

# Nicox Corporate Presentation

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

September 2022



# Forward-Looking Statements

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# Driving Innovation in Ophthalmology, Led by NCX 470 & an Experienced Team

## Differentiated pipeline with significant near-term clinical trial results from NCX 470

Lead asset NCX 470, with a potential best-in-class product profile targeting glaucoma, leverages Nicox's proprietary Nitric Oxide (NO) donating research platform. Results from the first Phase 3 trial (Mont Blanc) due November 2022

## Experienced Leadership, Board and Advisors with expertise to drive successful outcomes

Experienced team well positioned to bring NCX 470 to approval and to advance and build the pipeline to deliver future growth

## Cash position enhanced by global partnerships and out-licensed commercial products

Cash balance of €31.6 million<sup>1</sup> expected<sup>2</sup> to fund operations through Q4 2023

Current and potential future revenue and value from global partnerships

1. As of June 30, 2022

2. Assuming Nicox exercises the option to extend the interest-only period of the existing Kreos debt by 6 months, which is conditional upon the Mont Blanc trial on NCX 470 meeting its primary endpoint of non-inferiority to latanoprost



Potential best-in-class profile in intraocular pressure lowering, the leading cause of glaucoma

First pivotal Phase 3 topline data in November 2022

Large and established market<sup>1</sup>:

\$6 billion globally

\$1.3 billion prostaglandin analog market in United States

Nicox market research<sup>2</sup> estimates that NCX 470 net sales could be \$200 to \$500 million in the United States alone, depending on the magnitude of the Phase 3 results

1. IQVIA™ Analytics Link 2021

2. Nicox internal market research 2019 and 2021, based on intraocular pressure lowering compared to latanoprost, and assuming safety and tolerability at least equivalent to existing prostaglandin analogs





# Broad Global Leadership Experience



**Andreas Segerros**  
Chief Executive  
Officer



**Sandrine Gestin**  
VP, Finance



**Doug Hubatsch**  
EVP, Chief Scientific Officer



**Emmanuelle Pierry**  
General Counsel & Head,  
Legal

Former member of  
the Paris Bar



**Gavin Spencer**  
EVP, Chief Business Officer &  
Head, Corporate Development





# Board Bringing Extensive Experience in Ophthalmology and Pharmaceuticals



**JEAN-FRANÇOIS LABBE**  
Chairman of the Board



**LES KAPLAN**  
Director



**MICHELE GARUFI**  
Director



**LAUREN SILVERNAIL**  
Director



**ADRIENNE GRAVES**  
Director



**LUZI VON BIDDER**  
Director



# Unique Combination of Competencies

Capable of bringing NCX 470 to approval and driving future growth



- Corporate, Finance and Legal team have completed multiple transactions, restructuring and financing
- International R&D Management with deep ophthalmology experience
- World-recognized Key Opinion Leaders on the Clinical Advisory Board
- Board members with extensive experience in ophthalmology and pharmaceuticals from leading companies



# 2022: A Year of Change and Opportunity

Focus in on key, value creating, innovative assets and evaluate additions to development pipeline

Pivotal data due on lead asset in November 2022, providing the potential cornerstone for building the future of the company

New Chief Executive Officer, Andreas Segerros, brings broad experience and a strong background in ophthalmology, having launched Xalatan® whilst at Pharmacia

New Chief Scientific Officer brings ophthalmology experience, and additional hires in Clinical, CMC and Quality round out a full, ophthalmology-focused R&D organization





# Differentiated Pipeline Addresses Broad Ophthalmology Market

## Stages of Development

In-house Development Product Candidates	Preclinical	Phase 1	Phase 2	Phase 3	NDA	Marketed	Expected Milestones
<b>NCX 470   novel NO-donating prostaglandin analog</b> <i>Glaucoma &amp; Ocular Hypertension</i> (Ocumension for Chinese & SE Asian markets)	<div></div>	<div></div>	<div></div>	<div></div>	Mont Blanc Trial		Topline results in November 2022
	<div></div>	<div></div>	<div></div>	<div></div>	Denali Trial including Safety Extension		Topline results after 2024
<b>NCX 1728   NO-donating PDE5 inhibitor</b> <i>Glaucoma &amp; Ocular Hypertension &amp; Retinal Conditions</i>	<div></div>						Research data on MoA in retinal conditions

