



**Jefferies 2013 Global Healthcare  
Conference  
New York, June 3-6, 2013**

Michele Garufi, Chairman & CEO



# Disclaimer

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**This presentation contains certain forward-looking statements. Although the Company believes its expectations are based on reasonable assumptions, these forward-looking statements are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated in the forward-looking statements.**

**Risks factors which are likely to have a material effect on Nicox's business are presented in the 4th chapter of the « Document de référence, rapport financier annuel et rapport de gestion 2012 » filed with the French Autorité des Marchés Financiers (AMF) on March 22, 2013 and available on Nicox's website ([www.nicox.com](http://www.nicox.com)) and on the AMF's website ([www.amf-france.org](http://www.amf-france.org)).**

# Nicox: Our Foundation



## Helping people to enhance their sight

An international ophthalmic company with a diversified portfolio of innovative therapies and diagnostic tools addressing the medical needs of eye care practitioners and patients around the world.

# Nicox Overview

- Nitric Oxide(NO)-donating technology enabling advanced clinical-stage programs
  - Latanoprostene bunod, glaucoma drug candidate, in phase 3 program following positive phase 2b results
    - Worldwide licensing agreement with Bausch + Lomb
    - Global glaucoma market of \$5 billion<sup>(1)</sup>
- Commercial-stage company with entrance to market with AdenoPlus<sup>®</sup>
  - Only FDA-cleared diagnostic for acute conjunctivitis; launched in Oct. 2012
  - Worldwide in-license agreement with RPS<sup>®</sup>
- Management and Operations teams with successful track record in product development and commercial launches in the ophthalmic market
- Cash and cash equivalents of more than €72 million as of March 31, 2013 (~approx.\$92.7 million)

(1) Source: McKinsey & Co.

# Nicox's Growth Strategy

## Global Commercial Expansion

- Establishment of effective marketing & sales structures in the US and in the key European markets
- Collaborations and alliances with partners in the ophthalmic market for the rest of the world

## Leverage our World-Leading Nitric Oxide-donating Research Platform In Ophthalmology

- Focus our Research activities on ocular disorders where Nitric Oxide plays an important role
- Explore alternative funding options to ensure development of innovative, non-core early-stage projects

# Differentiated Global Growth Expansion in Ophthalmology

## *United States*

- In-licensing of new products
- Co-promotion deals
- Establishing field force targeting eye care specialists

