

# Nicox Corporate Presentation

An international ophthalmology company  
developing innovative solutions to help  
maintain vision and improve ocular health

June 19, 2024

# Forward-looking statements

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# Progress in achieving value inflection points expected for 2024-2025

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## Recent Highlights

Appointment of Gavin Spencer as Chief Executive Officer  
Value proposition of NCX 470 confirmed through Kowa partnership  
Restructuring of debt agreements with BlackRock  
Streamlining costs to concentrate on NCX 470 clinical development  
Extraordinary Shareholder Meeting to renew financing resolutions  
Equity financing of €3.3 million allowing completion of the debt restructuring, extending both the cash runway and the interest only period on our principal debt

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 IOP-lowering properties
- **Additional benefits**, e.g. retinal, seen in nonclinical models<sup>2,3</sup> to be explored post-Phase 3

## Global partnerships with Tier 1 ophthalmology players

- **€4.2m royalty revenue** in 2023 (+29% over 2022)
- **Continued sales growth** of VYZULTA<sup>®</sup> by Bausch + Lomb (+35% reported for 2023)
- Partnerships for NCX 470 in Japan with **Kowa** and in China with **Ocumension Therapeutics**
- **Pending approval of ZERVIA TE in China** through multi-product collaboration with Ocumension

## 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

# Upcoming milestones

Several positive milestones in 2024 and 2025

## NCX 470

- ❖ Completion of recruitment of U.S. patients Q4 2024
- ❖ Denali results – H2 2025
- ❖ Estimated worldwide sales over \$300 million<sup>1</sup>

## ZERVIAE







- ❖ Upcoming approval in China
- ❖ Estimated Chinese sales up to \$100 million<sup>2</sup>

## Corporate

- ❖ AGM for the approval of the 2023 accounts
- ❖ Ongoing business development discussions

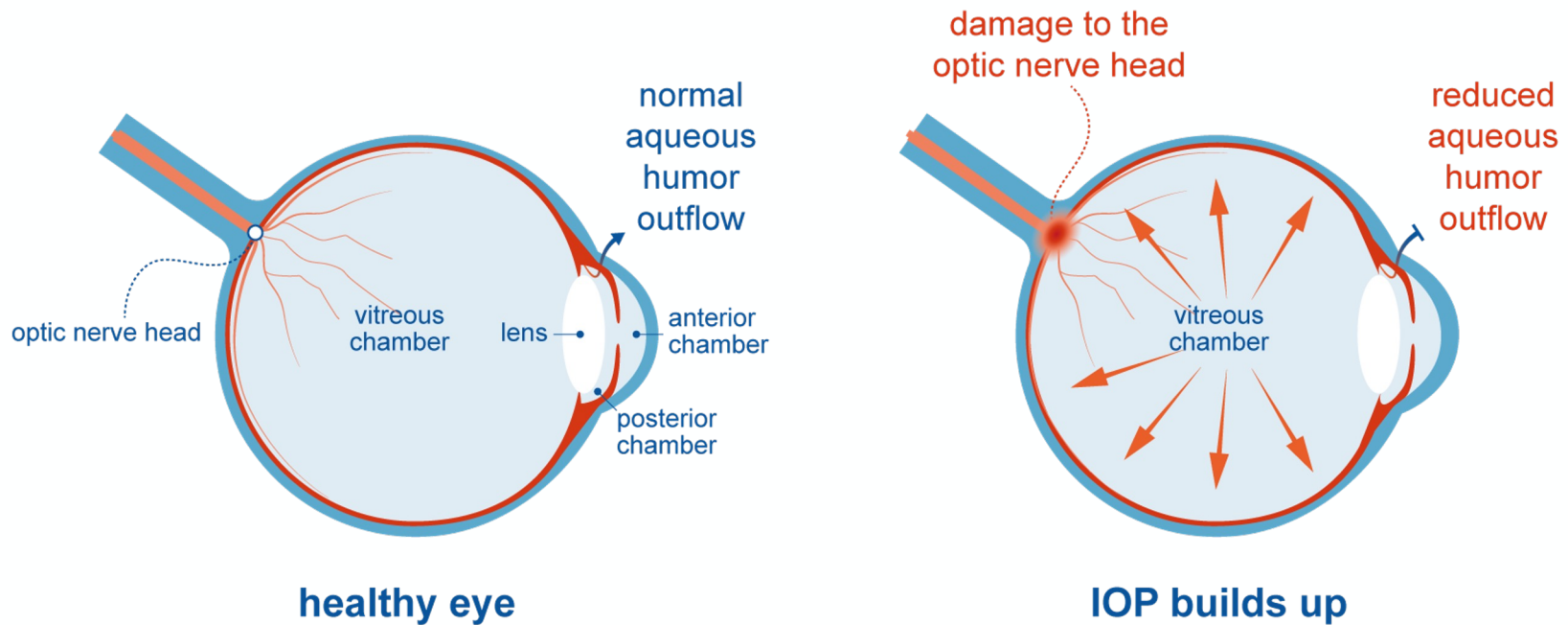
1. Within 8 years of launch in the U.S. and China  
2. Within 7 years if launch in China

