as part of a 10-patient European study as it awaits clearance from a CE mark application. It also reported supportive animal data on its next-generation implant, Prima, slated to start human studies by YE16. Our rNPV valuation is €10.28 per share, down from €10.50 previously.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/14	2.4	(11.6)	(1.18)	0.0	N/A	N/A
12/15	3.3	(15.6)	(1.23)	0.0	N/A	N/A
12/16e	3.0	(13.5)	(1.06)	0.0	N/A	N/A
12/17e	5.5	(23.5)	(1.85)	0.0	N/A	N/A

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

Iris II starts human studies

The Iris II implant contains 150 electrodes and is designed to partially restore vision in visually impaired patients by electrically stimulating the retina. Following safety data from an earlier device iteration (Iris I) comprising 50 electrodes, Pixium started a 10-patient study in early 2016 with the first implant occurring in France in January. A CE mark application filed in late 2015 for Iris II could lead to approval in H216. Iris II has more electrodes than the 60-electrode Argus II (the only approved competing retinal implant), which could potentially deliver a higher visual acuity.

Prima planned to start human testing by YE16

The next-generation implant, Prima, is inserted below the retina (sub-retinal) and could potentially provide sharper acuity than Iris II while offering a simpler and less invasive surgical technique. This could expand potential utilisation to the late-stage macular degeneration market. By targeting bipolar cells, Prima operates more upstream in the retinal signal processing than epi-retinal implants, reducing power requirements and allowing it to function wirelessly. Primate data presented at ARVO shows proof-of-concept of retinal signal responses to Prima prototype. A first-in-man study is planned by YE16 and commercialisation could occur in 2019.

Valuation: €10.28 per share including H116 cash

While we have raised our penetration forecasts, we also pushed back our US Prima launch timeline to 2021 (vs 2019 previously), and raised working capital/capex assumptions for future Iris or Prima launches. Our pipeline rNPV is €113.5m (vs €109.0m, previously). After including H116 estimated net cash of €17.5m, we obtain an equity valuation of €131.0m, or €10.28 per share (vs €10.50 previously). Upcoming catalysts, such as Iris II CE mark clearance and in-human testing of Prima, could de-risk the programmes and raise our valuation. We expect a cash burn rate of €14.9m in 2016, rising in the coming years due to higher R&D spending given plans for US Iris II trials and EU/US Prima studies, and Iris II launch activities. We assume Pixium will raise €20m in financing in 2016, and €30m in both 2017 and 2018. For illustrative purposes only, we have added these requirements to long-term debt, and our models do not include the potential dilutive impacts of future equity offerings.

15 July 2016

Price	**€7.81**
Market cap	**€99m**

Net cash (€m) at 31 December 2015	24.2
Shares in issue	12.7m
Free float	26%
Code	PIX
Primary exchange	Euronext Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	10.8	11.4	28.5
Rel (local)	4.7	14.7	46.5
52-week high/low		€8.40	€4.48

Business description

Pixium Vision is a French medical device company developing retinal implants for patients with retinitis pigmentosa and macular degeneration. A CE mark application was submitted in late 2015 on its initial product, Iris. A sub-retinal implant, Prima, is also being developed simultaneously.

Next events

H116 results	August 2016
Receipt of CE mark for Iris II	H216
First in-human dosing for Prima	H216

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Edison profile page

Iris II implant getting ready for prime time

Pixium Vision's higher-resolution successor to its Iris I neuromodulation-based sensory vision device, Iris II, is advancing through clinical testing. Many retinal diseases, such as retinitis pigmentosa (RP) and age-related macular degeneration (ARMD), permanently damage photoreceptor cells, impairing their ability to translate visual stimuli into electrical signals transmittable into the optic nerve and brain. The premise behind Pixium's vision restoration systems (VRS), such as Iris II and Prima, is to replace the signal processing functions of damaged retinal photoreceptors by electrically stimulating retinal cells, which would then transmit the information towards the brain via the optic nerve.