Out-Licensed Products		Preclinical	Phase 1	Phase 2	Phase 3	NDA	Marketed	Current Status
<b>NCX 4251</b> <i>Dry Eye Disease</i>	China	<div></div>	<div></div>	<div></div>				Partnered in China Available for out-licensing
<b>VYZULTA®</b> <i>Glaucoma &amp; Ocular Hypertension</i>	Worldwide	<div></div>	<div></div>	<div></div>	<div></div>			Growing U.S. and international sales
<b>ZERVIAE®</b> <i>Allergic conjunctivitis</i>	United States	<div></div>	<div></div>	<div></div>	<div></div>			Promoted in U.S.
	Chinese & SE Asian markets	<div></div>	<div></div>	<div></div>	<div></div>			Partner preparing Chinese NDA

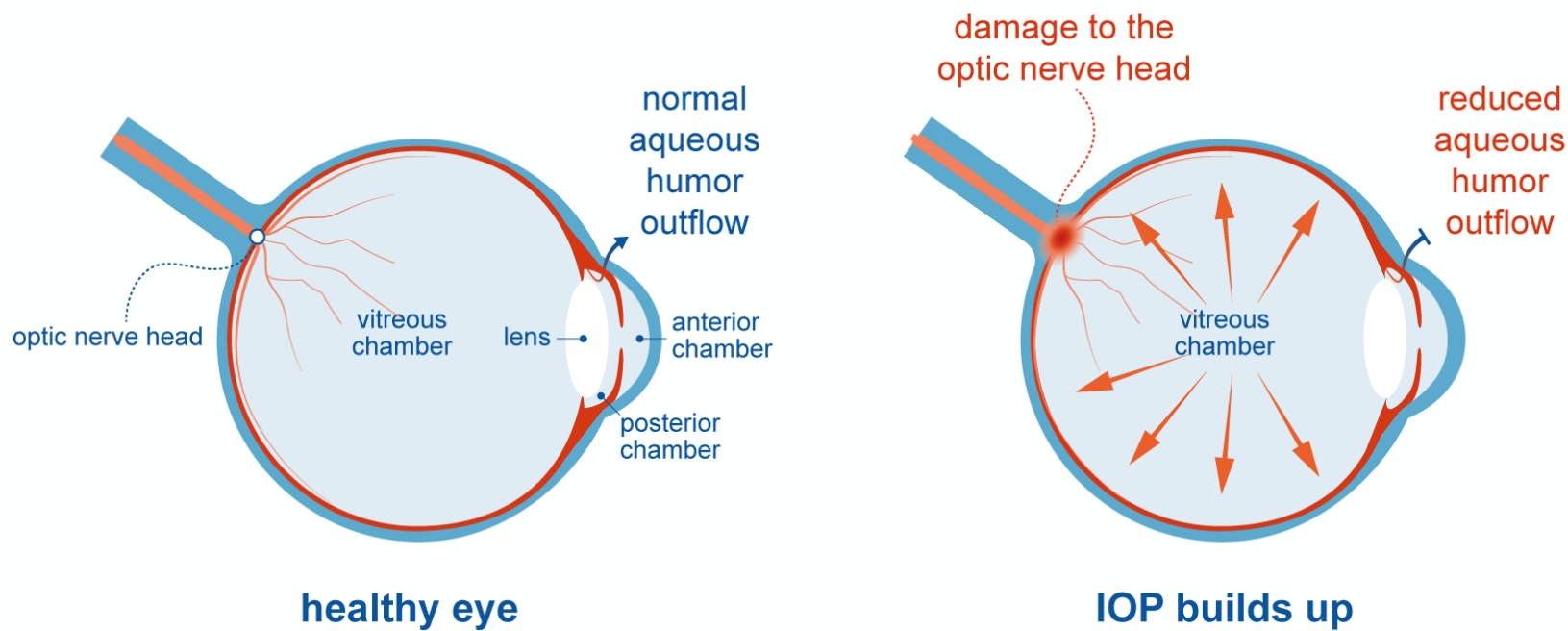


## NCX 470

Leveraging the potent intraocular pressure-lowering effects of nitric oxide and prostaglandin analogs for potential best-in-class treatment in glaucoma

# Glaucoma Snapshot

Elevated intraocular pressure (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



# Unmet Medical Need for Glaucoma Treatment

Despite having well established first line therapies, including the standard of care, latanoprost, there remains an unmet need for therapy with a greater IOP-lowering efficacy that is also safe and well tolerated

40% of patients do not achieve their target IOP on existing monotherapies<sup>1</sup>

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

Tolerability issues with some medications leads to discontinuations and/or compliance issues<sup>4</sup>