# An innovative portfolio led by NCX 470, a derisked product candidate with global potential

| 3 Product Candidates   | Stages of Development   |         |         |         |     |          | Expected Milestones   |
|--|---|---------|---------|---------|-----|----------|---|
|  | Preclinical   | Phase 1 | Phase 2 | Phase 3 | NDA | Marketed |   |
| <p><b>NCX 470   NO-donating bimatoprost eye drops</b><br/><i>Glaucoma &amp; Ocular Hypertension</i></p> <p>Licensed out to  in China<br/>欧康维视</p> <p>Licensed out to  in Japan</p>   | <p><b>Mont Blanc trial completed / Denali Phase 3 trial and Whistler Phase 3b ongoing</b></p> |         |         |         |     |          | <p>Denali topline results in H2 2025</p> <p>Whistler Phase 3 results in Q1 2025</p> <p>Initiation of development for Japan by Kowa</p> <p>Commercial partnership for U.S.</p> |
| <p><b>NCX 1728   NO-donating PDE5 inhibitor</b><br/><i>Retinal Conditions</i></p>  |   |         |         |         |     |          | <p>Development through collaborations</p>   |
| <p><b>NCX 4251   Fluticasone propionate nanocrystal susp.</b><br/><i>Dry Eye</i></p> <p>Licensed out to  in China<br/>欧康维视</p>  |   |         |         |         |     |          | <p>Chinese development</p>  |
| 2 Revenue Generating Products  | Preclinical   | Phase 1 | Phase 2 | Phase 3 | NDA | Marketed | Next Milestones   |
| <p><b>VYZULTA®   Latanoprostene bunod ophthalmic sol. 0.024%</b><br/><i>Glaucoma &amp; Ocular Hypertension</i></p> <p>Licensed out to  worldwide<br/>BAUSCH+LOMB</p>  |   |         |         |         |     |          | <p>Growth in U.S. and international sales</p>   |
| <p><b>ZERVIAE®   Cetirizine ophthalmic sol. 0.24%</b><br/><i>Allergic conjunctivitis</i></p> <p>Licensed out to  in the U.S.<br/>Your patients. Our purpose.</p> <p>Licensed out to  in China and SE Asia<br/>欧康维视</p> |   |         |         |         |     |          | <p>Chinese NDA approval and commercial launch</p>   |

# 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>

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

\*Intraocular Pressure

# 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 monotherapies<sup>1</sup> requiring ophthalmologists to adjust or change the medication

Many patients require >1 medication which leads to compliance issues<sup>2,3</sup>

Tolerability issues with some medications lead to discontinuations, patient management issues, and/or compliance issues<sup>4</sup>

