



REGAINING VISION, REGAINING LIFE

JPMorgan – TROUT conference San Francisco, January 11-14, 2015

### Disclaimer

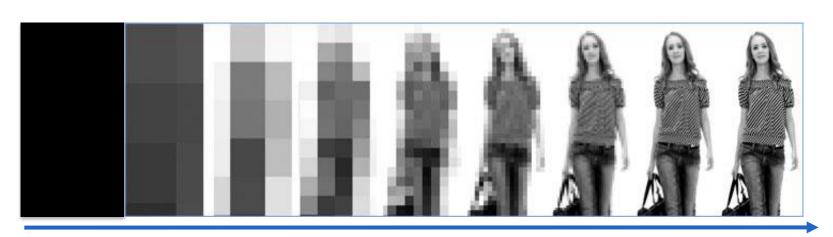
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### Pixium Vision: our mission

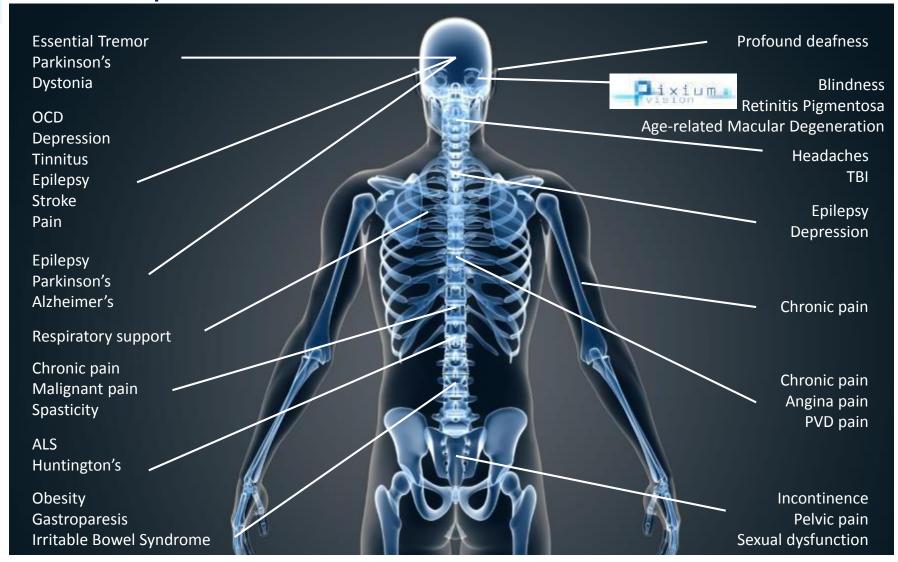


To provide the best-in-class vision restoration systems enabling the blind to regain greater autonomy





## Pixium Vision, pushing new frontier of "neuro-ophthal-modulation"





## An experienced management team

#### Bernard Gilly, Chairman



- 20+ years experience in the lifesciences sector
- Fovea Pharma (2005-2009)
   Chairman & CEO sold to Sanofi
- Sofinova (2000-2005) Managing Partner
- Transgene (1992-2000) -Chairman & CEO

#### Khalid Ishaque, CEO



- 20+ years experience in the medtech industry in neuromodulation
- Boston Scientific (1997-2014) -General Manager
   Neuromodulation International

Pierre Kemula, CFO



- 14 years experience in Corporate Finance / Financial Markets
- Ipsen VP IR, Finance & Treasury
- Strategy Consulting (Bossard; Roland Berger)

Guillaume Buc,



Karine Chevrie, RA/QA Dir



Robert Hill,



Sylvie Murgo,







### Pixium Vision

- 1 The only company with 2 proprietary retinal implant systems
  - An eco-system of global scientific & technological excellence
  - Intellectual Property & Know-How : Over 250 patents
- Attractive addressable >1 Billion Euro + market opportunity\*
  - 3 Two differentiated systems:
    - IRIS® system close to commercialization for Retinitis Pigmentosa (RP)
    - PRIMA to expand the market opportunity with AMD
    - Experienced and dedicated management executing the strategy

Establish Pixium Vision's position as a leader in Vision Restoration Systems



# Imagine how much blind people miss out on...

## Progress 15-17 months Observations





### Blindness

Costs and target pathologies

## Solving blindness from macular degeneration: a major market opportunity

#### Blindness epidemiology

- 285 million people in the world are visually impaired
- 40–45 million people in the world are totally blind
- In the US and Europe, blindness costs exceed tens of billions of USD per annum



## Retinitis Pigmentosa (RP)

- Genetic disease ~ 1/4000
- Blindness occurrence: ~ 3540 years old
- Worldwide prevalence: 1.5 to 2 million
- Prevalence in the US + EU: 350,000 - 400,000
- Incidence (US + EU): 15k-20k patients annually



#### Age-related Macular Degeneration (AMD)

- Age-related disease
- Later blindness occurence: 70+ years old
- Worldwide prevalence: 12 to 15 million
- Prevalence in the US + EU: 4 million
- Incidence (US + EU): 350k400k patients annually

#### Retinitis Pigmentosa is Pixium Vision's initial target market

Sources: World Health Statistics. World Health Organization -http://www.amd.org -NORC Cost of Vision Problems: The Economic Burden of Vision Loss and Eye Disorders in the United States -Study commissioned by Prevent Blindness in America and conducted by University of Chicago -European Forum Against Blindness (EFAB) Source: 2012 World Health Organization – by 2020 there will be 75 million blind people in the world and 314 million partially-blind people Fighting Blindness (UK): 25K in UK and over 2M worldwide CentralSight fact sheet End-Stage Age-related Macular Degeneration