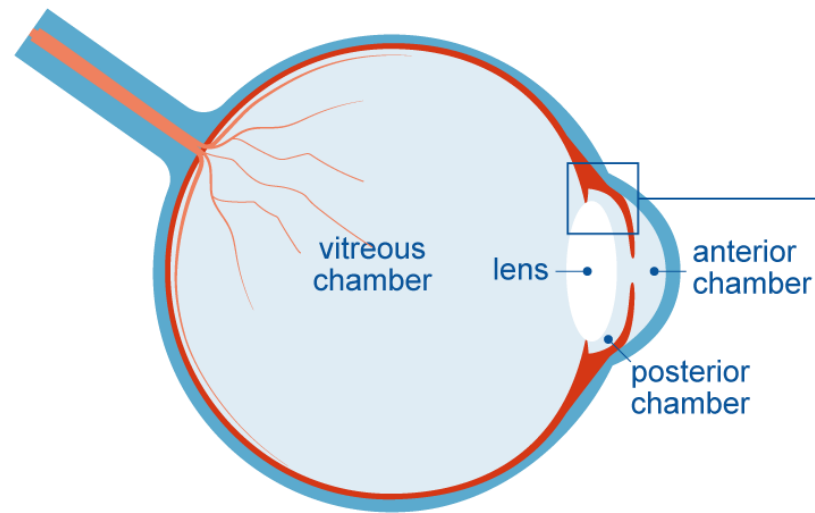
1. Kass et al, Delaying treatment of ocular hypertension: the ocular hypertension treatment study. Arch Ophthalmol, 2010; 128:276-287
2. Robin AL et al, Does adjunctive glaucoma treatment therapy affect adherence to the initial primary therapy? Ophthalmology. 2005; 112:863-868
3. Robin et al, Adherence 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



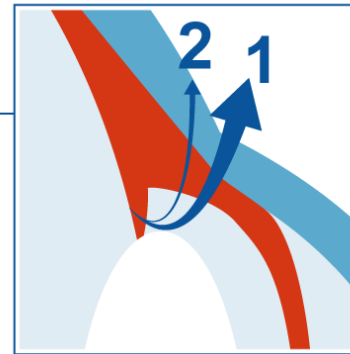
# NCX 470 Targets the Two Key Outflow Pathways for IOP Lowering

Potential for best-in-class efficacy with proven dual mechanism of action

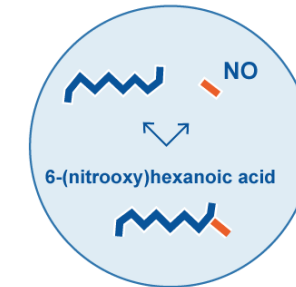
## Two pathways for aqueous humor outflow



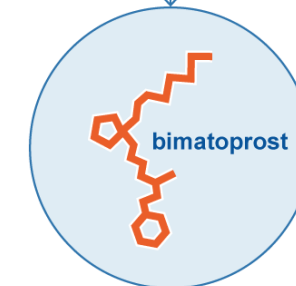
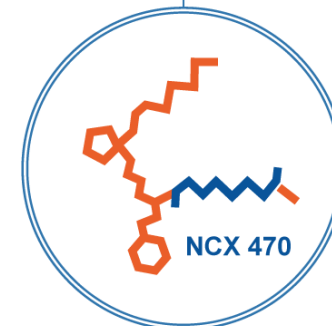
**1** Primary or conventional outflow normally accounts for ~60% to 80% of outflow



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



Stimulated by nitric oxide (NO)



Stimulated by PGAs\*

\*PGAs = Prostaglandin Analogs



# NCX 470 Targets >\$1 billion U.S. Glaucoma Opportunity

Glaucoma:  
progressive and  
irreversible vision  
loss

Approximately 3 million patients in the U.S. with open angle glaucoma<sup>1</sup>

First line, prostaglandin-based therapies represent a >\$1 billion opportunity in the U.S. alone  
40% of patients fail to reach target IOP with existing monotherapies, risking disease progression and vision loss

NCX 470: dual  
mechanism of  
action for potent  
IOP lowering

NCX 470 incorporates Nicox's proprietary NO-donating research platform and bimatoprost, a well-known prostaglandin-based therapy, in a single molecule

Robust Phase 2 trial already demonstrated statistical superiority of NCX 470 to latanoprost<sup>2</sup>

Nonclinical optic nerve/retinal damage models demonstrate potentially beneficial retinal protection effects<sup>3</sup>

