



## **Forward-Looking Statements**

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## Nicox at a glance

Ophthalmology-focused biopharmaceutical company, advancing NO¹-donating therapies

Late-stage Phase
3 program in
glaucoma – NDA<sup>2</sup>
filing targeted
for 2026



Commercialstage assets and R&D collaborations already in place



Global reach with strategic partnerships in Asia



Significant market opportunity - 80 million glaucoma patients worldwide<sup>3</sup>



- Nitric Oxide
- New Drug Application
- 3. World Glaucoma Association website: World Glaucoma Association » What is glaucoma?



## 2025 Opportunities Building on 2024 Achievements

1

Key Achievements in 2024

- ✓ Appointment of Gavin Spencer as Chief Executive Officer
- ✓ Nicox Board entirely renewed with appointment of Damian Marron as Chair and 3 new Board members
- ✓ Restructuring of debt agreements with BlackRock
- ✓ Streamlining costs to concentrate on NCX 470 clinical development
- ✓ Royalty and Equity financing of over €19 million
- ✓ Value proposition of NCX 470 confirmed through Kowa partnership
- ✓ Completion of recruitment of all patients in the Denali trial
- ✓ Approval and launch of ZERVIATE in China
- ✓ Research and licensing option agreement with Glaukos for NCX 1728

2

**Strategic Horizons** 

- Denali results in 2025 to crystallize NCX 470 strategic value
- Business development and partnerships
- Potential strategic transactions



# Consistently Delivering Innovations in Ophthalmology ...

... with NCX 470 the Next Derisked Asset Advancing Toward NDA Filing in the U.S. and China

Commercial Value of Lead
Asset NCX 470 in
Late-Stage Phase 3
Development

- A potentially differentiated profile targeting ~\$6bn worldwide glaucoma market
- Positive results from the first Phase 3 trial<sup>1</sup>, Mont Blanc, demonstrating competitive Intraocular Pressure (IOP) lowering properties
- ➤ Whistler² exploratory trial results support dual mechanism of action
- ➤ **Additional benefits**, e.g. retinal, seen in nonclinical models<sup>3,4</sup> to be explored post-Phase 3

Global Partnerships with Tier 1 Ophthalmology Players

- Partnerships for NCX 470 in Japan with Kowa and in China with Ocumension Therapeutics
- > ZERVIATE commercialised in China, part of multi-product collaboration with Ocumension
- Research and option agreement with Glaukos for NCX 1728
- > VYZULTA® commercialized<sup>5</sup> by Bausch + Lomb

Deep Ophthalmology
Experience

- Two FDA approved products
- Extensive development expertise has generated a focused portfolio of products and product candidates
- Business and corporate development track record, including M&A



<sup>.</sup> Nicox Press release October 31, 2022

<sup>2.</sup> Nicox Press Release May 14, 2025

Bastia et al., J Ocul Pharmacol Ther. 2022, 38: 496-504

<sup>4.</sup> Sgambellone et al., Transl Vis Sci Technol. 2023, 1;12(9):22.

<sup>5.</sup> VYZULTA revenue sold to Soleus Capital in October 2024

## **Upcoming Milestones**

#### **NCX 470**

- ❖ Denali results Q3 2025
- Estimated potential worldwide sales over \$300 million<sup>1</sup>
- Phase 3 clinical trial initiation
   in Japan expected H2 2025

#### **ZERVIATE**

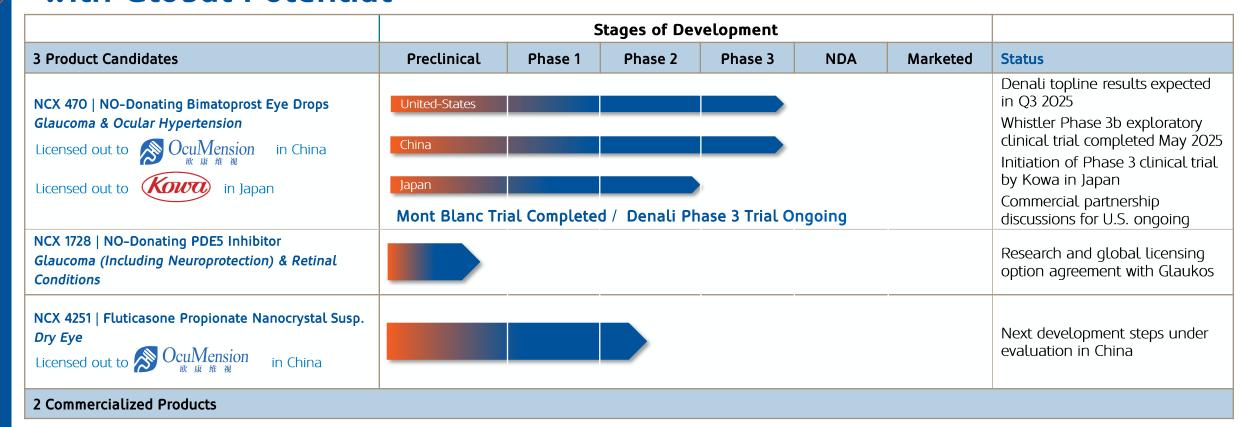
\* Recurrent revenue

### Corporate

- Ongoing partnership discussions
- Potential NCX 1728 license option exercise with Glaukos