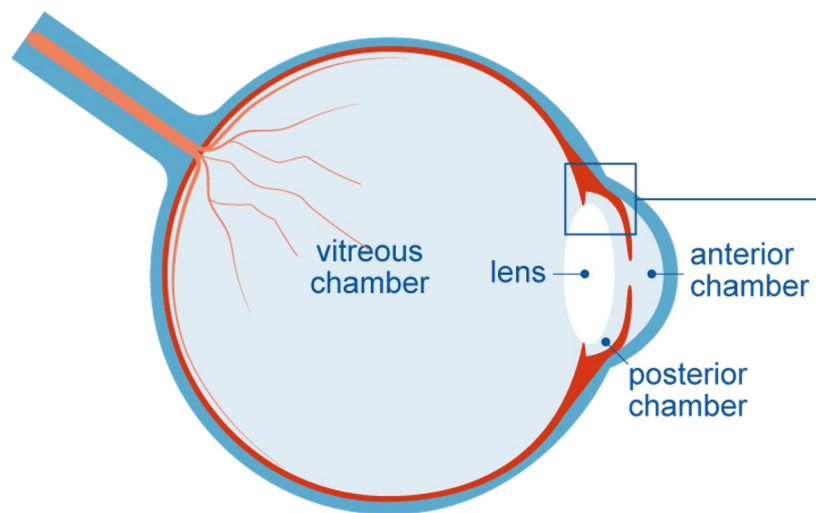
1. Kass et al, Delaying treatment of ocular hypertension: the ocular hypertension treatment study. *Arch Ophthalmol*, 2010; 128:276-287
2. Robin AL et al, Does adjunctive glaucoma treatment therapy affect adherence to the initial primary therapy? *Ophthalmology*. 2005; 112:863-868
3. Robin et al, Adherence in glaucoma: Objective measurements of once-daily and adjunctive medication use. *Am J Ophthalmol*. 2007;144:533-540
4. Beckers HJM et al. Side effects of commonly used glaucoma medications: comparison of tolerability, chance of discontinuation, and patient satisfaction. *Graefes Archive for Clinical and Experimental Ophthalmology* 2008;246(10):1485-90



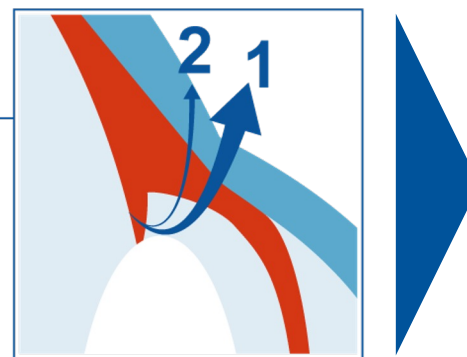
# NCX 470 acts through a dual mechanism<sup>1</sup> for IOP lowering

Non-clinical optic nerve/retinal damage models also demonstrate potentially beneficial retinal effects<sup>2</sup>

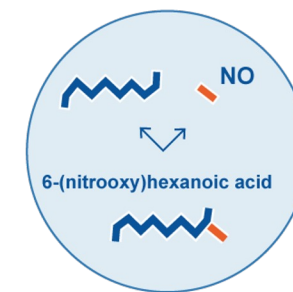
## Two pathways for aqueous humor outflow



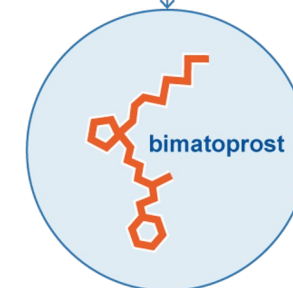
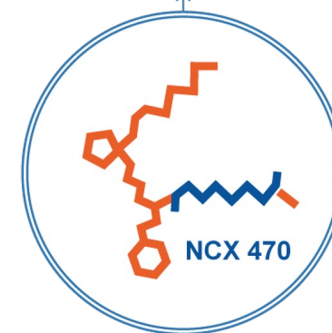
**1** Primary or conventional outflow normally accounts for ~60% to 80% of outflow



**2** Secondary or uveoscleral outflow normally accounts for ~20% to 40% of outflow



Stimulated by nitric oxide (NO)



Stimulated by prostaglandins (PGAs)

1. Same mechanism of action as Nicox's first commercialized NO-donating product, latanoprostene bunod  
 2. Bastia et al. J Ocul Pharmacol Ther. 2022, 38: 496-504

# Positive NCX 470 Mont Blanc topline results<sup>1,2,3</sup>

Phase 3 clinical program intended to support planned U.S. & China NDA submissions

Designed to demonstrate safety and efficacy of NCX 470 0.1% vs. latanoprost 0.005%, defined by IOP reduction 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 study design selected the 0.1%

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

NCX 470 was statistically superior to latanoprost in intraocular pressure reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6

## DENALI: Enrolling subjects

N=~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 H2 2025

1. Nicox Press release October 31, 2022  
 2. Mansberg et al., 2023, World Glaucoma Congress, Abstract # P-339  
 3. Fechtner et al., 2023, World Glaucoma Congress, Abstract # P-288