First Phase 3:  
results in  
November 2022

Two Phase 3 trials, Mont Blanc and Denali, each designed for ~670 subjects/~50 sites in the U.S. & China

Mont Blanc topline results read-out November 2022, Denali topline results after 2024

1. <https://www.cdc.gov/features/glaucoma-awareness/index.html>

2. Walters et al., A Randomized, Controlled Comparison of NCX 470 (0.021%, 0.042% and 0.065%) and Latanoprost 0.005% in Patients with Open-Angle Glaucoma or Ocular Hypertension: The Dolomites Study. J Glaucoma 2022

3. J Ocul Pharmacol Ther. 2022, 38: 496-504

# NCX 470 Market Potential in the U.S.

Potential best-in-class therapeutic profile vs. standard of care (latanoprost)

Existing Branded and Generic  
Prostaglandin Analog (PGA) Label  
Claims<sup>1</sup>

**IOP Lowering of 6 mmHg to 8 mmHg**

No label claims of superiority over  
other prostaglandin analogs

**Latanoprost has ~80% of U.S. PGA  
prescription volume<sup>2</sup>**

Based on market research<sup>3</sup> on IOP lowering,  
NCX 470 potential driven the by magnitude of  
the lowering vs. latanoprost

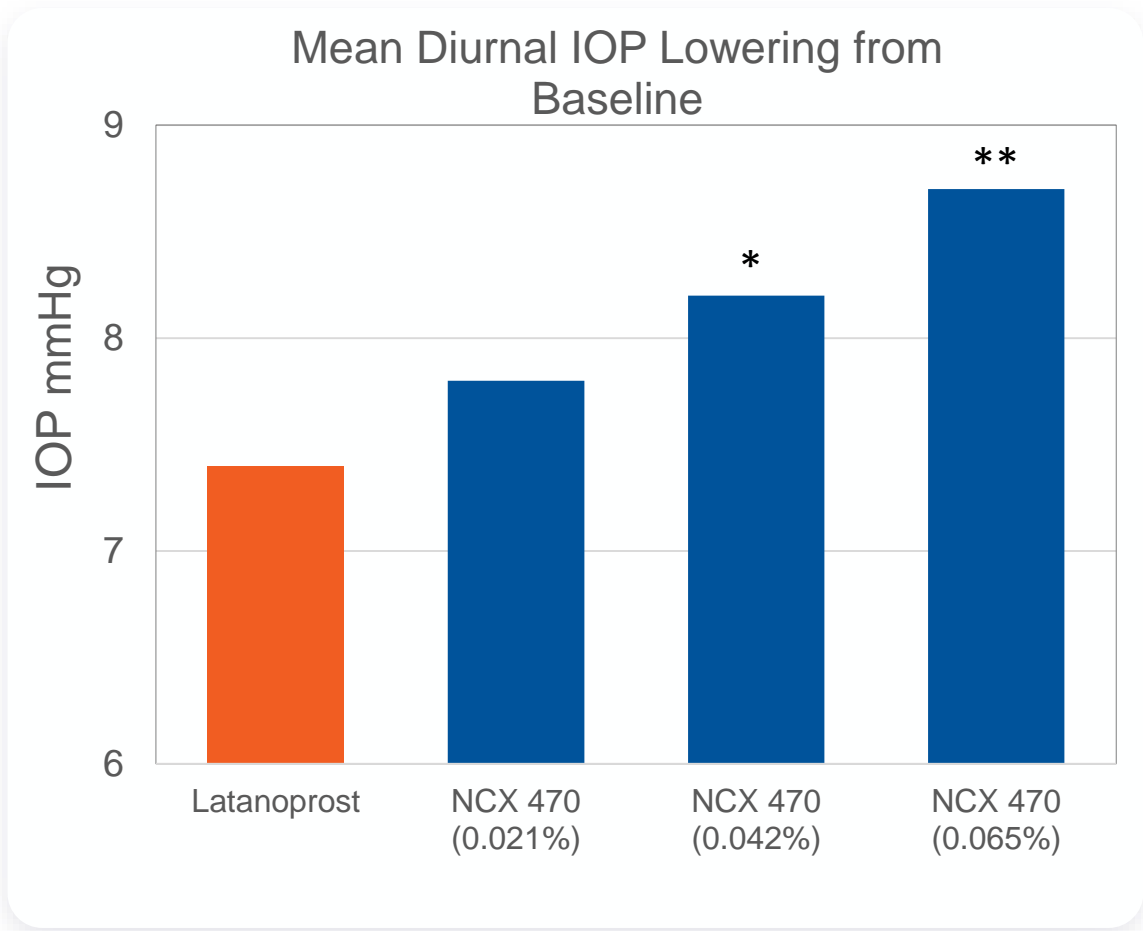
**\$200 million to \$500 million net sales  
potential in the U.S. alone based on  
Phase 3 data demonstrating superiority  
in IOP-lowering over latanoprost**