The primary difference between the Iris II epi-retinal[1] implant and the Iris I is that Iris II has 150 electrodes, compared to 50 on the Iris I. The higher electrode count and density of Iris II could improve the level of visual resolution perceived by the user. The higher resolution capacity of Iris II can help better differentiate this device compared to existing VRS implants, such as Second Sight's (EYES, Nasdaq) Argus-II epi-retinal implant (currently the only approved implant VRS device in the US and Europe, and 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 VRS devices in the future).

The Iris I has been studied in eight patients across five European sites to date, with favourable safety data. Pixium has used the six-month data from these subjects as part of its Iris II CE mark filing in December 2015, and has committed to follow these patients for 12-18 months to further study longer-term performance and be better positioned to provide further supportive data to enquiries from European regulators or reimbursement authorities. Given the similarities between the Iris I and Iris II devices and their assembly, Pixium believes the existing safety data on Iris I support its CE mark filing for the Iris II.

Iris II European study commences human testing

Subsequent to the CE mark filing, Pixium started a European clinical study on Iris II, and in January 2016 implanted the first human Iris II implant in a 47-year old RP patient at the University Hospital in Nantes, France. The study plans to recruit 10 patients and monitor them at pre-defined intervals for up to 18 months post-implantation, and assess performance in functional visual tasks between when the headset is activated and when it is disabled. The firm received clearance from regulators in France, Austria, Germany and most recently (late May 2016) the UK for the Iris II clinical study, and Moorfields Eye Hospital is registered as a clinical trial site. The company expects that all its future Iris implantations (either for clinical studies or subsequent to commercial clearance) will use the higher electrode-density Iris II implant, rather than Iris I.

The firm anticipates commercial Iris II approval and potential launch in H216. In 2016, Pixium intends to make an Investigational Device Exemption (IDE) application for authorization to commence clinical trials on the Iris II in the US in H216, although we expect initial implantations will likely start in 2017.

Prima inches closer to human studies

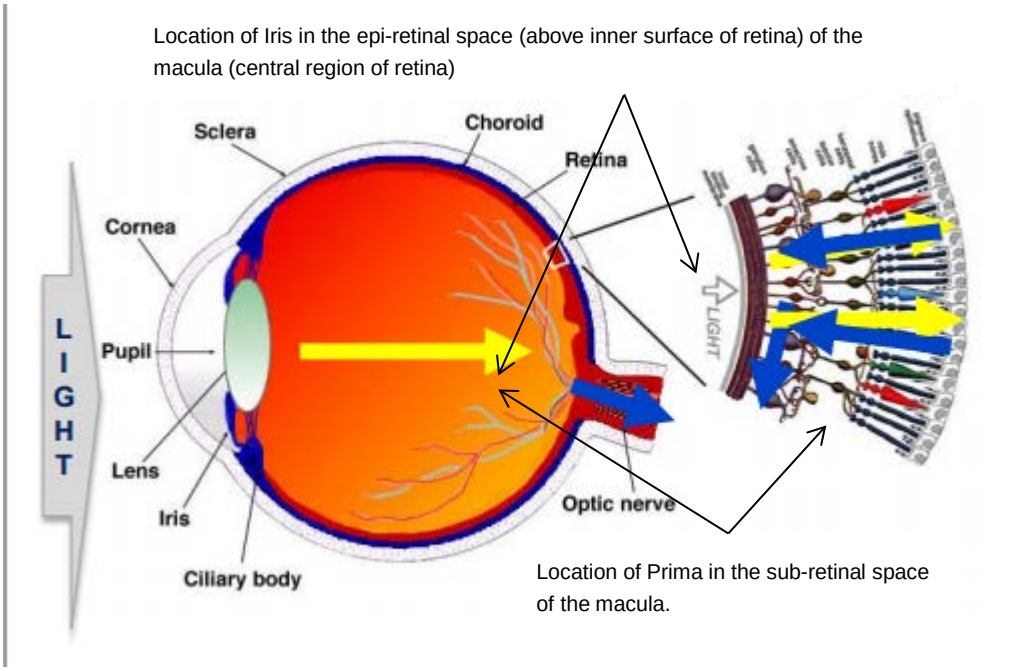
While Pixium readies Iris II for further human testing and potential commercial launch, it is also advancing its next-generation VRS platform, Prima, for human feasibility studies. The Prima is a miniaturized wireless sub-retinal implant that can potentially offer better visual resolution than Iris II, while also requiring a less complex surgical procedure for instillation. Like the Iris systems, the Prima system comprises three components:

[1] Lying at the surface of the retina.