## *5 Largest EU Countries*

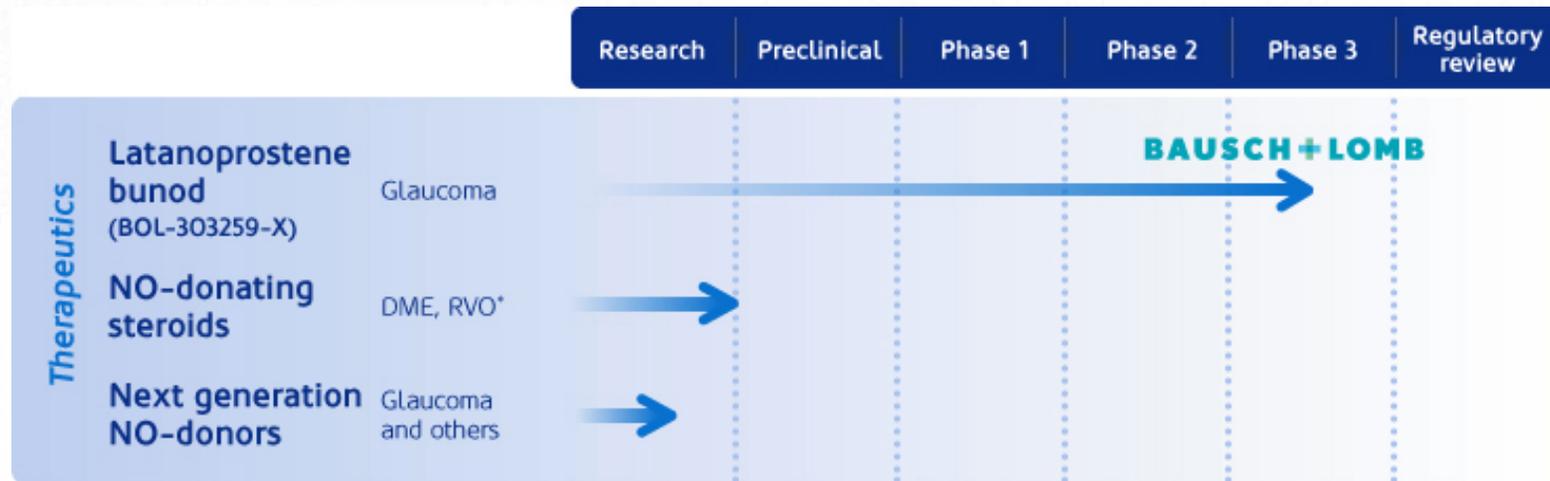
*France, UK, Spain, Germany, Italy*

- Acquisition and in-licensing of commercial & late-stage projects
- Establishing sales network independently and through acquisition/alliances

## *ROW*

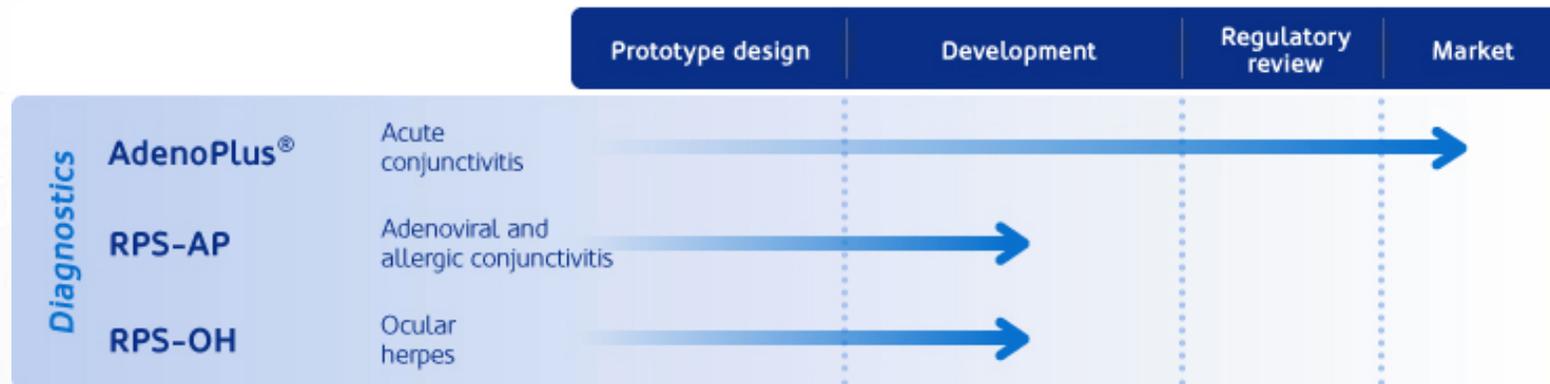
- Partner with local companies with relevant expertise and distribution channels