# An Innovative Portfolio Led by NCX 470, a Derisked Product Candidate with Global Potential



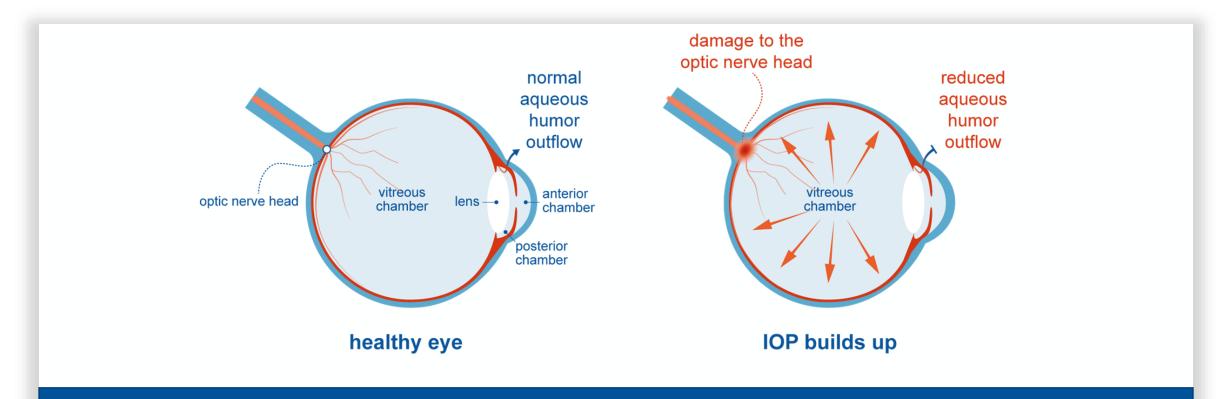






# Glaucoma: a Worldwide Ophthalmic Condition with Unmet Medical Needs

Elevated IOP\* Contributes to Irreversible Optic Nerve Damage, Leading to Progressive Vision Loss



As published in the landmark EMGT study "...each mmHg of decreased IOP was related to an approximately 10% lowering [of risk of vision loss progression]"



<sup>1.</sup> Heijl et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002; 120: 1268-1279

#### Unmet Medical Needs for Glaucoma Treatment

Despite having well established first-line therapies, including the standard-of-care, latanoprost, patients do not react to glaucoma medications in the same way, and therefore ophthalmologists need multiple treatment options

✓ 40% of patients do not achieve their target IOP on existing monotherapies¹ requiring ophthalmologists to adjust or change the medication

✓ Many patients
require >1
medication which
leads to
compliance
issues²³

✓ Tolerability
issues with some
medications lead
to
discontinuations,
patient
management
issues, and/or
compliance
issues⁴

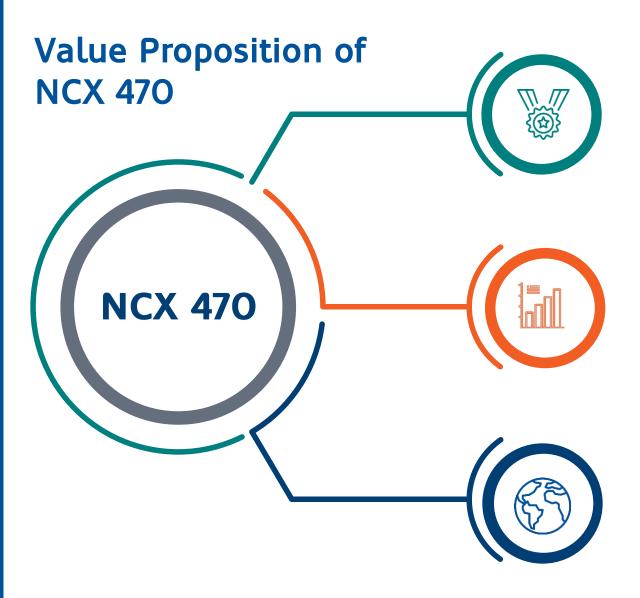


<sup>1.</sup> Kass et al, Delaying treatment of ocular hypertension: the ocular hypertension treatment study. Arch Ophthalmol, 2010; 128:276-287