1. an implantable portion containing electrodes designed to communicate with retinal cells
2. a portable visual interface (bio-inspired camera) in the form of spectacles integrating a camera and an information transmission system, and
3. a handheld device allowing the user to adjust settings.

While Iris II is an epi-retinal device (implanted at the surface of the retina, designed to stimulate retinal ganglion cells), the Prima sub-retinal device is implanted underneath the retina. Instead of stimulating the retinal ganglion cells (more downstream in the visual signal processing), Prima aims to stimulate bipolar cells (more mid-stream in physiological visual signal processing). In normal visual function, healthy photoreceptor cells (located on the outer portion of the retina, or closer to the choroid and sclera) send information to bipolar cells (located within the retina), which then relay information into ganglion cells (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 also requires less electrical energy than Iris (since functioning inner retinal cells amplify the raw electrical signals before sending them to the optic nerve). The reduced energy requirement lends itself to Prima being capable of operating through a wireless photovoltaic approach, which eliminates the need for permanent trans-scleral wires (as needed by Iris II) and allows the eye to remain intact.

Exhibit 1: Schematic of eye displaying location of Iris and Prima implants



Source: Edison Investment Research, Pixium Vision presentation

Overall, because the device uses wireless micro photodiode implants (not requiring permanent wire attachments), the surgical procedure to install the device can be easier and less invasive than implanting the Iris II. Pixium continues to work on refining the surgical technique ahead of its first expected human implant (planned in late 2016) in Europe.

Pixium and a team at Stanford University provided preclinical data at the Association for Research in Vision and Ophthalmology (ARVO) conference earlier in 2016. Data studied on ex-vivo[2] blind primate retina (an animal model close to the human retina) confirmed that there are localised, pixel (location-specific) responses in the retinal ganglion cells, following sub-retinal stimulation using the

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

Prima prototype. Safety and efficiency testing is being carried out on rodents and other animal models as well.

Improved potential resolution of Prima could open door to ARMD market

Pixium believes the Prima could potentially allow for higher resolution than Iris II; animal studies suggest that Prima could reach up to 20/250 in humans (reflecting 8% of the resolution seen by healthy individuals, and generally enough for crude facial recognition). This could be sufficient to provide meaningful improvements and justify implantations in patients with late-stage ARMD (such as those with retinal scarring or geographic retinal atrophy reducing best-corrected vision in both eyes to below 20/200). Hence, 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. Altogether, Prima's potential additional detail and contour resolution enhancement could be advantageous for the visual functioning of many late-stage ARMD patients.

Also like Iris, the Prima uses asynchronous time-based image sensor (ATIS) technology for the imaging camera and sensor, which enables real-time delivery of pertinent 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, 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, processing and bandwidth requirements. Given the wireless photovoltaic approach used by Prima (versus transscleral wires), bandwidth and energy conservation are critical for optimal functioning. The Prima requires clear optical media to function effectively, so patients with significant corneal scarring may be contraindicated (and any cataracts would need to be removed prior to implantation).

Financial forecasts and commercial assumptions

We have made adjustments to our financial model with regards to Iris and Prima. We continue to assume Iris II sales in RP, and Prima sales occurring in both RP and ARMD indications. As Prima has yet to be implanted in humans, we apply a lower probability of success (10% vs 40%) in our valuation. Over time, given its potential for improved vision and a less invasive implantation, Prima may cannibalise Iris sales in RP.