# Mont Blanc Phase 3 efficacy trial design<sup>1</sup>

Designed to evaluate NCX 470 vs. established therapy, latanoprost

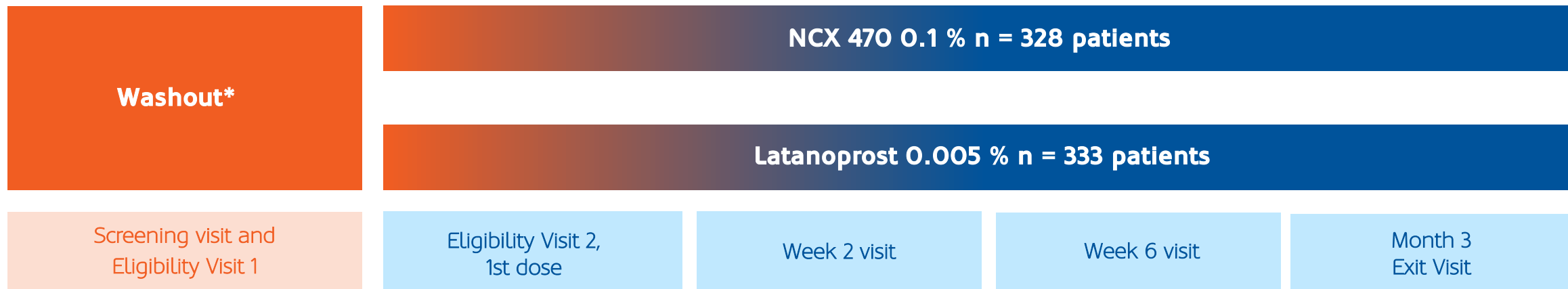
Randomized, controlled, double-masked, parallel design trial. Patients with open angle glaucoma or ocular hypertension were randomized 1:1 to once-daily treatment with NCX 470 0.1% or latanoprost 0.005%

## 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)



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

1. 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

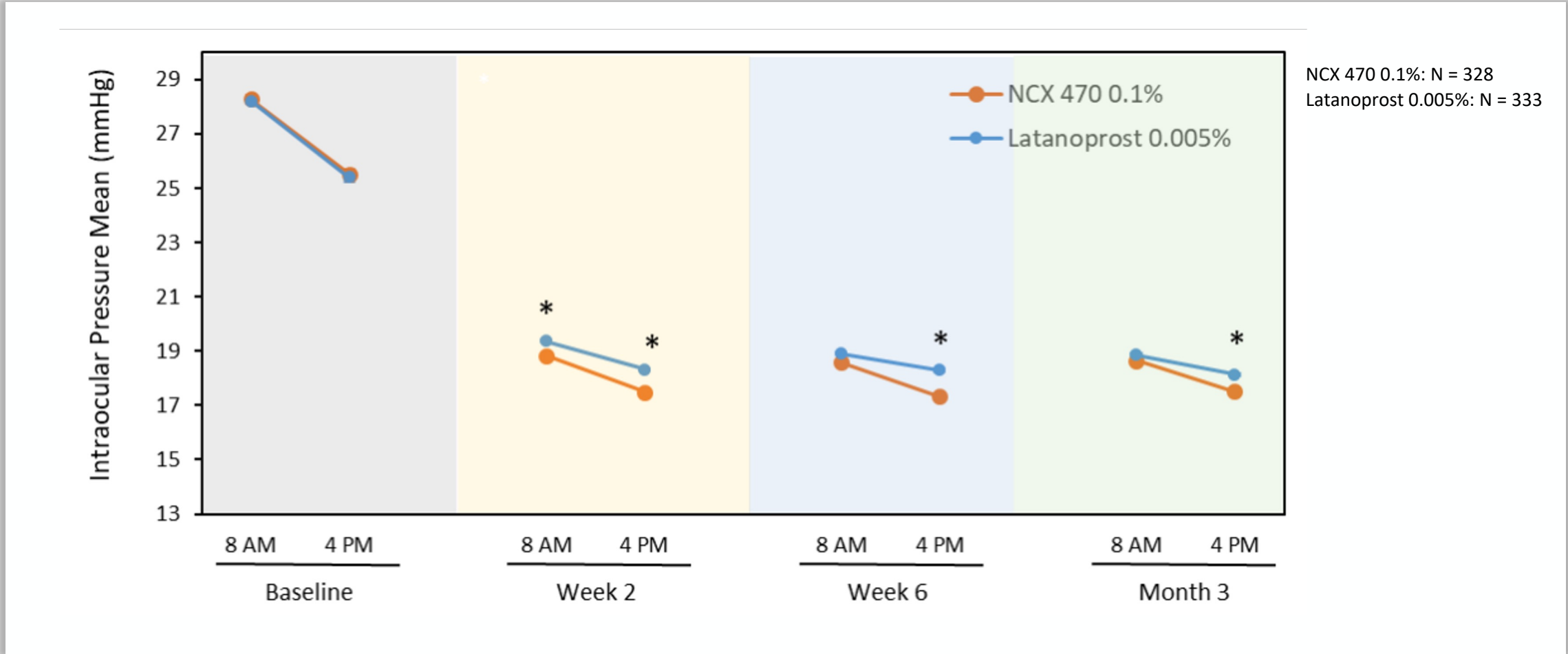
# Baseline characteristics, demographics and disposition<sup>1</sup>