# Innovative Ophthalmology Pipeline

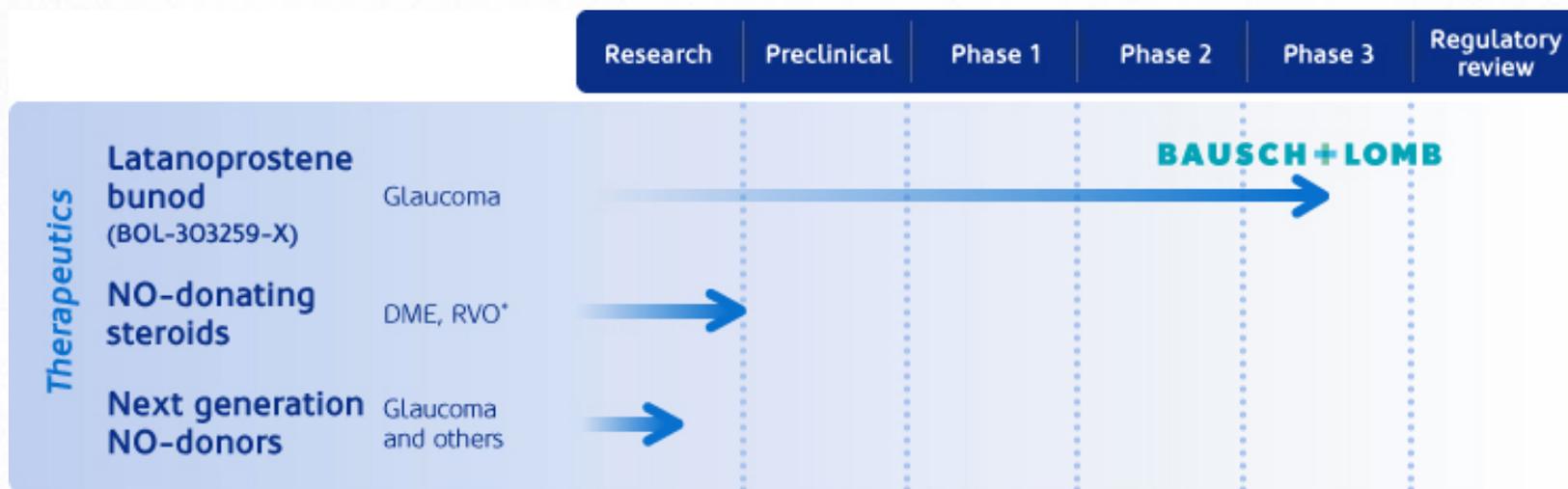


\*DME: Diabetic Macular Edema. RVO: Retinal Vein Occlusion

<p><b>Pipeline Expansion: A New Range of Eyecare Products</b></p>	<ul style="list-style-type: none"> <li>• Exclusive supply and distribution agreement with private European ophthalmics company – March 2013</li> <li>• Novel products developed for a major therapeutic class w/ differentiated formulation</li> <li>• Expect launch in late 2013</li> </ul>
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# Ophthalmology: Focus on Therapeutics



\*DME: Diabetic Macular Edema. RVO: Retinal Vein Occlusion

## Global Ophthalmic Market

- 2010: \$10.3 billion
- 2017 forecast: \$13.2 billion

Source: Ophthalmology Therapeutics Market to 2017, GBI Research, Oct. 2011

# Leading Nitric Oxide-donating Research Platform

## Nitric Oxide (NO)

A key signaling molecule in a variety of biological processes

- Strong heritage of innovation in NO technology
  - World-leading specialized Research Center (Bresso, Italy):
    - R&D studies covering many therapy areas such as cardiovascular, inflammation and ophthalmology
    - 28 chemical families covering products and therapeutics that generated more than 520 granted patents/patent applications
    - More than 400 research papers published in peer-reviewed journals
- Broad program of next generation of NO-donating compounds in active research
- Long-term collaborations with industry leaders that have generated so far €87 million of revenues
  - AstraZeneca, Merck, Pfizer, Bausch + Lomb, *etc...*

# Innovative NO-donating Ophthalmic Portfolio

## Nitric Oxide Involved in Eye Physiology and Pathophysiology

### IOP lowering / glaucoma

- Latanoprostene bunod with B+L in Phase 3
- Additional NO-prostaglandins
- Next generation NO-donors

### Diabetic Macular Edema (DME) Retinal Vein Occlusion (RVO)

- Intravitreal NCX-434 and NCX-422 NO-steroids ready to start IND-enabling studies