**NCX 470 has the potential for best-in-  
class IOP-lowering efficacy**

1. IQVIA NPA 2021  
2. <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm> for Lumigan, Travatan Z, Xalatan  
3. Nicox internal market research 2019 and 2021, assuming safety and tolerability at least equivalent to existing PGAs

# NCX 470 Dolomites Phase 2 Trial

Statistical superiority to standard of care in IOP lowering



## Phase 2 Dolomites Trial Summary

Met the primary non-inferiority endpoint of reduction from baseline in mean diurnal IOP at Day 28 in the 433-patient evaluation of 3 doses of NCX 470 vs. standard of care, latanoprost

Statistical superiority was achieved with the 0.042% and 0.065% doses with up to 1.4mmHg greater IOP reductions from baseline than latanoprost at the 0.065% dose

NCX 470 was generally well tolerated: hyperemia levels peaked at 22% at the 0.042% dose

Linear dose response suggests potential for greater efficacy, with a higher dose, 0.1%, selected for Phase 3 trials

\*p<0.05, \*\*p=0.0009.  
Walters et al., A Randomized, Controlled Comparison of NCX 470 (0.021%, 0.042% and 0.065%) and Latanoprost 0.005% in Patients with Open-Angle Glaucoma or Ocular Hypertension: The Dolomites Study. J Glaucoma 2022



# NCX 470: Two Phase 3 Trials Support Planned U.S. & China NDA Submissions

Mont Blanc topline results due in November 2022

Both trials are randomized, controlled, double-masked, parallel design. 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%)

## MONT BLANC TRIAL

N=~670

~50 clinical sites in the U.S. & one site in China

Adaptive study design selected the 0.1% dose for the duration of the trial

Topline results due in November 2022

## DENALI TRIAL

N=~670

~60 clinical sites in the U.S. & China

Includes a 12-month safety extension

Trial jointly conducted and equally financed by Ocumension Therapeutics

Topline results expected after 2024

### Primary Endpoint:

Mean intraocular pressure reduction from time-matched baseline at 8AM and 4PM at the Week 2, Week 6 and Month 3 Visits



# NCX 470: Dual Mechanism of Action for Potent IOP lowering

Potential to provide best-in-class IOP lowering, leveraging both PGA and nitric oxide (NO) mechanisms of action

Promising Phase 2 data with higher NCX 470 doses demonstrating superior IOP lowering vs. latanoprost

First glaucoma monotherapy to be tested against standard of care latanoprost in a Phase 3 program powered for superiority

Major Near-Term, Clinical Value Inflection Point:

Topline results from the Phase 3 Mont Blanc trial due in November 2022





## NCX 1728

Novel class of molecules for IOP lowering and retinal conditions



# NCX 1728: Lead Compound in a New Class of NO-donating Molecules

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

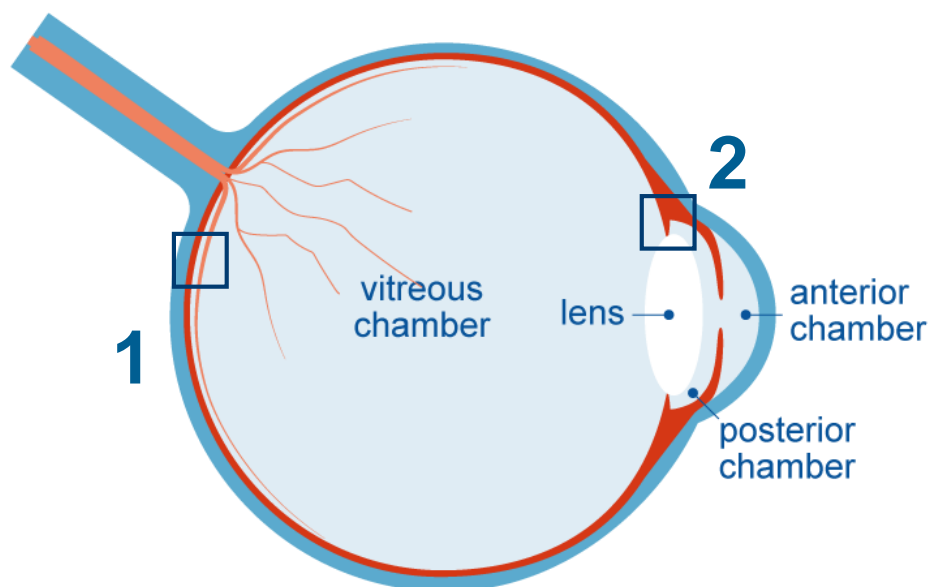
Potential in IOP  
lowering and  
retinal conditions