|   | NCX 470 0.1%<br>N = 328 | Latanoprost 0.005%<br>N = 333 |
|---|-------------------------|-------------------------------|
| Mean Diurnal Baseline (8am+4pm) IOP, mmHg, Study Eye (SD) | 26.9 (2.04)             | 26.8 (2.02)                   |
| Gender, n (%)   |                         |                               |
| Female  | 200 ( 61.0%)            | 188 ( 56.5%)                  |
| Male  | 128 ( 39.0%)            | 145 ( 43.5%)                  |
| Age, Years (SD)   | 63.6 (10.12)            | 62.7 (11.73)                  |
| Completed the Study                                       | 314 (95.7%)             | 316 (94.9%)                   |
| Discontinued Prior to Study Completion                    | 14 (4.3%)               | 17 (5.1%)                     |
| Reasons for Discontinuation                               |                         |                               |
| Adverse Event   | 8 (57.1%)               | 6 (35.3%)                     |
| Lost to Follow-up   | 1 (7.1%)                | 4 (23.5%)                     |
| Physician Decision  | 0                       | 0                             |
| Sponsor or IRB Decision                                   | 1 (7.1%)                | 2 (11.8%)                     |
| Protocol Violation  | 0                       | 1 (5.9%)                      |
| Withdrawal by Subject                                     | 3 (21.4%)               | 3 (17.6%)                     |
| IOP greater than 36 mmHg                                  | 0                       | 0                             |
| Other   | 1 (7.1%)                | 1 (5.9%)                      |

1. 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.