## The loss of the photoreceptor function is a major cause of blindness

The eye transforms light into electric signals

Cornea

Cornea

Pupil

G

H

T

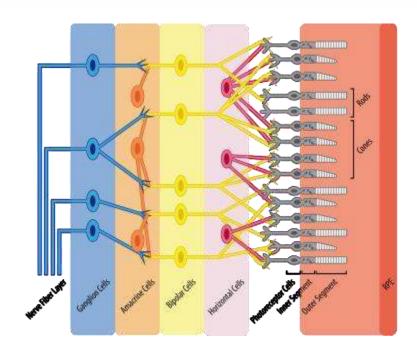
Ciliary body

Choroid

Retina

Optic nerve

Photoreceptor degeneration does not affect the rest of the retina



- Photoreceptor cells convert light into signals
- The human retina contains 6 million cone cells responsible for central vision

- RP and AMD are linked to photoreceptor degeneration
- However, bipolar cells, ganglion cells and downstream visual pathways remain INTACT and FUNCTIONAL in the vast majority of RP and AMD patients

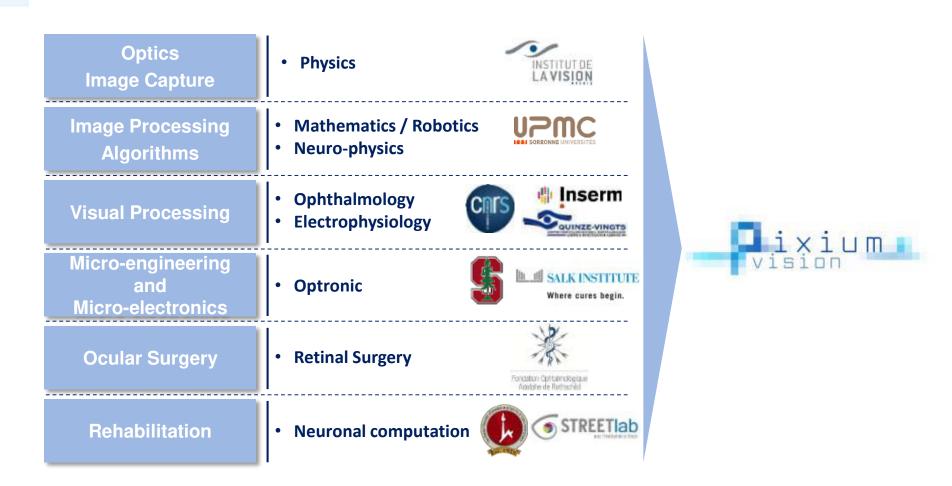




#### **Pixium Vision**

The convergence of excellence providing a solid intellectual property

## Pixium Vision systems are supported by global expertise, resulting in a strong patent position



Pixium Vision has built a strong Intellectual Property & Know-How with more than 250 patents



## Pixium continues to strengthen its IP position

#### New initiatives

- 7 patents granted with IRIS® since January 2015
- 5 new patent applications filed on both IRIS® and PRIMA further strengthen the portfolio

#### **Defensive**

The company strives to protect its competitive patent position with:

- 1 patent maintained in Europe following opposition claim by a competitor
- 2 US competitor European patents revoked following successful oppositions led by Pixium Vision