In addition to IOP lowering, NO has a role in ocular perfusion which may be beneficial in a number of orphan retinal conditions for which there is no standard treatment

Nonclinical program  
focused on  
evaluating MoA

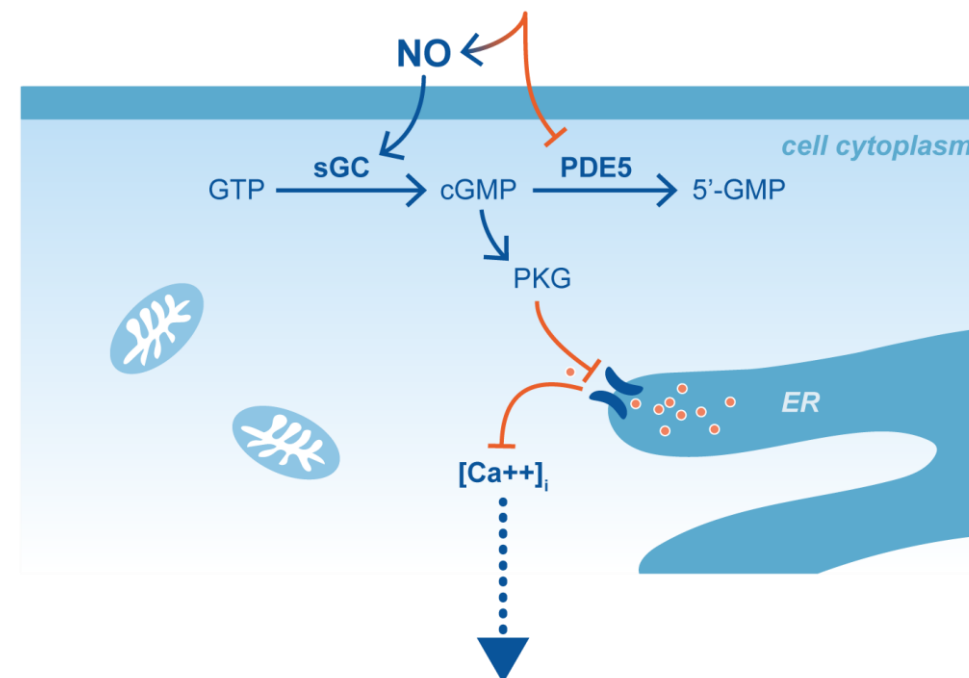
Nonclinical studies underway to evaluate the mechanism of action in models of orphan retinal conditions

# NCX 1728: NO-Mediated IOP Lowering and Improved Ocular Perfusion



**Two potential target tissues for NO-mediated effects**

## NCX 1728 NO-donating PDE5 inhibitor



**Improved ocular perfusion and reduced intraocular pressure**





# NCX 4251

Novel treatment with unique mode of application in dry eye disease



# NCX 4251: Novel Approach to Dry Eye Disease

Novel corticosteroid presentation leverages Nicox's unique formulation expertise

Novel, patented ophthalmic nanocrystal suspension of fluticasone propionate, a well-established corticosteroid. Fluticasone has 10x affinity for the glucocorticoid receptor vs. dexamethasone, commonly used in ophthalmology

Planned to be the first topical ophthalmic fluticasone product, a two-week, once-daily treatment leveraging Nicox's proprietary formulation technology

Targeting dry eye disease, a \$3.4 billion prescription market in the U.S.