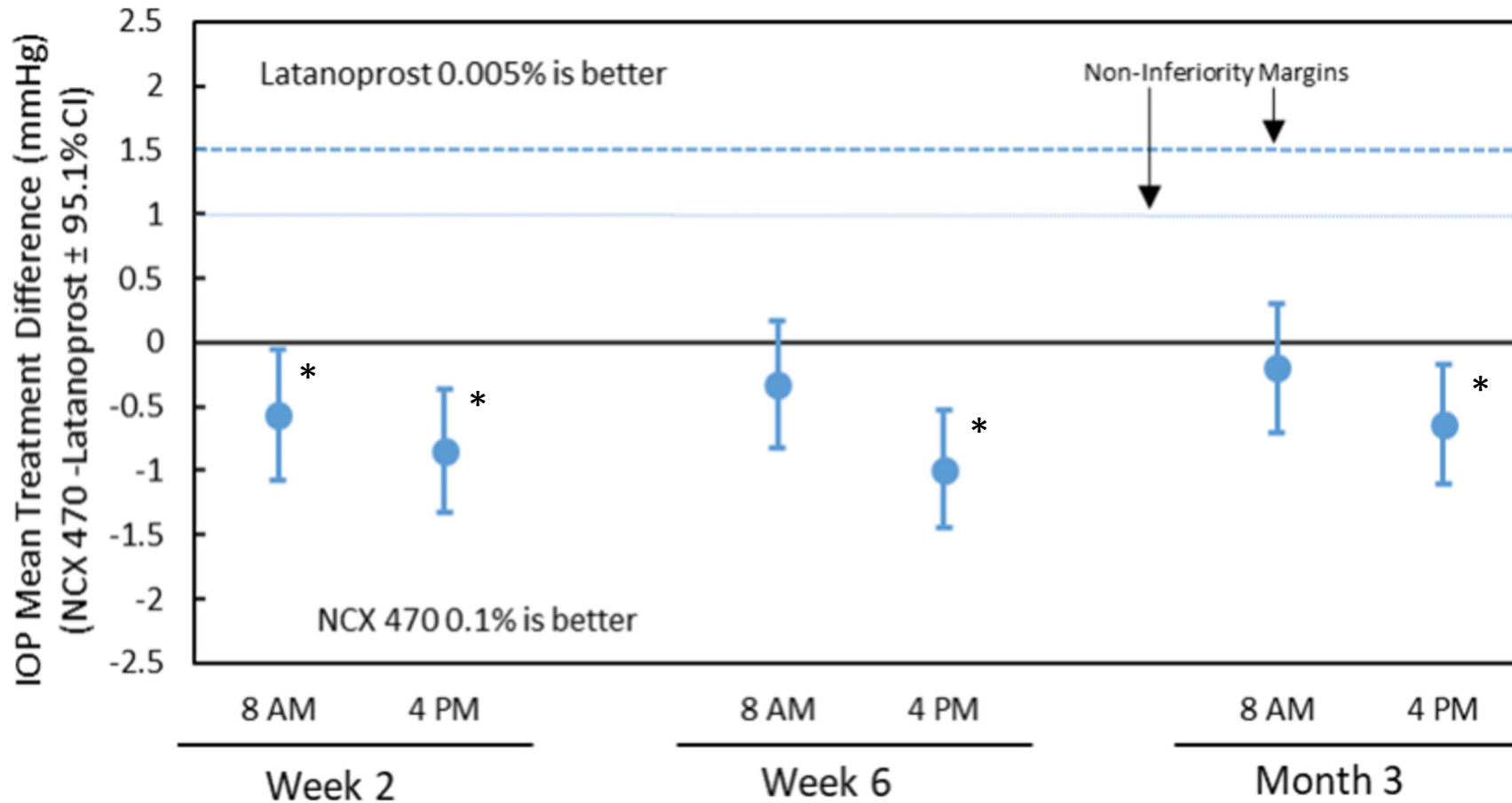
# Significant, sustained IOP-lowering effects

IOP-lowering from baseline was 8.0 to 9.7 mmHg for NCX 470 vs. 7.1 to 9.4 mmHg for latanoprost



- Denotes statistically significant differences vs latanoprost (p<0.049)
- Fechtner et al., AJO, published, 2024 - <https://doi.org/10.1016/j.ajo.2024.03.002>

# NCX 470 0.1% achieved non-inferiority and demonstrated an IOP-lowering greater than Latanoprost 0.005% of up to 1.0mmHg



To be non-inferior, the treatment difference between NCX 470 and latanoprost had to meet BOTH criteria:

- For all 6 timepoints, the upper limit of all confidence intervals (95.1%) were required to be less than or equal to 1.5 mmHg and
- At least 4 of the 6 timepoints were required to be less than or equal to 1.0 mmHg
- NCX 470 0.1% demonstrated an IOP lowering effect greater than latanoprost 0.005% of up to 1.0 mmHg

\* Denotes statistically significant differences vs latanoprost (p<0.049)



# NCX 470 topline results demonstrate robust efficacy and safety<sup>1</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**

**Data from the post hoc analysis:**


- **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 significant greater proportion of patients who received NCX 470 showed an IOP reduction of greater than 10 mmHg from baseline**, compared to those on latanoprost

## 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

1. 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 – Presentations at key ophthalmology conferences




- Poster 1: Intraocular Pressure Reduction with NCX 470 versus Latanoprost Across the Spectrum of Baseline Intraocular Pressures
- 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  $\geq 10$  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 Non-inferiority to Latanoprost in Phase 3 Mont Blanc Clinical Trial. Fechtner et al., 2023, AGS Abstract #232



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## **DR. TOM WALTERS, MD**

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## **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

# Value proposition of NCX 470



**Novel molecule** with competitive positive impact on lowering intraocular pressure (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>: ~**\$6 billion** worldwide reported

**Over 3 million patients and over 36 million prescriptions<sup>4</sup> in the United States alone** with additional safe and effective alternatives to first-line 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.