<sup>2.</sup> Robin AL et al, Does adjunctive glaucoma treatment therapy affect adherence to the initial primary therapy? Ophthalmology. 2005; 112:863–868

<sup>3.</sup> Robin et al, Adherence in glaucoma: Objective measurements of once-daily and adjunctive medication use. Am J Ophthalmol. 2007;144:533-540

Beckers HJM et al. Side effects of commonly used glaucoma medications: comparison of tolerability, chance of discontinuation, and patient satisfaction. *Graefe's Archive for Clinical and Experimental Ophthalmology* 2008;246(10):1485-90



- ✓ Novel molecule with positive impact on lowering IOP, the leading cause of glaucoma
- ✓ **Positive pivotal Phase 3 topline results** from the Mont Blanc trial<sup>1,2,3</sup>
- ✓ First non-combination product to demonstrate statistical non-inferiority to a prostaglandin analog in a pivotal trial, thereby meeting the efficacy requirements for U.S. approval
- ✓ Large and established glaucoma drug market<sup>4</sup>: valued at ~\$6 billion worldwide
- ✓ Over 3 million patients and over 36 million prescriptions⁴ in the United States alone with additional safe and effective alternatives to firstline therapy required
- ✓ Over \$300 million global peak net sales forecast<sup>5</sup> for NCX 470
- ✓ Only late-stage New Chemical Entity in glaucoma in the U.S.

4 IOVIΔ<sup>TM</sup> Δnalytics Link 2O21



<sup>1.</sup> Nicox Press release October 31, 2022

<sup>2.</sup> Mansberg et al., 2023, World Glaucoma Congress, Abstract # P-339

<sup>3.</sup> Fechtner et al., 2023, World Glaucoma Congress, Abstract # P-288 b

<sup>5.</sup> Nicox market research, partner and internal estimates – Press Release July 10, 2023

## NCX 470 Timing

A Near-Term Asset Close to Completion of Development

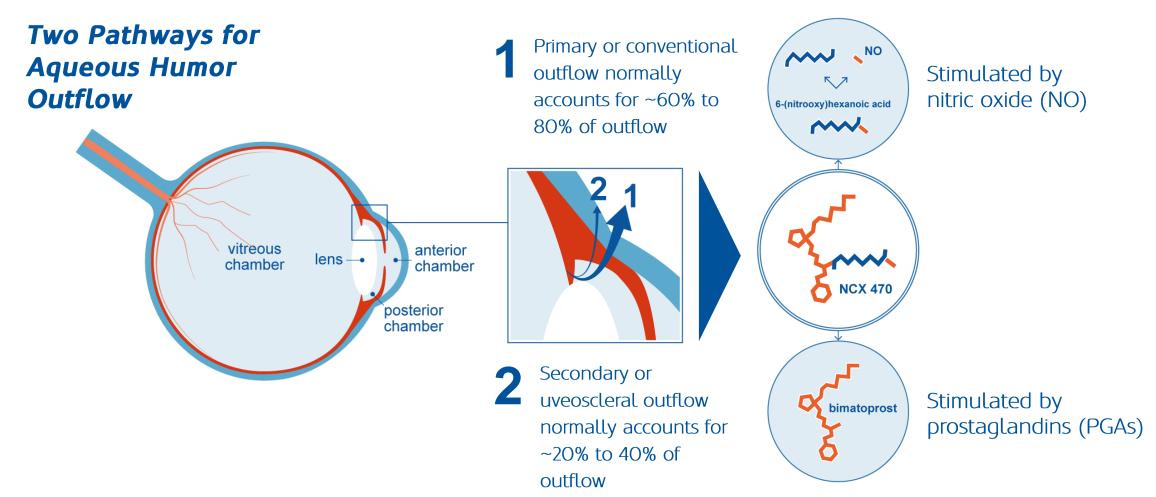


- Composition of matter patent to 2029 expected to be extended to 2034 in the United States and formulation patent to 2039.
- Additional marketing exclusivity may be available based on the status as a New Chemical Entity
- Chinese NDA expected to be submitted shortly after the US submission



# NCX 470 Lowers IOP Through a Validated<sup>1</sup> Dual Mechanism Pathway

Clinically Validated with the First NO-Donating PGA, VYZULTA®





## Positive NCX 470 Mont Blanc Topline Results<sup>1,2,3</sup>

Phase 3 Clinical Program Intended to Support U.S. & China NDA Submissions

Designed to demonstrate safety and efficacy of NCX 470 0.1% vs. latanoprost 0.005%, studies will evaluate reduction of IOP from time-matched baseline at pre-established time points