### Ocular inflammation

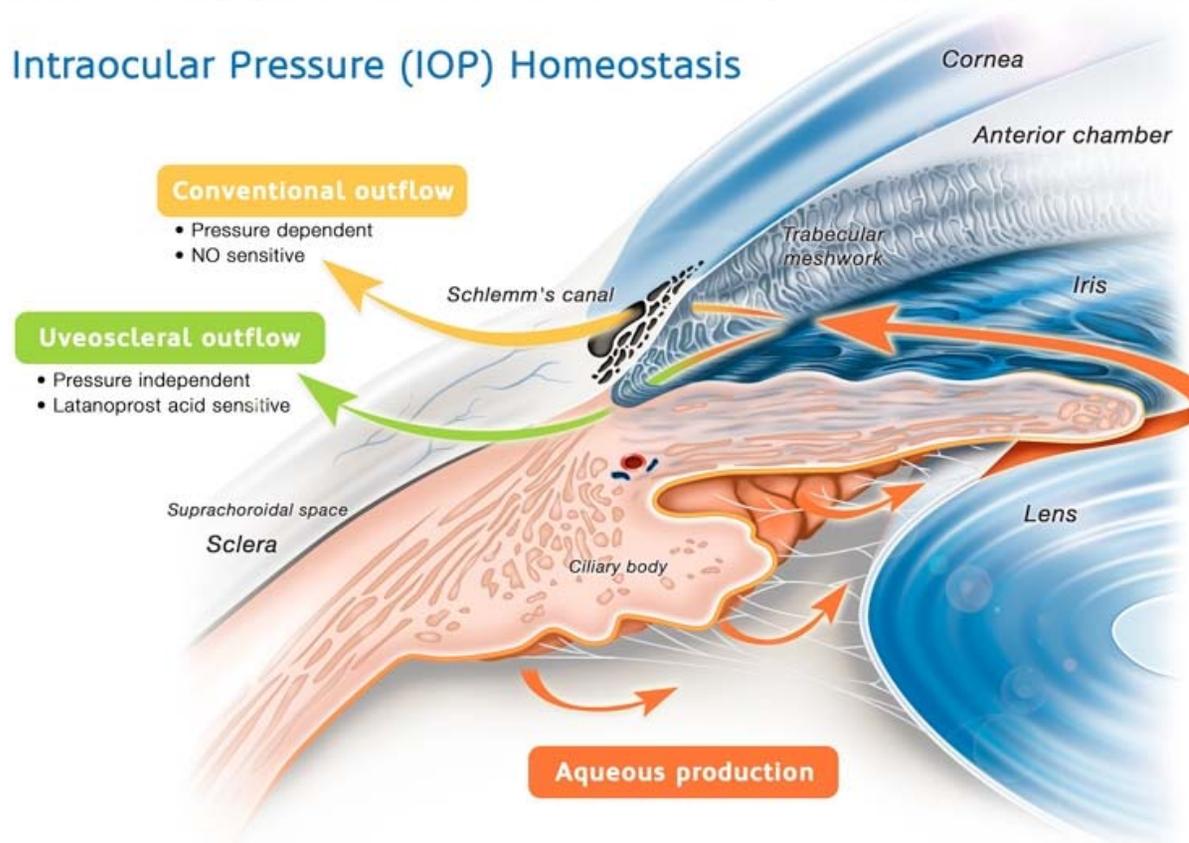
- Research project on NO-steroids

# Glaucoma Drug Candidate In Phase 3 with B+L

Latanoprostene bunod, first NO-donating PGF2 $\alpha$  analog for the potential treatment of glaucoma and ocular hypertension

- Phase 3 program initiated by Bausch + Lomb in January 2013
- Only compound that showed superiority to latanoprost in clinical trials:
  - Primary efficacy endpoint met in Phase 2b study - reduction in mean diurnal IOP on day 28
  - Positive results compared to latanoprost on a number of secondary endpoints including responder rate and duration of action
- Worldwide licensing agreement signed with Bausch + Lomb in 2010

# Strategy Focusing on Dual Mechanism of Action NO/cGMP and FP Receptor-mediated IOP



Latanoprostene bunod targets two distinct anatomical compartments each contributing to aqueous humor outflow