Supporting the technology development and industrialization

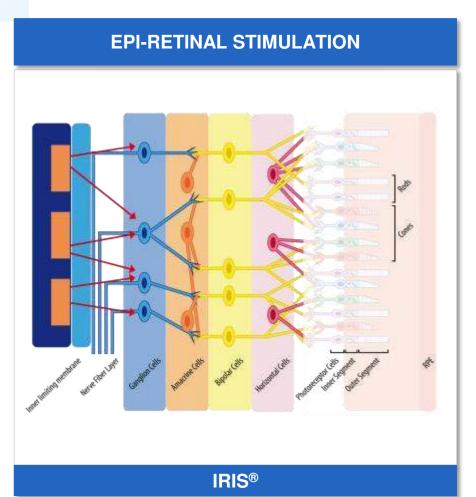


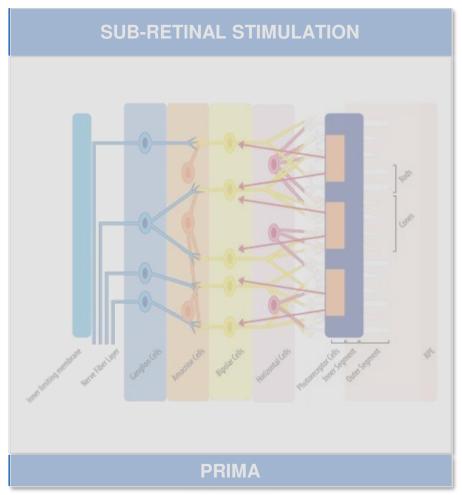


### **IRIS®**

A state of the art Vision Restoration System

## Pixium Vision, the only company to develop two proprietary retinal implant systems



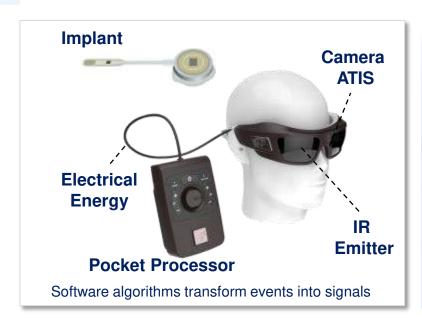






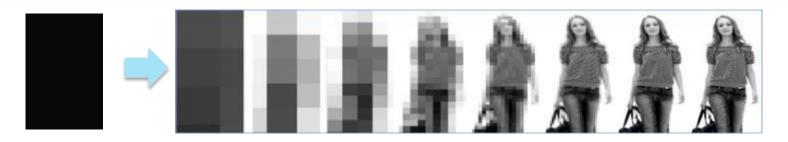


## IRIS®, a technically advanced system targeting Retinitis Pigmentosa





Initial goal is to deliver light and shape perception, and to localize objects giving the patient the ability to negotiate an unfamiliar environment





## IRIS®: A technically advanced and differentiated VRS



	Device Features	IRIS®	Main Competitor	IRIS <sup>®</sup> Advantage
Technology	Camera	Neuromorphic Event Based	Frame Based	How the human brain works
	Patient Programming - Tuneability	Yes	No	All patients respond and learn differently; IRIS is flexible to patient needs
	Number of Electrodes	150 electrodes	60 electrodes	Allow smarter stimulation combinations
Surgery	Surgical Procedure	2.5 hours	Up to 4 hours	Easier to implant;
	Explant and Replacement	Yes	Replacement not proven	Technology is always evolving and improving; patients need the option of upgrading to new technologies in the future



## SPECTRUM



## How Neuromorphic Image Sensors Steal Tricks From the Human Eye

By prioritizing the dynamic parts of a scene, machines can capture images more efficiently

By Christoph Posch, Ryad Benosman & Ralph Etienne-Cummings Posted 26 Nov 2015

http://spectrum.ieee.org/biomedical/devices/how-neuromorphic-image-sensors-steal-tricks-from-the-human-eye?utm\_source=feedburner-robotics&utm\_medium=feed&utm\_campaign=Feed:+leeeSpectrumRobotics+(IEEE+Spectrum:+Robotics)



## IRIS®, illustration of smart design



#### Competitor

Proprietary epi-retinal tack that allows release of implant on the retina i.e. explantation

Illustration of proprietary epi-retinal tack that **does not** allow explantation



Silicon ring (not fitted here) allows release of intra-ocular implant section



Spring does not allow for release of intraocular implant section

Patented: a key feature allowing patients to replace / upgrade





## IRIS®: A clear path to market Aiming for a leading market position

### IRIS®: Continue to build evidence for CE Mark

#### **Ongoing Clinical Trial**

- Incidence, severity and duration of all adverse events at 4, 6, 9, 12 and 18 months
  - Assessment of the capability of patients to *perform visual tasks* with and without the device at 4, 6, 9, 12 and 18 months

#### **Regulatory Path**



#### **Clinical Centers**



Paris & Nantes



Graz



**Hamburg & Bonn** 

#### **Rehabilitation Program**

- Programs tailored for each patient
- Rehabilitation programs will enable further software improvements
- Patients' vision improves during the course of their rehabilitation program



### A lean and specialized commercial organization

#### 25 to 30 key ophthalmic surgery centers in Europe



These centres give access to ~80% of qualifying patients\*

#### Market development process

#### **Ongoing:**

- KOL engagement Discussions with patient associations Participation in major scientific and medical conferences



**Country/market assessments** to select and prioritize centers



Recruitment of a lean internal technical/clinical specialist sales team focused on:

- Commercial & educational activities
- Training & support of orthoptists

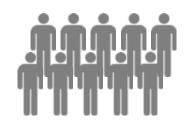


Sales team to reach a peak of 2 to 3 team members per country & sales admin employees



## IRIS® path to the US market

Gather results from European clinical trial







2

## File an Investigational Device Exemption (IDE)

- Pre IDE planned for Q2/Q3 2016
- Pixium Vision anticipates that FDA will require clinical results from at least 30 patients with 2 years followup





3

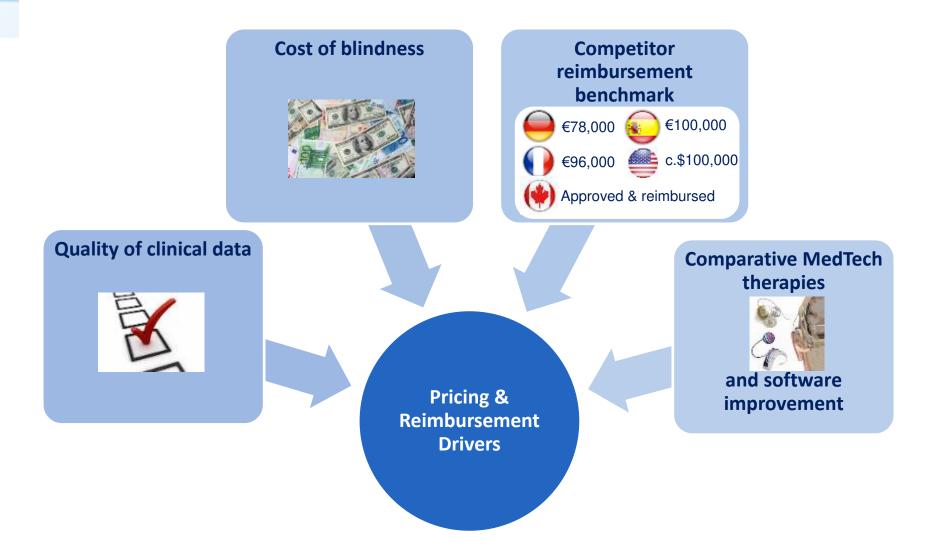
#### Obtain Pre-Market Approval (PMA)