# MONT BLANC: Primary Objective of Non-Inferiority Achieved

N=691

56 clinical sites in the U.S. & one site in China

Adaptive design selected the 0.1% concentration

Second efficacy objective, statistical superiority to latanoprost, was not achieved

NCX 470 was statistically superior to latanoprost 0,005% in IOP reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6

#### **DENALI: Fully Enrolled**

 $N = \sim 670$ 

~80 clinical sites in the U.S. & China

Includes a 12-month safety extension

Jointly conducted and equally financed with Chinese partner Ocumension Therapeutics

Topline results expected in Q3 2025



# Mont Blanc Phase 3 Efficacy Trial Design<sup>1</sup>

Designed to Evaluate NCX 470 vs. Established Therapy, Latanoprost

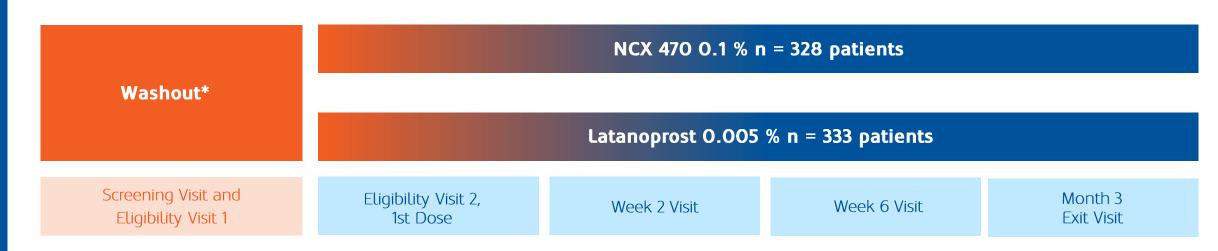
Randomized, controlled, double-masked, parallel design trial. Patients with open angle glaucoma or ocular hypertension were randomized 1:1 to once-daily treatment with NCX 470 0.1% or latanoprost 0.005%

#### **Primary Endpoint:**

Mean IOP reduction from time-matched baseline at 8 AM and 4 PM at the week 2, week 6 and month 3 visits

#### **Enrollment:**

The trial enrolled 691 patients across all arms (including ~30 patients on NCX 470 0.065% in the adaptive design part)



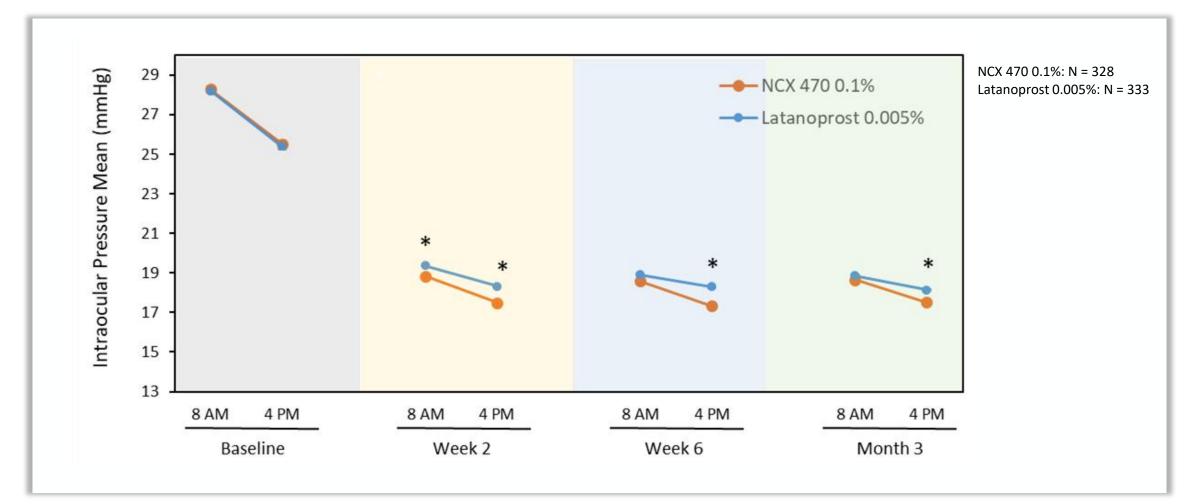
<sup>\*</sup> Wash-out period according to the patient's previous IOP-lowering treatment

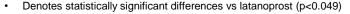


<sup>1.</sup> This schematic reflects the dosage arms which continued in the trial and do not include the NCX 470 0.065% dose which was only in the adaptive design portion of the trial

## Significant, Sustained IOP-Lowering Effects

IOP-Lowering from Baseline Was 8.0 to 9.7 mmHg for NCX 470 vs. 7.1 to 9.4 mmHg for Latanoprost