We now assume initial Iris sales in the EU will occur in 2017 (vs H216 previously), and we continue to model US commercialisation (through the PMA pathway) in 2018, although this assumption could be ambitious as the IDE for a US study has not been adopted yet. We expect the company will start human studies on Prima in late 2016, and ramp up to commence an IDE for a US Prima study in 2017 as well. We continue to model Prima launch in Europe in 2019. We now anticipate PMA approval and US commercial introduction for Prima in early 2021, as we believe that the FDA review process for Prima will take longer than the European CE mark process, and that the FDA may require more comprehensive Prima study data than the European regulators.

Exhibit 2: Pixium Vision upcoming catalysts

Event	Timing
Receive CE mark clearance for Iris II	H216*
Start human studies for Prima implant (Europe)	H216*
Initial Iris II sales in Europe	2017**
Start human studies for Iris II and Prima in US	2017**
PMA approval and Iris II commercialisation in US	2018**
CE mark approval and EU commercialisation for Prima	2019**
PMA approval for Prima and US commercialisation	2021**

Source: *Company guidance. **Edison Investment Research estimates

We have increased our peak penetration assumptions for both RP and ARMD, as we assume that a larger proportion of the estimated populations with profound vision loss (20/200 or worse) of the RP (targeted by Iris and Prima) and ARMD (Prima) will obtain treatment. As a means of comparison, we previously estimated that peak transplantations for Prima in ARMD would occur in 2022 and be approximately 1,400 in the US and 2,200 in Europe; we now assume peak Prima ARMD transplantations to occur in 2024, with about 3,700 in Europe and 2,500 in the US. Given the lack of treatment alternatives for potential late-stage ARMD patient populations of over 830,000 persons in Europe[3] and over 550,000 in the US, we believe this adjustment is plausible, as it still represents a minor fraction of the pool of affected patients.

Exhibit 3: Financial forecasts for Iris and Prima

	2017e	2018e	2019e	2020e	2021e	2022e	2023e	2024e
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	32	249	683	869	806	590	427	329
Average revenue per treatment (€)	78,000	78,811	80,214	81,758	83,354	85,022	86,723	88,468
Total EU revenue (€000) for IRIS-RP	2,525	19,607	54,789	71,086	67,206	50,152	37,041	29,141
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	0	25	203	494	660	691	496	263
Average revenue per treatment ($)	N/A	144,000	145,376	148,105	150,972	153,957	156,852	160,124
Total US revenue ($000) for IRIS-RP	0	3,627	29,497	73,134	99,690	106,405	77,784	42,120
Prima in Retinitis pigmentosa								
Unit sales in EU	-	-	108	391	719	874	876	878
Average revenue per treatment (€)	N/A	N/A	81,900	81,900	81,900	82,922	84,580	86,272
Total EU revenue (€000) for PRIMA-RP	-	-	8,881	32,050	58,903	72,469	74,108	75,784
Unit sales in US	-	-	-	-	94	346	618	702
Average revenue per treatment ($)	N/A	N/A	N/A	N/A	151,200	153,276	156,241	159,272
Total US revenue ($000) for PRIMA-RP	-	-	-	-	14,277	52,992	96,576	111,735
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	-	-	176	640	1,395	2,797	3,738	3,748
Total EU revenue (€000) for PRIMA-ARMD	-	-	14,399	52,423	114,241	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	-	-	-	-	336	1,229	2,198	2,494
Total US revenue ($000) for PRIMA-ARMD	-	-	-	-	50,764	188,415	343,380	397,281
Assumed $/EUR rate	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11
Worldwide total revenue (€000)	2,525	22,875	104,643	221,446	388,756	668,080	893,772	924,786

Source: Edison Investment Research

Valuation: Adjusting US Prima launch, working capital

While our longer-term revenue assumptions have increased, we have also adjusted our model to account for a longer than previously expected US launch timeframe for Prima (2021 vs 2019 previously). We have also increased assumptions for the working capital and capex expenditure that could be necessary for manufacturing and commercial supply for the Prima and Iris implants. Given these adjustments, we now obtain a risk-adjusted firm NPV (enterprise value) of €113.5m (vs €109.0m, previously) which, after adding €17.5m of estimated net cash at 30 June 2016, provides an equity valuation of €131.0m, or €10.28 per share.