Eye Care Professionals require improved short-term treatment for flares and bridging to chronic therapy

Unique delivery device applies drug directly to the eyelid margin, potentially reducing steroid side-effects

Phase 2 trial supports potential clinical utility in dry eye disease

Post-hoc analysis of 224-subject Phase 2b Mississippi trial showed a statistically and clinically significant reduction in dry eye symptoms versus placebo

Nicox reached alignment with U.S. FDA on a 505(b)(2) development path for NCX 4251 and is currently looking for partnerships outside of China to advance development of this program



# Mississippi: Post-Hoc Results Puts Dry Eye Disease in Sight



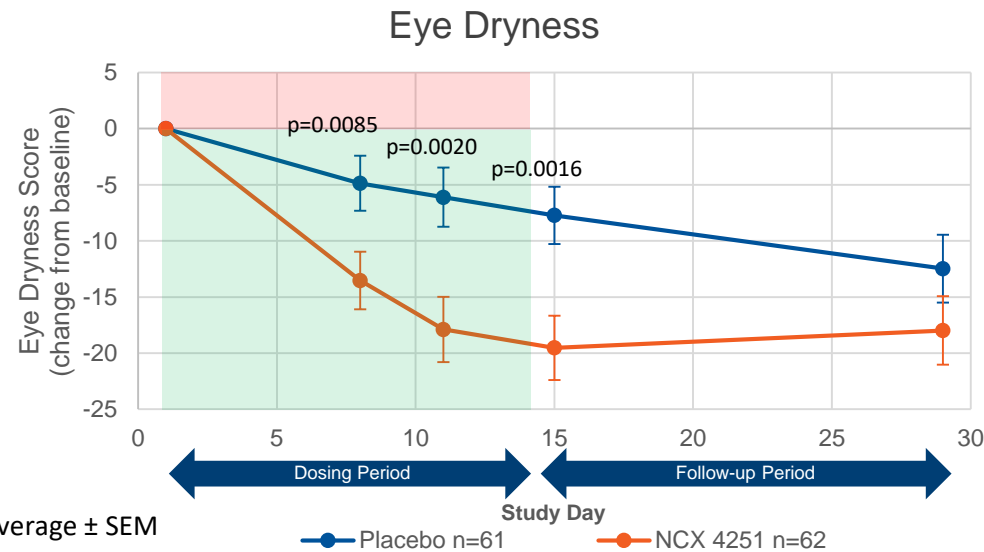
**Unique eyelid margin application** designed to minimize corticosteroid-induced ocular adverse events

## Phase 2 Mississippi<sup>2</sup> Trial Summary

The trial evaluated NCX 4251 in patients with acute exacerbations of blepharitis. Topline results of the trial did not meet primary endpoint of difference between NCX 4251 and placebo in the proportion of patients with complete cure of eyelid redness, debris, and discomfort

Positive post-hoc results from the Mississippi Phase 2 trial suggest NCX 4251 may be effective in dry eye disease. Patients with a baseline score of  $\geq 2.0$  (on a scale of 0 to 4) for fluorescein staining demonstrated a statistically significant difference in change from baseline vs. placebo for eye dryness score and several other symptoms

NCX 4251 was found to be safe and well tolerated over 14 days with no serious adverse events (all events in the NCX 4251 arm were mild)



**Reduction from baseline in eye dryness score<sup>1</sup> in patients with inferior corneal fluorescein staining score of  $\geq 2$**

1. Eye dryness measured on a visual analog scale (0 to 100)  
 2. Mississippi: U.S. Multi-Center, Randomized, Double-Masked, Placebo-Controlled, Phase 2b Study Evaluating the Safety and Efficacy of NCX 4251 Ophthalmic Suspension, 0.1% QD for the Treatment of Acute Exacerbations of Blepharitis, ClinicalTrials.gov Identifier: NCT04675242



**Nicox Corporate**



# 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



# Partnering Deals Include Potential Future Payments & Royalties

NCX 470



*Potential best-in-class treatment for IOP lowering*

6% to 12% royalties on future net sales<sup>1</sup> in China and Southeast Asia

Ocumension pays 50% of the Denali Phase 3 clinical trial costs

VYZULTA



*First eye drop for glaucoma approved in 20 years with a novel approach to reduce IOP*

\$5 million net milestone at \$100 million net sales

6% to 12% net<sup>2</sup> royalties on global sales

ZERVIAE



*First and only eye drop formulation of cetirizine for allergic conjunctivitis*

Phase 3 completed by Ocumension<sup>3</sup> in China: Up to \$17.2 million in sales milestones plus 5% to 9% royalties on net sales

Commercialized by Eyeavance (a wholly-owned subsidiary of Santen Pharmaceutical Co.) in the U.S.