Fechtner et al., AJO, 2024 Aug;264:66-74



# Mont Blanc Topline Results Demonstrate Robust Efficacy and Safety<sup>1,2</sup>

All Comparisons Are Based on NCX 470 0.1% and Latanoprost 0.005%

#### **Topline Results from this Pivotal Trial:**

- IOP-lowering effect from baseline was 8.0 to 9.7 mmHg for NCX 470 vs. 7.1 to 9.4 mmHg for latanoprost
- **Statistical non-inferiority was met vs. latanoprost** in the primary efficacy analysis. This trial therefore met the efficacy requirements for approval in the U.S.
- While NCX 470 failed to meet statistical superiority to latanoprost in a pre-specified secondary efficacy analysis of time-matched change from baseline IOP, NCX 470 was numerically superior to latanoprost at all time points and **statistically significant** (p<0.049) at 4 of 6 timepoints

#### **NCX 470 Was Well Tolerated**

- The most common adverse event was ocular hyperemia in 11.9% of NCX 470 patients vs. 3.3% of latanoprost patients
- There were no ocular serious adverse events and no treatment-related non-ocular serious adverse events
- 4.3% of patients on NCX 470 discontinued compared to 5.1% on latanoprost



2. Fechtner et al, American Journal of Ophthalmology, 2024, 264:66-74

<sup>1.</sup> This data reflects the dosage arms which continued in the trial and do not include the NCX 470 0.065% dose which was only in the adaptive design portion of the trial

# NCX 470 Post hoc Analysis Further Differentiates vs Standard of Care

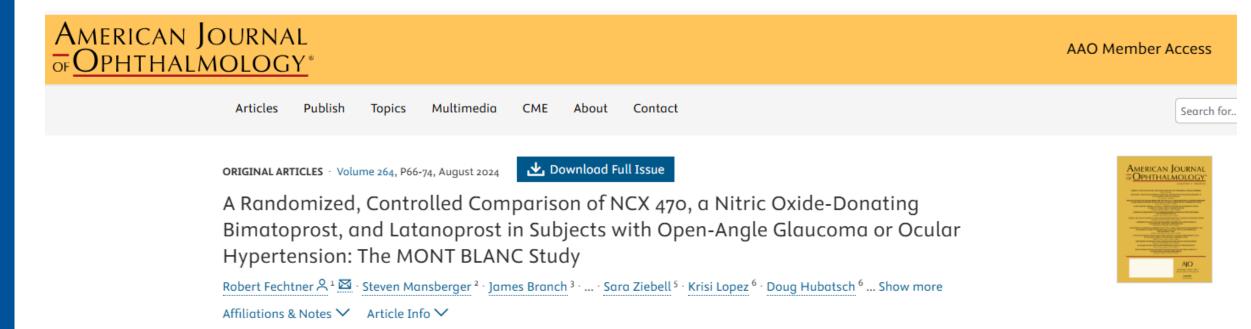
All Comparisons Are Based on NCX 470 0.1% and Latanoprost 0.005%

- Statistically significantly greater percentage of patients **achieve** ≤ **18mmHg IOP on NCX 470** compared to latanoprost
- Mean percentage reduction in IOP greater on NCX 470 than on latanoprost
- In eyes with an initial IOP of  $\leq$  28 mmHg the IOP-lowering effect from baseline was statistically significantly greater for NCX 470 compared to latanoprost at the majority of timepoints measured
- NCX 470 demonstrates a consistent lowering of IOP regardless of the baseline IOP, whereas the reduction in IOP with latanoprost is dependent on the baseline IOP
- A statistically significantly greater proportion of patients who received NCX 470 showed an IOP reduction of greater than 10 mmHg from baseline, compared to those on latanoprost

The full data from the Mont Blanc Phase 3 trial is available on the Nicox website Homepage at www.nicox.com



## Mont Blanc Results Published in a Prestigious Journal



<u>Authors' Conclusion:</u> The NO-donating prostaglandin analogue NCX 470 0.1% was well-tolerated and lowered IOP more than latanoprost in subjects with OAG or OHT at all 6 time points. With a dual mechanism of action that enhances both uveoscleral and trabecular outflow, **NCX 470 could become an important first-line therapy for IOP reduction in glaucoma.** 



# NCX 470 – Presentations at Key Ophthalmology Conferences



Poster: Diurnal IOP Control Responder Analysis with NCX 470 Versus Latanoprost in the Phase 3 MONT BLANC Trial



- Poster 1: Intraocular Pressure Reduction with NCX 470 versus Latanoprost Across the Spectrum of Baseline IOPs
- Poster 2: Intraocular Pressure Reduction with NCX 470 versus Latanoprost In Previously Treated Versus Treatment-Naïve Patients