# Latanoprostene Bunod

## ***Primary Endpoint Met In Phase 2b Study***

- Phase 2b study to identify the most efficacious and safe dose of latanoprostene bunod for the reduction of IOP
  - Randomized, investigator-masked
  - 413 patients randomized, received latanoprostene bunod (various concentrations) or latanoprost 0.005% once a day in the evening for 28 days
- Primary endpoint met
  - Statistically significant reduction in mean diurnal IOP compared with latanoprost 0.005% for two doses of latanoprostene bunod on day 28
  - Differences >1mmHg ( $p < 0.01$ )
- Responder rate
  - Definition: proportion of patients achieving an IOP of 18mmHg or less
  - 68.7% for the most efficacious dose of latanoprostene bunod, compared to 47.5% for latanoprost 0.005% ( $p = 0.006$ )
- Duration of action
  - Consistently better control of IOP over 24 hours
- Latanoprostene bunod safety comparable to latanoprost

# Latanoprostene Bunod

## ***Phase 3 Clinical Program Initiated In January 2013***

- Includes two separate studies, APOLLO and LUNAR:
  - Randomized, multi-center, double-masked, parallel-group
  - Combined total of ~800 patients in North America and Europe
  - Pivotal for US registration
- Phase 3 studies to compare the efficacy and safety of latanoprostene bunod with timolol maleate in lowering IOP:
  - Patients will receive latanoprostene bunod once daily or timolol maleate 0.5% twice daily during three months of treatment
- Primary endpoint:
  - Reduction in mean IOP measured at specified time points during three months of treatment
- Additional secondary endpoints will also be evaluated
- Open-label safety phase:
  - Patients will receive latanoprostene bunod once daily for an additional 9 months in the APOLLO study and for an additional 3 months in the LUNAR study

# Latanoprostene Bunod

## ***A Strong Partnership with Bausch + Lomb***

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- Worldwide licensing agreement signed with Bausch + Lomb in 2010
- Bausch + Lomb granted exclusive worldwide rights to develop and commercialize latanoprostene bunod
  - \$10 million initial license payment in March 2010
  - \$10 million paid in April 2012 following B+L decision to pursue development
  - Potential development, regulatory, commercialization and sales based milestones, which could total an additional \$162.5 million
  - Tiered double-digit royalties on the sales
  - B+L responsible for funding all development and commercialization activities
- Nicox has the option to co-promote latanoprostene bunod products in the United States

# NO-steroids: NO-donating glucocorticoids

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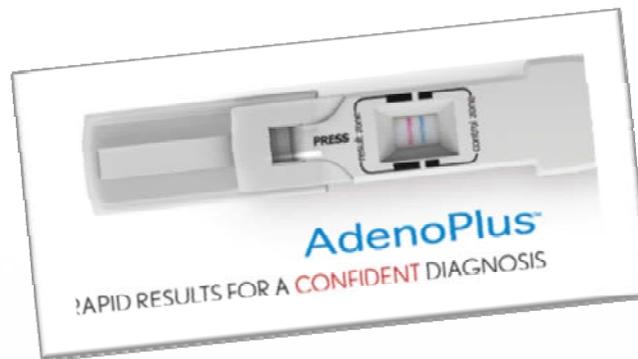
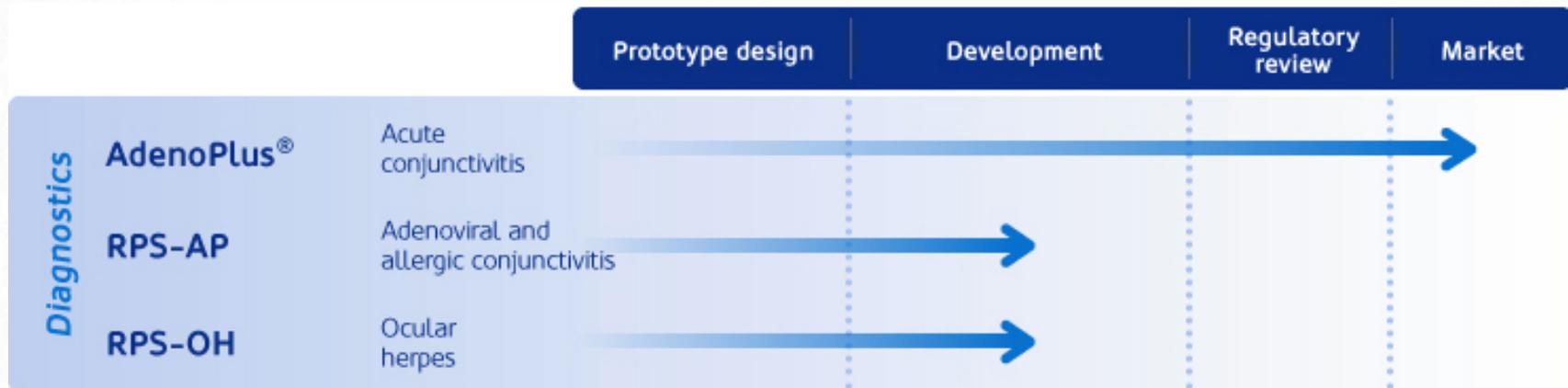
- Target profile and Mechanism of Action:
  - Intravitreal administration or potential as eye drops
  - Low liability for increase in IOP
  - Potential of retinal cell protection
  - Reduce oxidative stress and inflammatory cytokines
- Competitive advantages:
  - Two lead compounds (NCX-434 and NCX-422) ready for IND-enabling program
  - Sustained and potent activity following intravitreal administration
  - Show little or no IOP increase in experimental models
  - Reduce oxidative and inflammatory markers