 US launch of IRIS<sup>®</sup> to start 2019





## IRIS® pricing and reimbursement drivers



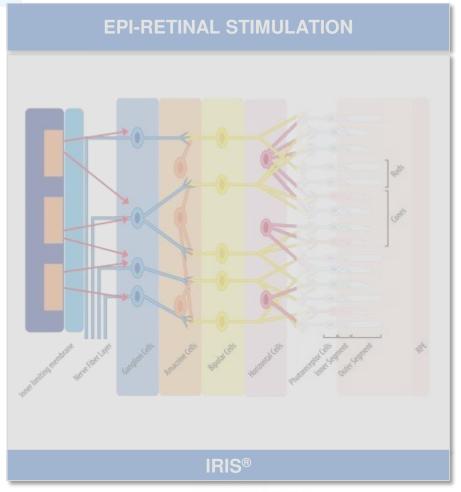


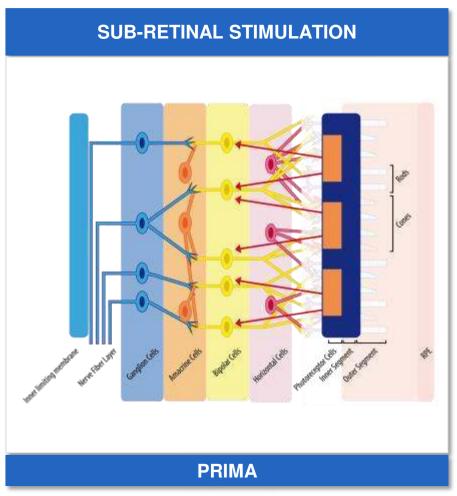


### **PRIMA Vision Restoration System**

Building on IRIS® leading market position

## Pixium Vision, the only company to develop two proprietary retinal implant systems











### Treating Macular Degeneration AMD:

"Tiny implantable solar panels could help the blind see one day"

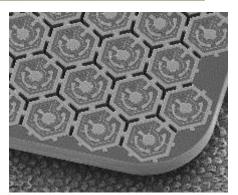


#### Treating blindness

Bionic eyes

A new device may restore vision to those whose sight is dwindling





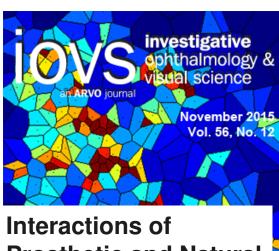


## Photovoltaic restoration of sight with high visual acuity



#### Nature

Medicine (2015) doi:10.1038/nm.3851 http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.3851.





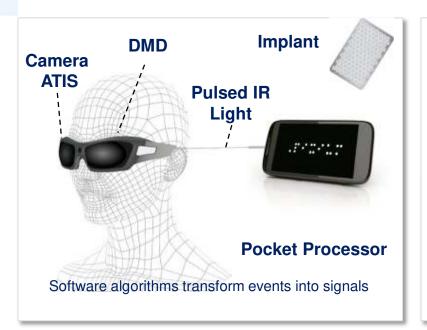


http://iovs.arvojournals.org/article.aspx?articleid=2474145&res ultClick=1



### The PRIMA System, more optimal approach for AMD

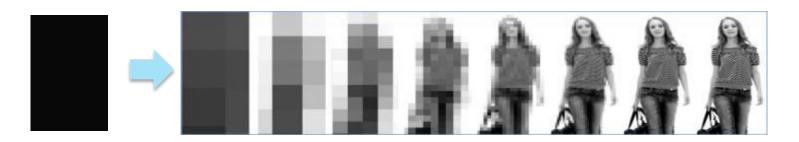
A technically advanced system designed to deliver further clinical benefits





- Physiological signal processing
- Simpler and shorter surgical procedure
- Retinal chips in modules up to several 1000 electrodes
- Advanced processing algorithms
- Reduced energy requirements enabling miniaturization of components

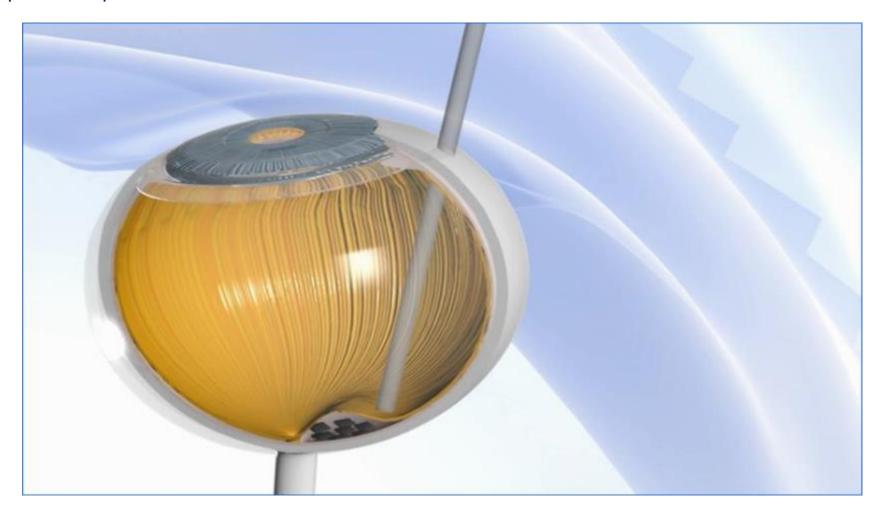
#### Goal is to deliver improved visual perception to the level of direct facial recognition