- Effects of NCX 470, a Nitric Oxide (NO)-Donating Bimatoprost, in in-vitro 3D-Human Trabecular Meshwork (TM) / Schlemm's Canal (SC) Co-Culture Tissue Model. Galli et al., 2023, WGC Abstract # P-337
- NCX 470, a Nitric Oxide Donating Bimatoprost versus Latanoprost has Greater Proportion of Subjects Achieving ≥10 mmHg IOP Decrease in Phase 3 Trial. Mansberger et al., 2023, WGC Abstract # P-339
- NCX 470, a Nitric Oxide Donating Bimatoprost Compared with Latanoprost Adaptive Design Period Results from the Phase 3 Mont Blanc Clinical Trial. Fechtner et al., 2023, WGC Abstract # P-288



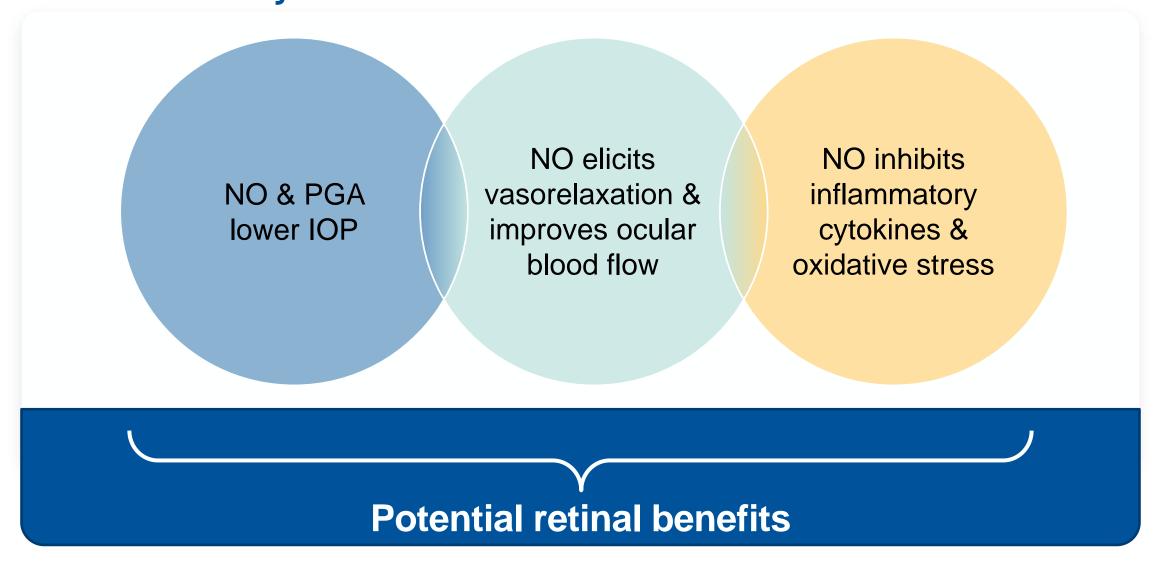
NCX 470, a nitric oxide (NO)-Donating Bimatoprost, Preserves Rabbit eyes from Biochemical and Functional changes associated with endothelin-1 (ET-1)-induced Ischemia/reperfusion Injury of the Optic Nerve and Retina Impagnatiello et al., 2023, ARVO Abstract #2580



NCX 470, a Nitric Oxide Donating Bimatoprost, Demonstrates Noninferiority to Latanoprost in Phase 3 Mont Blanc Clinical Trial. Fechtner et al., 2023, AGS Abstract #232



# **Nitric Oxide May Protect the Retina**

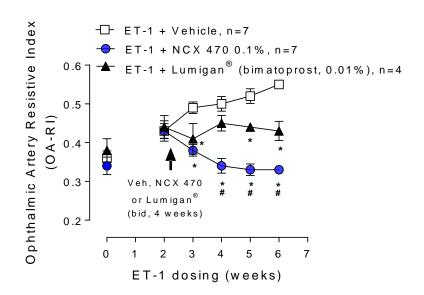




### NCX 470 Shows Retinal Cell Protection in a Nonclinical Model<sup>1,2</sup>

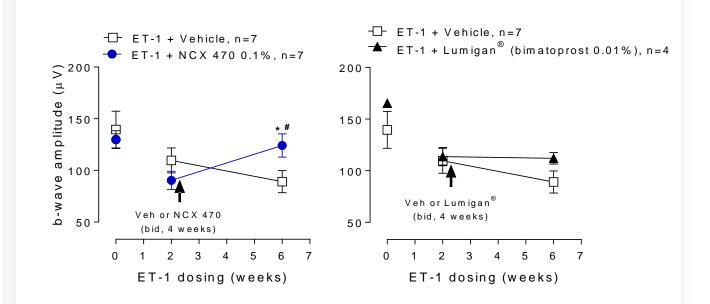
Improved ocular perfusion and retinal function in damaged eyes vs. Lumigan®

#### Ocular hemodynamics (Echo-doppler - Ophthalmic artery)



Detrimental effect of ET-1 on ophthalmic artery hemodynamics reversed in eyes receiving NCX 470. Lumigan® only was only partially effective

# Retinal function (Scotopic Electroretinogram - rod/cone responses)



Photoreceptor response decline induced by ET-1 was almost completely reversed in eyes treated with NCX 470.