# Next Generation NO-donors

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- Target profile:
  - Topically effective
  - Extended NO donation enabling long duration of action
  - Retain efficacy over repeated administration (no tolerance)
  - NMEs with new IP
- Competitive Advantages:
  - Compounds specifically designed to target selected disorders associated with NO deficiency
  - NO donation can be titrated without the constraints of the dosing of the parent drug
  - Broad potential by combining with different other therapeutics

# Ophthalmology: Focus on Diagnostics



# AdenoPlus®

## *For The Differential Diagnosis Of Acute Conjunctivitis*

**First and only FDA-cleared, CLIA-waived,  
rapid point-of-care diagnostic test  
that aids in the differential diagnosis of acute conjunctivitis**



- AdenoPlus® detects adenovirus in only 10 min.
- Marketed to US eye care practitioners by Nicox's specialized sales force
- CE marked in Europe

# AdenoPlus®

## ***Addressing an Unmet Medical Need***

- Over 6 million cases of acute conjunctivitis are contracted each year in the U.S.<sup>(1)</sup>
  - Most often caused by a bacterium, virus or allergen
  - Misdiagnosed in up to 50% of cases using signs and symptoms alone<sup>(2)</sup>
- Adenoviral form is highly contagious
  - Causes approx. 1 out of 4 cases seen by eye care professionals<sup>(2)</sup>
  - Antibiotics, although ineffective against this form, are still widely prescribed
- AdenoPlus® allows for better therapeutic decisions based on diagnostic evidence
  - May avoid spread of disease
  - May help in reducing the potential for misuse of antibiotics, reducing unnecessary costs and avoiding potential adverse reactions

(1) 2005 Thomson Healthcare Medstat  
(2) O'Brien TP, Jeng BH, McDonald M, et al. *Curr Med Res Opin.* 2009 Aug; 25(8):1953-61.