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

Exhibit 4: 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	Retinitis Pigmentosa	CE mark application filed	86.4	6.78	40.0%	2017	157 in 2021
Prima	Retinitis Pigmentosa	Preclinical	27.6	2.16	10.0%	2019	176 in 2024
Prima	Age-related Macular degeneration	Preclinical	105.3	8.27	10.0%	2019 (EU); 2021 (US)	681 in 2024
Corporate costs & expenses							
G&A expenses			(22.2)	(1.74)			
Net capex, NWC & taxes			(83.7)	(6.57)			
Total rNPV			113.5	8.91			
Net cash (debt) (H116e)			17.5	1.38			
Total equity value			131.0	10.28			
FD shares outstanding (000) (H116e)			12,740				

Source: Edison Investment Research

In addition to clinical and regulatory risks, the success probabilities (40% for Iris, 10% for Prima) applied in our risk-adjusted NPV also include and account for the inherent risk in generating and sustaining demand for implantable devices among stakeholders (patients, ocular health professionals and reimbursement authorities). We note that in 2015, there were only 75 implantations for Second Sight's Argus II device (approved by both FDA and CE mark) worldwide, including 32 in North America (two units were implanted in North America in Q116 and 10 worldwide). Hence there may be a material perception barrier and market acceptance barrier that needs to be overcome among stakeholders, in order to achieve the penetration levels we forecast. This will depend largely on the performance of the Iris and Prima implants; currently Argus II is estimated to provide visual acuity improvement to 20/1262 (approximately 1.6% of normal visual acuity) and should Iris and/or Prima achieve material improvements to such levels (Prima is projected to potentially reach 20/250 or 8% of normal acuity), then we believe the market penetration assumptions in our model can be reached, despite the relatively low uptake of the Argus II to date.

We also highlight that while Prima accounts for the majority of our pipeline valuation, our current model only assumes a 10% probability of success for this product. Pixium expects to complete preclinical electrical safety studies in the coming months, which could bring the product closer to human testing and potentially lower its development risk. This catalyst, and other Prima-related milestones (such as commencing human studies and/or showing early signs of safety), could increase our success probability forecast. As a means of comparison, raising the Prima success probability to 15% or 20% would raise the firm rNPV (excluding net cash) to €154.3m or €195.2m, respectively. Subsequent human data showing material visual acuity and functional improvements in late-stage ARMD patients could further de-risk the programme. Our 40% probability of success (unchanged) for Iris II takes into consideration the demonstrated safety data among patients who have already used the device. The granting of a CE mark for Iris II, anticipated by the company in H216, would be a catalyst to justify an increase in our probability estimate for this programme.

Financials

Pixium's gross cash position was €20m in cash at the end of Q116, down from €24.4m at YE15 (net cash at YE15 was €24.2m after considering €0.2m in short-term debt/advances). We expect a cash burn rate (operating cash flow plus net interest minus net capex) of €14.9m in 2016, increasing to €29.4m in 2017 and €26.9m in 2018. We expect the 2016 burn rate to be lower than the 2015 rate of €17.6m, given that as the Iris II CE mark dossier has been filed, we believe research expenses

on the product should decrease in 2016. The anticipated increase in cash burn in 2017 and beyond is partly due to increased R&D spending as expected for human trials in the US for Iris II, and in both the US and Europe for Prima (both of which we expect will be in full swing in 2017). In addition, capex and working capital requirements are forecast to increase to accommodate initial Iris II commercialisation in Europe in 2017, and in the US in 2018 (assuming PMA approval).