Lumigan® had no significant effect



<sup>\*</sup> p<0.05 vs. vehicle at the same time point, # p<0.05 vs. Lumigan® Student's t-test

<sup>1.</sup> Bastia et al., J Ocul Pharmacol Ther, 2022, 38: 496-504:

<sup>2.</sup> Impagnatiello et al. ARVO 2023, abstract # 2580

## U.S. Glaucoma Clinical Advisory Board with Leading Experts

#### DR. ROBERT D. FECHTNER, MD, CHAIRMAN

Professor and Chair of the Department of Ophthalmology at SUNY Upstate Medical University, Syracuse, NY

#### DR. SANJAY G. ASRANI, MD

Professor of Ophthalmology at Duke University in Durham, North Carolina, and Director of the Duke Eye Center of Cary and the Duke Glaucoma OCT Reading Center

#### DR. DONALD BUDENZ, MD MPH

Kittner Family Distinguished Professor and Chairman, Department of Ophthalmology, UNC Chapel Hill School of Medicine

#### DR. STEVEN MANSBERGER, MD MPH

Vice-Chair, Senior Scientist, and Director of Glaucoma Services and Ophthalmic Clinical Trials for the Devers Eye Institute in Portland, Oregon. Clinical Professor of Ophthalmology at Oregon Health Science University

#### DR. TOM WALTERS, MD

President of Texan Eye P.A. and Medical Director of Eye LASIK Austin, Advanced Ophthalmic P.A., Keystone Clinical Research

#### DR. ROBERT N. WEINREB, MD

Distinguished Professor and Chair, Ophthalmology, Director of both the Shiley Eye Institute and the Hamilton Glaucoma Center, holder of the Morris Gleich, MD Chair in Glaucoma, and Distinguished Professor of Bioengineering





# Chinese Partner and Nicox Shareholder, Dedicated to Ophthalmology with Manufacturing and Commercial Capabilities

Based in China Created in 2018 Dedicated to Ophthalmology Listed on the Hong Kong Stock Exchange Since 2020 \$600 Million Market Cap Portfolio of 25
Products with
10 Commercialised
\$34 Million
Revenue in 2023
(+55%)

444 Employees, Including 232 in Commercial

- Ocumension's focus on ophthalmology and their local manufacturing and commercial capabilities makes them the ideal partner for NCX 470 in China
- Total of €18 million paid to Nicox in milestones (non-dilutive financing) plus cost contributions to Denali (50%) and Mont Blanc (one Chinese site)
- Nicox to receive royalties of 6% to 12% of future net sales on the territories licensed to Ocumension





# Global Enterprise with a Strong Pharmaceutical Business and Japanese Glaucoma Franchise

Founded in Japan in 1894 Active Worldwide in Multiple Domains Including Life Sciences

~8000 Employees with an Annual Group Revenue of \$4.9 Billion

The Pharmaceutical
Sector is an
Important One with
an International
Presence

Team of Medical Representatives in Japan and a Franchise in Glaucoma

- Kowa's direct commercial experience in glaucoma in Japan positions them as a strong partner for NCX 470
- Signed in February 2024 with a €3 million upfront payment to Nicox for exclusive rights to NCX 470 in Japan
- €4 million received, €2 million expected on Phase 3 initiation in H2 2025 and Nicox to potentially receive up to a further €24.5 million in milestones and 7% to 12% royalties on net sales



#### Future Commercialization of NCX 470

#### To Secure the Long-Term Future of the Company

- The Company is considering a number of options to ensure the commercialization of NCX 470 and concretize the future strategy:
  - New license agreements
  - Joint venture structures with companies having complementary products
  - M&A
  - Extension of the pipeline with other products under license or acquired, with associated funding
- Nicox has the team to:
  - Complete the development of NCX 470
  - Continue our existing collaborations
  - Deliver on a long-term strategy



## **Existing Commercial Products and Partnerships**



- ✓ Same mechanism of action as NCX 470
- ✓ Launched by Bausch + Lomb in 2017 in the United States
- ✓ Marketed in >15 countries and territories
- ✓ Revenue sold to Soleus Capital in October 2024