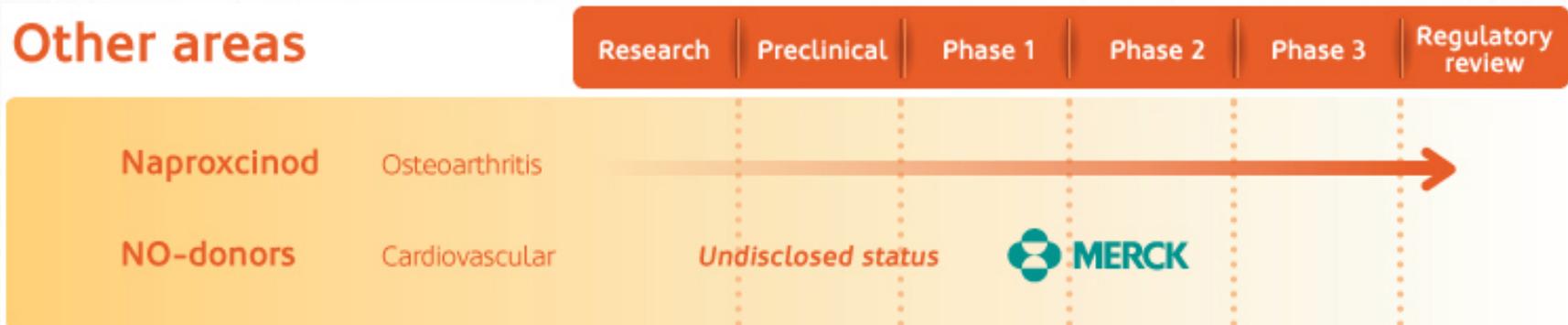
# Worldwide In-licensing Agreement With RPS®

- Innovative point-of-care ocular diagnostic tests
  - AdenoPlus® for adenoviral conjunctivitis – marketed
  - RPS-AP test for the combined detection of adenoviral and allergic conjunctivitis – in development
  - RPS-OH test for ocular herpes – in development
  - Exclusive option for an undisclosed additional product
- Nicox granted exclusive marketing rights to US eye care professionals
  - ROW: Nicox granted full exclusive rights
- Financial terms
  - License and option fees paid to RPS®: \$4 million
  - Potential milestone payments up to \$2 million; single-digit royalties
  - Nicox will also pay half of the development costs for the two development-stage products, subject to an agreed budget



# Leveraging Non-core Assets Through Alliances

## Other areas



## Naproxcinod

**2 options are evaluated to progress the development of naproxcinod:**

- Out-licence for the treatment of the signs and symptoms of osteoarthritis of the knee
- OR**
- Out-licence for development as an adjuvant for the treatment of muscular dystrophy



- New approach to NO donation discovered during joint research program
- Merck exploiting this new approach in certain cardiovascular indications, for which it holds worldwide rights
- Next announcement at the potential entry of a candidate in Phase 2

# Naproxcinod repurposing in Muscular Dystrophies

- Duchenne and Becker muscular dystrophies (DMD and BMD) are severe progressive diseases affecting about 3/10,000 live-born males (DMD)
- The dystrophin protein is associated with neuronal NOS, and is absent and truncated in DMD and BMD respectively
- Naproxcinod was found to target two key pathological events for the treatment of muscular dystrophies:
  - Local inflammation
  - Reduced generation of nitric oxide (NO)

- About naproxcinod:
  - Belongs to the CINOD class (Cyclooxygenase Inhibiting Nitric Oxide Donators)
  - Combines the properties of NO with naproxen, a non-steroidal anti-inflammatory drug (NSAID)
  - Clinical stage, phase 2-ready, with significant clinical exposure in more than 4000 patients for treatment of osteoarthritis and demonstrates both nitric oxide (NO) and NSAID properties