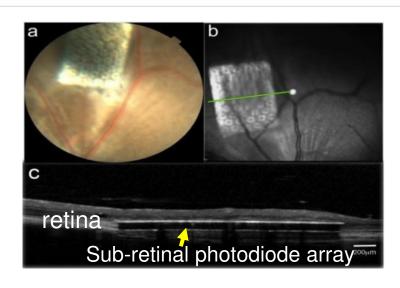
## PRIMA, a sub-retinal implant

Prima to directly stimulate the retinal cells that were directly connected to the photoreceptors

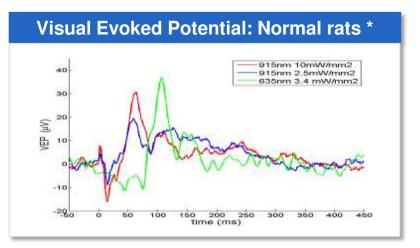


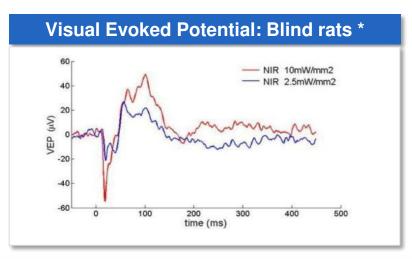


## PRIMA: Validated in pre-clinical models Nature Medicine 2015: Photovoltaic restoration of sight with high visual acuity



- Proof of concept achieved in rats
- Safety demonstrated in rats and pigs
- Scale-up of manufacturing process ongoing
- First in man expected in 2016





In rats with retinal degeneration, PRIMA elicited retinal responses with a spatial resolution of  $64 \pm 11$  mm, corresponding to *half of the normal visual acuity in healthy rats* 



- Ref: J. Neural. Eng 9: 046014(2012)
- IEEE EMBS Neural Engineering Conference 22 April 2015
- Nature Medicine (2015) doi:10.1038/nm.3851 http://www.nature.com/nm/journal/vaop/ncurrent/full/nm.3851.html

## PRIMA rat data, published in Nature Medicine, show restoration of half of normal visual acuity

- 70 μ m-wide pixels provide highly localized stimulation of retinal neurons in rats
- Electrical receptive fields recorded in retinal ganglion cells were similar in size to the natural visual receptive fields
- Similarly to normal vision, the retinal response to prosthetic stimulation exhibited:
  - flicker fusion at high frequencies
  - adaptation to static images
  - nonlinear spatial summation



PRIMA implant

photoreceptors

Inner nuclear layer

Ganglion cells (GCL)

Multi-electrode array (MEA)

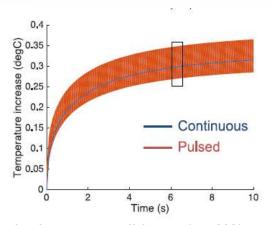
Healthy rat retina sandwiched between a transparent MEA which records electrical field at the ganglion cell layer (GCL) level

In rats with retinal degeneration, PRIMA elicited retinal responses with a spatial resolution of  $64 \pm 11$  mm, corresponding to *half of the normal visual acuity in healthy rats* 

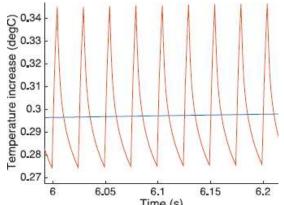


## Thermal Safety of PRIMA is demonstrated with temperature rise well within required standards

Model of retinal temperature rise in typical use (5ms, 40Hz) of NIR beam



- In typical use conditions (5mW/mm2, 5ms pulses at 40Hz, with 2-4.5mm diameter implant and 4.5mm beam), the temperature increase predicted by the model will be within the range of 0.17-0.43°C
- These power settings are well above levels shown in previous trials to allow stimulation of animal retina.



- Pulsing light generates temperature spikes of about 0.05°C, oscillating around the blue line corresponding to the average power, a negligible variation within the natural temperature range in the body.
- Pulsing allows reduction of the chip temperature increase in a quasi-linear manner vs duty cycle (% of time when light is on).