NCX 4251



*Novel treatment with unique mode of application in dry eye disease*

Up to \$11.3 million in future milestones plus 5% to 10% royalties on net sales in China by Ocumension<sup>4</sup>

Available for out-licensing outside China

1. Ocumension has rights in Chinese, SE Asian markets and Korea
2. Net of royalties payable to Pfizer, per the terms of the contract signed with Pfizer in August 2009
3. Ocumension has rights in Chinese and SE Asian markets
4. Ocumension has rights in Chinese markets



# Financial Highlights

Cash balance expected to support current operations through Q4 2023

## Estimated Financial Position and Ownership as of June 30, 2022<sup>1</sup>

Cash, Cash Equivalents	€31.6 million
Debt <sup>2</sup>	€20.6 million
Cash runway <sup>3</sup>	Q4 2023
Outstanding Shares <sup>4</sup>	43.2 million
Management and Employees Ownership <sup>5</sup>	<2%
Key Institutional Investor	HBM Partners 7.0%

## Analyst Coverage

Bryan Garnier	Dylan Van Haaften
Edison Investment Research	Pooya Hemami
H.C. Wainwright	Yi Chen
Kepler Cheuvreux	Arsene Guekam

1. Unaudited results

2. Includes Kreos Capital bond financing agreement (€18.6 million) and a non-dilutive loan facility credit agreement (€2 million) guaranteed by the French state related to the COVID-19 pandemic

3. The cash runway is calculated assuming the development of NCX 470 alone. NCX 4251 is licensed to Ocumension for Chinese markets and is available for out-licensing elsewhere. The cash runway assumes Nicox exercises the option to extend the interest-only period of the existing Kreos debt by 6 months, which is conditional upon the Mont Blanc trial on NCX 470 meeting its primary endpoint of non-inferiority to latanoprost

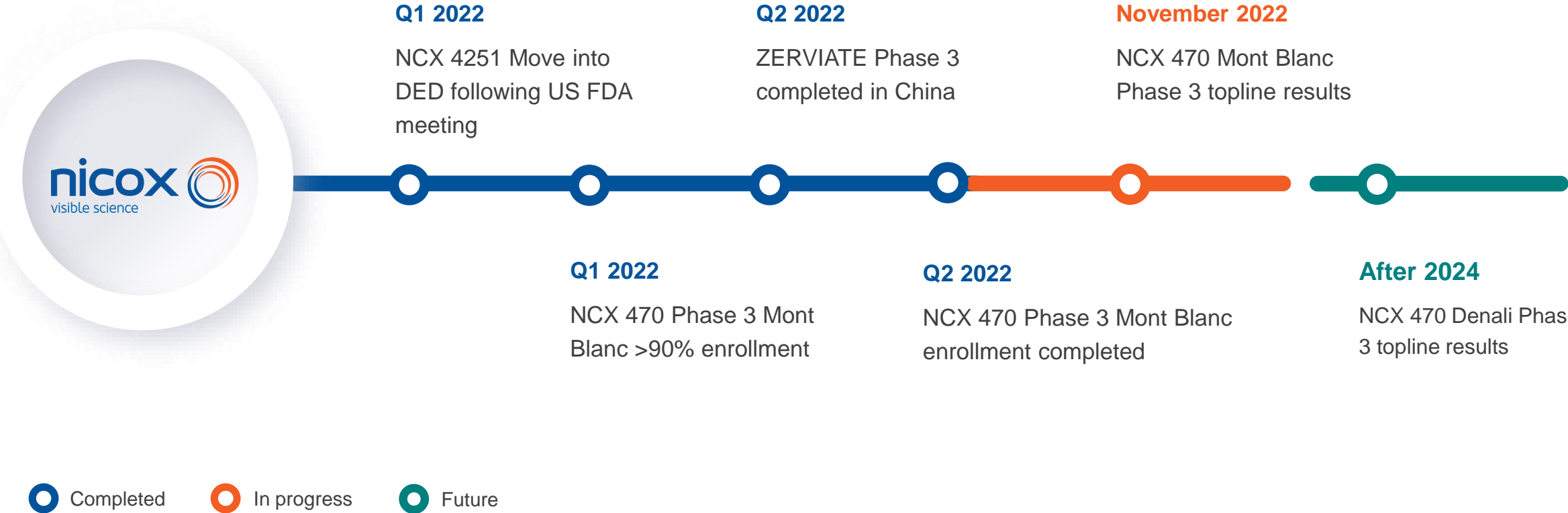
4. Existing outstanding shares as of August 1, 2022

5. To the best of our knowledge, based on issued share capital



# Value-Creating Milestones

## Building a high-value ophthalmology pipeline



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