1. Nicox Press release October 31, 2022
2. Mansberg et al., 2023, World Glaucoma Congress, Abstract # P-339
3. Fechtner et al., 2023, World Glaucoma Congress, Abstract # P-288 b
4. IQVIA™ Analytics Link 2021
5. Nicox internal estimate – Press Release July 10, 2023

# NCX 470 Commercial Potential and Timing

A near-term asset arriving at completion of development



\*\*Subject to securing a U.S. commercial partner

- 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
- Peak annual net sales potential in the U.S. alone was estimated at between \$115 and \$165 million<sup>1</sup>
- Peak annual global net sales of NCX 470 could be over \$300 million<sup>2</sup> within 8 years of the date of launches in the U.S. and China

1. By year 8 from launch, based on Nicox commissioned market research in 2023, announced [here](#).  
2. Excluding Europe

Chinese partner and largest 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

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
- Nicox to potentially receive up to €27.5 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

VYZULTA

**BAUSCH+LOMB**

Marketed in >15 countries and territories, including the U.S.

Nicox receives 6% net<sup>1</sup> royalties on global sales – VYZULTA sales increased 35% in 2023 vs. 2022  
 \$5 million net milestone payable to Nicox at \$100 million net sales  
 Patent extended in the United States to 2029

ZERVIAE<sup>2</sup>

**OcuMension**  
 欧康维视

Approval expected in China in 2024<sup>3</sup>

5% to 9% royalties on annual net sales  
 Potential for up to \$17.2 million in sales milestones by Ocumension  
 Will be manufactured by Ocumension in their state-of-the art Chinese factory and commercialized by their existing sales team

1. Net of royalties payable to Pfizer, per the terms of the contract signed with Pfizer in August 2009  
 2. ZERVIAE is also commercialized in the U.S. by Harrow  
 3. Ocumension has rights in Chinese and Southeast Asian markets

# A refocused global leadership team



**Gavin Spencer**  
Chief Executive Officer



**Sandrine Gestin**  
VP, Finance and HR



**Doug Hubatsch**  
EVP, Chief Scientific Officer



**Jean-François Labbe**  
Chairman of the Board



**Michele Garufi**  
Director



**Les Kaplan**  
Director



**Gavin Spencer**  
Chief Executive Officer



**Sonia Benhamida**  
Observer  
BlackRock

**Maurizio Petitbon**  
Observer  
BlackRock



# Financial highlights

Cash balance expected to support current operations through end of February 2025

## Financial Position and Ownership of the Nicox Group<sup>1</sup>

|  |  |
|--|--|
| Cash, Cash Equivalents as at 31 March 2024                   | €12.4 million <sup>2</sup>   |
| Long term debt <sup>2</sup> as at 31 March 2024 <sup>3</sup> | €20.5 million  |
| Cash runway <sup>4</sup>                                     | February 2025  |
| Outstanding Shares <sup>5</sup>                              | 63.5 million including 13.2 million to be issued on June 21 <sup>st</sup> , 2024 |
| Management, Board and Employees Ownership <sup>6</sup>       | 1.6%   |
| Key Institutional Investors <sup>6</sup>                     | Ocumension Therapeutics 4.8%<br>HBM Healthcare Investments (Cayman) 3,1%         |

## Analysts coverage

|                 |         |
|-----------------|---------|
| H.C. Wainwright | Yi Chen |
|-----------------|---------|

1. Figures are non audited. Nicox Group is Nicox SA and its affiliates. 2. Cash and Cash Equivalents as at 31 March 2024 increased by the proceeds of the Equity financing of 3.3 million euros in June 2024. 3. This figure does not include the Armistice put option granted in the November 2022 equity financing, payable in the case of a merger by acquisition (fusion par absorption), merger (fusion par création d'une nouvelle société), division (scission), or a change of control within the meaning assigned in article L.233-3 I of the French commercial code (Code de commerce) where the consideration for such transaction is Nicox shares at a value of less than €1.70, the exercise price of the warrants, Armistice can request that Nicox purchases the warrants granted to Armistice at their Black Scholes value (using pre-defined terms). 4. Based exclusively on the development of NCX 470. 5. Existing outstanding shares as of June 21, 2024. 6. To the best of our knowledge, based on share capital to be issued as of June 21, 2024.

# Investment highlights



## ✓ A proven track record in clinical development and business development

- Two product approvals in the U.S., one pending 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.**

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