Our model assumes that Pixium will raise €20m in financing in 2016, and €30m in both in 2017 and 2018. For illustrative purposes only, we have added these requirements to long-term debt. Note that our financial and valuation models do not include the potential dilutive impacts of future equity offerings. We do not expect Pixium to start generating sustainable positive recurring operating cash flows until H219, at which point we forecast Prima will start generating meaningful sales for the company (in addition to Iris II).

Exhibit 5: Financial summary

€(000)	2014	2015	2016e	2017e	2018e
31-December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	2,427	3,296	3,000	5,525	25,875
Cost of Sales	0	0	0	(1,894)	(12,154)
General & Administrative	(2,299)	(2,680)	(3,200)	(5,781)	(8,864)
Research & Development	(10,963)	(15,169)	(12,500)	(20,000)	(22,000)
EBITDA	(10,835)	(14,552)	(12,700)	(22,150)	(17,143)
Depreciation	(813)	(1,144)	(1,131)	(1,415)	(1,628)
Amortization	0	0	0	0	0
Operating Profit (before exceptionals)	(11,648)	(15,697)	(13,831)	(23,565)	(18,771)
Exceptionals	0	0	0	0	0
Other	0	0	0	0	0
Operating Profit	(11,648)	(15,697)	(13,831)	(23,565)	(18,771)
Net Interest	37	52	313	22	(413)
Profit Before Tax (norm)	(11,611)	(15,644)	(13,518)	(23,543)	(19,184)
Profit Before Tax (FRS 3)	(11,611)	(15,644)	(13,518)	(23,543)	(19,184)
Tax	0	0	0	0	0
Profit After Tax and minority interests (norm)	(11,611)	(15,644)	(13,518)	(23,543)	(19,184)
Profit After Tax and minority interests (FRS 3)	(11,611)	(15,644)	(13,518)	(23,543)	(19,184)
Average Number of Shares Outstanding (m)	9.8	12.7	12.7	12.7	12.7
EPS - normalised (€)	(1.18)	(1.23)	(1.06)	(1.85)	(1.51)
EPS - normalised and fully diluted (€)	(1.18)	(1.23)	(1.06)	(1.85)	(1.51)
EPS - (IFRS) (€)	(1.18)	(1.23)	(1.06)	(1.85)	(1.51)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	9,932	11,087	12,456	14,191	16,563
Intangible Assets	9,259	8,822	8,822	8,822	8,822
Tangible Assets	673	2,265	3,634	5,369	7,741
Current Assets	44,866	27,682	32,795	35,607	44,977
Short-term investments	0	0	0	0	0
Cash	42,132	24,354	29,467	30,102	33,173
Other	2,735	3,328	3,328	5,505	11,805
Current Liabilities	(4,051)	(3,498)	(3,498)	(1,588)	(2,514)
Creditors	(4,051)	(3,498)	(3,498)	(1,588)	(2,514)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(245)	(315)	(20,315)	(50,315)	(80,315)
Long term borrowings	(167)	(164)	(20,164)	(50,164)	(80,164)
Other long term liabilities	(78)	(151)	(151)	(151)	(151)
Net Assets	50,503	34,956	21,438	(2,105)	(21,288)
CASH FLOW					
Operating Cash Flow	(8,426)	(15,584)	(12,700)	(26,237)	(22,516)
Net Interest	37	52	313	22	(413)
Tax	0	0	0	0	0
Capex	(1,772)	(2,106)	(2,500)	(3,150)	(4,000)
Acquisitions/disposals	0	0	0	0	0
Financing	42,705	56	0	0	0
Net Cash Flow	32,543	(17,582)	(14,887)	(29,364)	(26,930)
Opening net debt/(cash)	(9,420)	(41,965)	(24,190)	(9,302)	20,062
HP finance leases initiated	0	0	0	0	0
Other	1	(193)	0	0	0
Closing net debt/(cash)	(41,965)	(24,190)	(9,302)	20,062	46,991

Source: Edison Investment Research, Pixium Vision accounts. Note: 2014 and 2015 revenues include tax credits and subsidies, which are forecast at $3m per year through 2018.

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