These results are more than 4 times below the recommended thermal safety limit of 2°C for active implanted medical devices

Source: Retinal safety of near infrared radiation in photovoltaic restoration of sight - BIOMEDICAL OPTICS EXPRESS 4 Dec. 2015

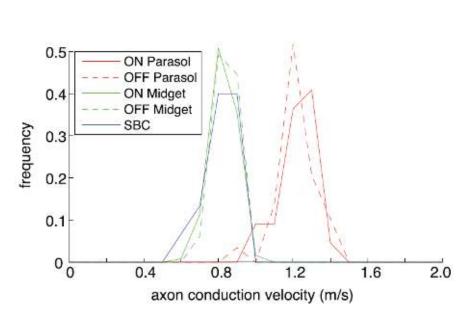


## Spike speed to differentiate RGC types



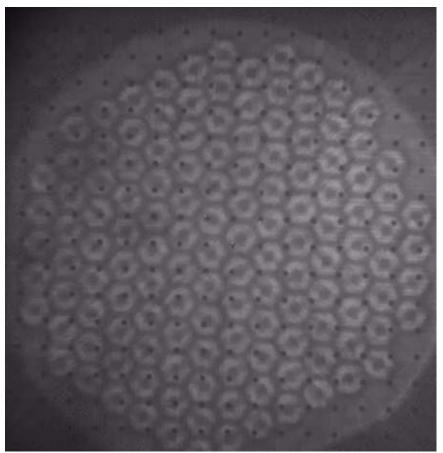
7 pixels stimulation, 75μm pixels, 1.25mW.mm<sup>-2</sup>, 5ms, 5Hz

4ms video



Anatomical Identification of Extracellularly Recorded Cells in Large-Scale Multielectrode Recordings.

Peter H. Li, E.J. Chichilnisky

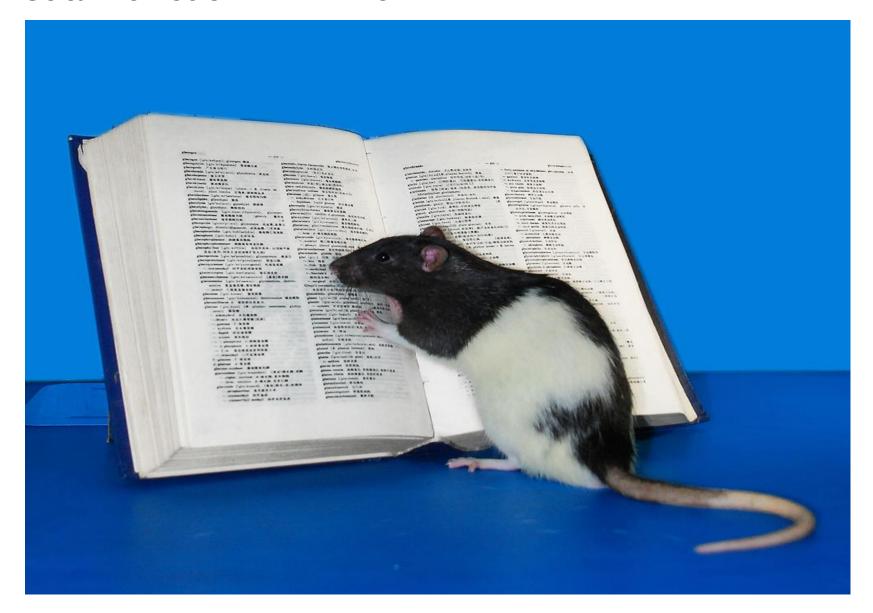


Calculated spike speed:  $0.73 \pm 0.2 \text{m.s}^{-1}$ 

Measure of the interspike interval necessary to differentiate between ON and OFF cell types



### Visual Function – in vivo ?





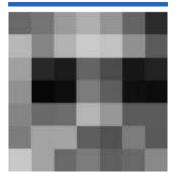


### In short

## Pixium Vision Creating a world of Bionic Vision



IRIS 50



IRIS <sub>150</sub>



PRIMA 1 chip 400 electrodes



PRIMA 4 chips 1600 electrodes



**Today IRIS** 

- Epi-retinal implant in clinical with novel proprietary Neuromorphic sensor
- Toward Higher Resolution 150 electrodes

Commercial Launch: 2016 in EU

#### **Tomorrow PRIMA**

- Sub-retinal implant with proprietary passive wireless microphotodiodes
- Toward Facial Recognition