# Preclinical studies in muscle dystrophy with naproxcinod

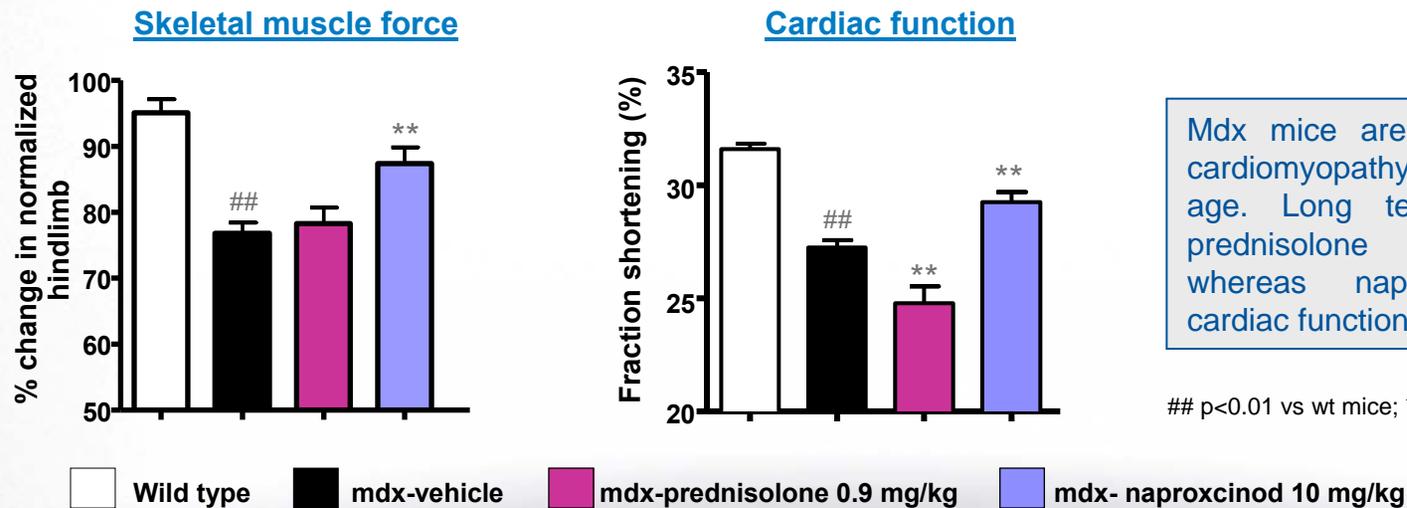
- Research studies have shown that naproxcinod is effective on key mechanisms underlying Duchenne and Becker muscular dystrophy:
  - Local inflammation
  - Muscle regeneration
  - Muscle blood flow

**In a long term (9 months of treatment) confirmatory study\*,  
naproxcinod improves skeletal and cardiac muscle function  
and reduces skeletal muscle inflammation in *mdx* mice**

*\* Collaboration with a leading US center (Children's National Medical Center, Washington DC)*

*Example of results:*

*Naproxcinod significantly improves skeletal muscle force and cardiomyopathy in *mdx* mice*



Mdx mice are known to develop cardiomyopathy at 9-10 months of age. Long term treatment with prednisolone exacerbates it, whereas naproxcinod improves cardiac function.

## p<0.01 vs wt mice; \*\* p<0.01 vs mdx-vehicle

# Seasoned Leadership Team

## **Michele Garufi, PharmD**

**Co-Founder, Chairman and  
Chief Executive Officer**

**30+ years in international pharma**  
*Co-founder of other Research and  
Pharma start-ups*

## **Elisabeth Robinson, Ph.D.**

**Co-Founder, President,  
Nicox Research Institute**

**20+ years in pharma development**  
*Recordati Italy, Techint Engineering &  
Genzyme*

## **Eric Castaldi**

**Chief Financial Officer**  
**20+ years in finance**

*Cordis Corporation, Safety Kleen &  
My Kinda Town*

## **Gavin Spencer, Ph.D.**

**Executive Vice President,  
Corporate Development**

**18+ years in product experience**  
*Novartis Consumer Health &  
Boots Healthcare International*

## **Jerry St. Peter**

**Executive Vice President,  
General Manager**

**23+ years in specialty pharma**  
*Merck & Co., Inspire Pharmaceuticals &  
Muro Pharmaceuticals*

## **Philippe Masquida**

**EVP, Managing Director, EU &  
International Operations**

**22+ years in pharma & ophthalmology**  
*Allergan, Merck, Sanofi Aventis &  
Laboratoires Thea*

# Financial Highlights

*As of March 31, 2013:*

**Debt**

- No long-term debt

**Cash & Cash Equivalents**

- €72.1 million (~\$92.7mm)

*As of March 31, 2013:*

**Basic Shares Outstanding**

- 72.9 million



# Nicox S.A.

*Helping people to enhance  
their sight*

(NYSE Euronext Paris: COX)