#### ZERVIATE1



First Commercial Sale in China in Q4 2024

#### **ZERVIATE**<sup>2</sup>



Launched<sup>3</sup> in the United States in 2020

- ✓ 5% to 9% royalties on annual net sales in China
- ✓ Potential for up to \$17.2 million in sales milestones by Ocumension<sup>4</sup>
- ✓ Manufactured by Ocumension in their state-of-the art Chinese factory and commercialized by their existing sales team since the end of 2024

√ 8% to 15% royalties on annual net sales in the United States

- 1. Ocumension has rights in Chinese and Southeast Asian markets
- 2. ZERVIATE is commercialized in the U.S. by Harrow, who also have rights for Canada.
- 3. Initially launched by Eyevance, who was acquired by Santen. Harrow acquired the ZERVIATE rights from Santen in 2023.
- 4. The majority of these milestones are on sales over \$100 million. Due to changes in the Chinese allergic conjunctivitis market, peak sales may not reach \$100 million



### NCX 1728: Research Collaboration with Glaukos

Combining NO-Release with PDE5 Inhibition MOA for this novel class of molecules is based entirely on NO-mediated activity

NO-mediated effects are enhanced and prolonged by concomitant phosphodiesterase-5 (PDE5) inhibition within the same molecule

Potential in Multiple Ophthalmic Conditions

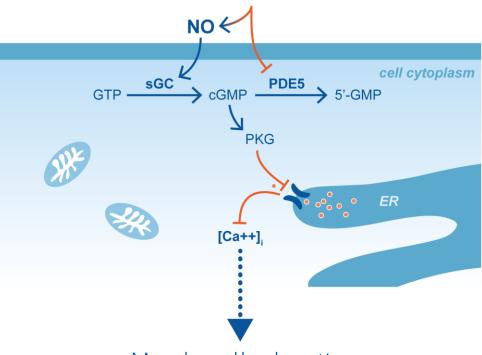
NO is an important mediator in both IOP control and in ocular blood flow and plays a role in a number of retinal conditions where dysfunctional ocular perfusion are key features in disease progression

# Collaboration with Glaukos

Exclusive research and global licensing option agreement

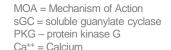
Pre-clinical research program exploring indications for the treatment of glaucoma, including neuroprotection, and in the treatment of retinal diseases

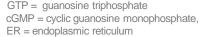
NO-donating PDE5 inhibitor



Muscle cell relaxation

- Vasorelaxation
- Enhancement of ocular blood flow
- Ocular tissues oxygenation
- Prevention of retinal damage







# **Experienced Leadership Team**



**Gavin Spencer Chief Executive Officer** 







Sandrine Gestin
VP, Finance and HR





Doug Hubatsch

EVP, Chief Scientific Officer





Emmet Purtill

VP Business Development





Damian Marron
Chairman of the Board



Christine Placet
Director



Marc Le Bozec
Director



**Gavin Spencer Chief Executive Officer** 

Sonia Benhamida Observer BlackRock



# **Financial Highlights**

Cash Balance Expected to Support Current Operations to the end of 2025

Financial Position and Ownership of Nicox SA <sup>1</sup>	
Cash, Cash Equivalents as at 31 December 2024	€10.5 million
Long Term Debt as at 31 December 2024	€15.1 million
Cash Runway <sup>2</sup>	To the end of 2025 <sup>3</sup>
Outstanding Shares <sup>4</sup>	69.8 million
Key Investors	Soleus Capital 6.2% Ocumension Therapeutics 4.4% HBM Healthcare Investments (Cayman) 2.9%

Analysts Coverage	
H.C. Wainwright	Yi Chen

- 1. Figures are audited. Nicox SA has a 100%-owned subsidiary, Nicox Ophthalmics. The figures for this subsidiary would have no impact on the figures of this slide if presented on a Group basis
- 2. Based exclusively on the development of NCX 470.
- 3. Including Kowa milestones expected in 2025
- 4. Outstanding shares as of March 31, 2025.



### **Investment Highlights**



- Two product approvals in the U.S., one in China
- Business Development deals in the U.S., Japan, China, and globally with Tier 1 companies

#### ✓ NCX 470, a Derisked, Late-Stage Development Program

- Positive Mont Blanc Phase 3 efficacy data and well tolerated
- Same-design Second Phase 3 trial, Denali, advancing as planned
- Validation by partnerships with Kowa and Ocumension Therapeutics

#### ✓ Large Potential Market

- ~\$6 billion worldwide glaucoma market
- Successful track record of VYZULTA® under partnership with Bausch + Lomb

#### ✓ High Strategic Transaction Potential

- Business Development
- M&A







#### Nicox S.A.

Sundesk Sophia Antipolis Emerald Square Bâtiment C rue Evariste Galois, 06410 Biot, France T: +33 (0)4 97 24 53 00

communications@nicox.com www.nicox.com