First in man: 2016



# Giving sight, giving life: making an impact in lives of people who have lost their sight

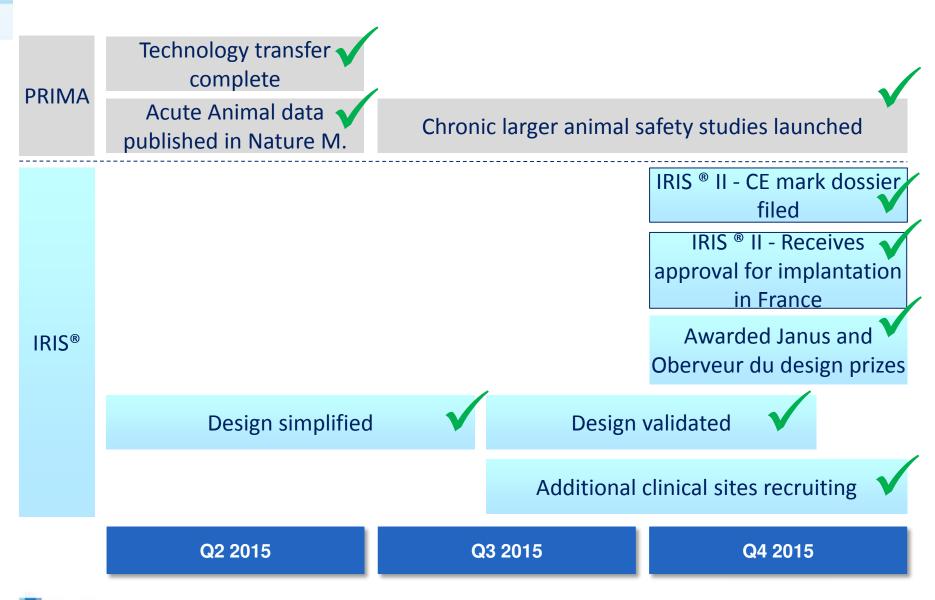






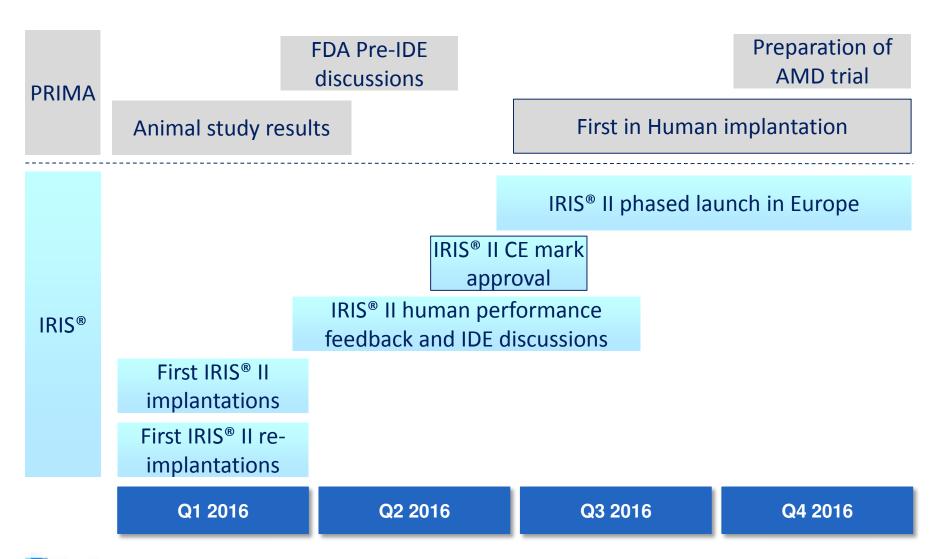
# Continuing to move forward, more to come

## Execution accelerating throughout 2015...





## ... setting the scene for a rich 2016 newsflow









Pixium Vision is listed on Euronext (Compartment C) in Paris.

LISTED ISIN: FR0011950641; Mnemo: PIX

EURONEXT IRIS® is a trademark of Pixium-Vision SA

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**Pixium-Vision.com** 



### Thank You





@PixiumVision
#PixiumVision



## 1H 2015 - Update

# Strong cash position with €28.1m in cash at September 30, 2015

#### Other operating income of the first nine months

	First nine mo	First nine months		
in thousand euros	2015	2014		
Operating income / other income	2 652.0	1 564.3		

#### **Cash flow statement summary**

	First nine mo	First nine months	
in thousand euros	2015	2014	
Opening cash and cash equivalents	42 131.7	9 420.2	
(Decrease) / Increase in cash position	(14 049.5)	33 383.6	
O/W net cash flows from operating activities	(12 088.2)	(7 538.6)	
Closing cash and cash equivalents	28 082.2	42 803.6	



# Strong cash position with €31m in cash at June 30, 2015

ral Summary	P&L	summary
-------------	-----	---------

in thousand euros	H1 2015	H1 2014
Operating income / other income	1 737.7	1 104.1
Research and Development	(7 999.1)	(4 510.6)
General and Administrative	(1 766.5)	(930.1)
Operating income	(8 027.9)	(4 336.5)
Net profit	(7 953.8)	(4 325.7)
Earnings per share	(0.63) €	€ (0.62)

#### Cash flow statement summary

in thousand euros	H1 2015	H1 2014
Opening cash and cash equivalents	42 131.7	9 420.2
(Decrease) / Increase in cash position	(11 050.6)	32 383.4
O/W net cash flows from operating activities	(9 504.2)	(4 530.1)
O/W net cash flows from investing activities	(1 571.6)	(1 629.1)
Closing cash and cash equivalents	31 081.2	41 803.6





# Thank You

www.pixium-vision.com

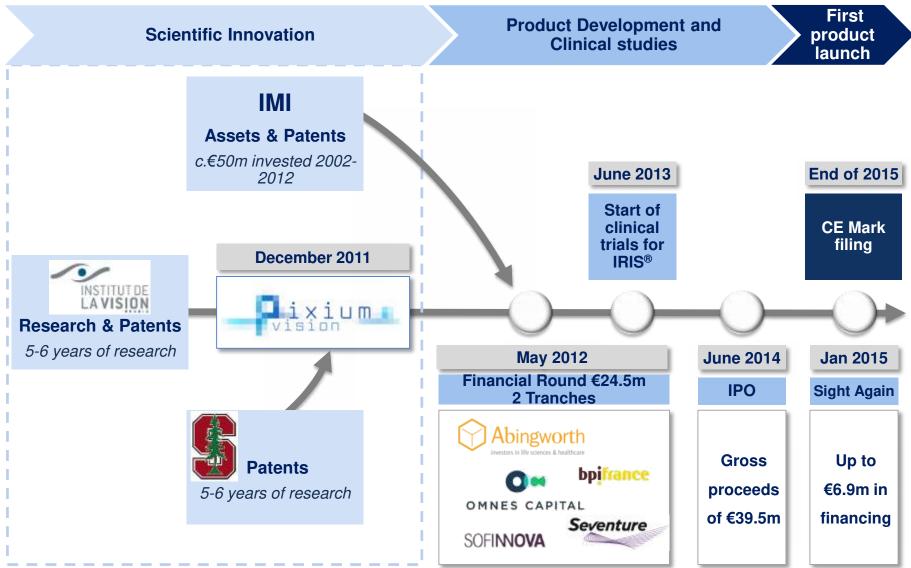




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# The Pixium Vision story relies on the convergence of technology and financing

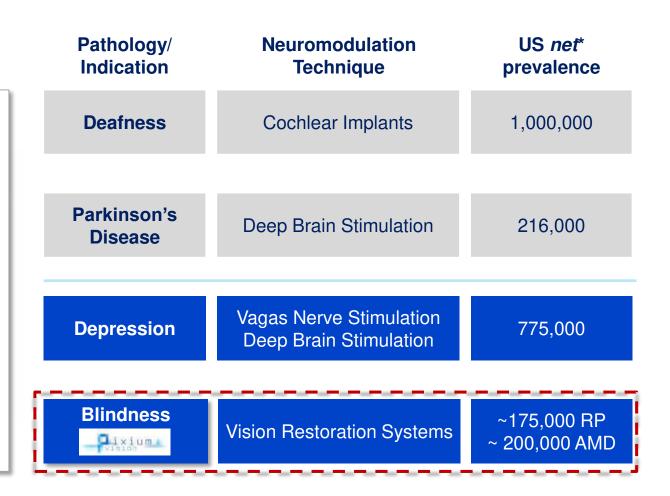


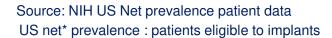


# With its technology, Pixium Vision is well positioned in the fast growing neuromodulation market

## What is Neuromodulation?

- Induction of biological responses from electrical stimulation on nerves or zone where nerve activity is affected
- \$5Bn+ market by 2018 implying a high double digit growth rate (around 15%)





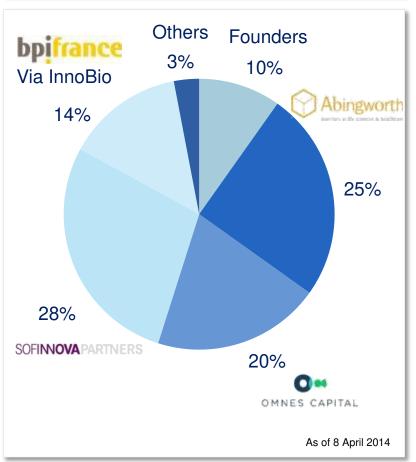




## Shareholder structure

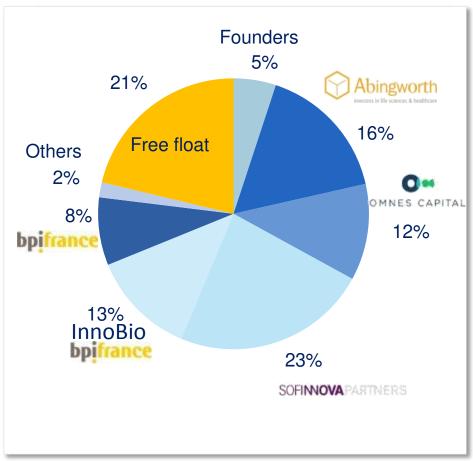
#### **Pre-IPO shareholder structure**

On a non-diluted basis



#### Post-IPO shareholder structure

On a non-diluted basis
(with full exercise of the extension clause and overallotment option exercised at 95.8%)





# Competitive landscape

System	Number of Electrodes	Epi-Retinal Or Sub-Retinal	Features & Benefits	Clinical Results	Regulatory Status
Pixium Puixium	<ul> <li>IRIS®: 50 to 150</li> <li>PRIMA: several thousand</li> </ul>	<ul> <li>IRIS<sup>®</sup>: Epi-Retinal</li> <li>PRIMA: Sub- retinal</li> </ul>	<ul> <li>2h surgery</li> <li>Explantable</li> <li>Neuromorphic Camera</li> <li>Tunable software</li> </ul>	<ul> <li>Short term study on 19 patients</li> <li>10 Patients CE mark study ongoing</li> </ul>	• CE Mark filing end of 2015
Second Sight	Argus II : 60     electrodes	• Epi-retinal	CMOS camera	<ul><li>Argus I: 6 patients</li><li>Argus II: IDE on 30 patients</li></ul>	<ul> <li>Argus-II CE Mark Feb 2011</li> <li>FDA HDE Feb 2013</li> </ul>
retina implant	Alpha IMS	• Sub-Retinal	<ul><li>Visual field of 12°</li><li>Non explantable</li></ul>	<ul><li>11 patients from 2005 to 2009</li><li>30 patients CE mark</li></ul>	• CE Mark July 2013
Na Retina	• 500 electrodes	Insufficient data	No camera	<ul> <li>Launch scheduled for 2016</li> </ul>	Pre-clinical     phase

