





## Forward-Looking Statements

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Risk factors which are likely to have a material effect on Nicox SA's business are presented in the 3<sup>rd</sup> chapter of the "Document d'Enregistrement Universel, rapport financier annuel et rapport de gestion 2021" filed with the French Autorité des Marchés Financiers (AMF) on April 29, 2022 under number D.22-0392 available on Nicox SA' website (www.nicox.com).

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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. Topline results from the first Phase 3 trial (Mont Blanc) in early November 2022

Blanc trial on NCX 470 meeting its primary endpoint of non-inferiority to latanoprost

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 outlicensed commercial products

Cash balance of €25.6 million<sup>1</sup> expected<sup>2</sup> to fund operations until November 30, 2023

Current and potential future revenue and value from global partnerships







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

First pivotal Phase 3 topline results in early 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





# Broad Global Leadership Experience



Andreas Segerros
Chief Executive
Officer

**PHARMACIA** 







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 Phase 3 results on lead asset due in November 2022, providing the potential cornerstone for building the future of the company

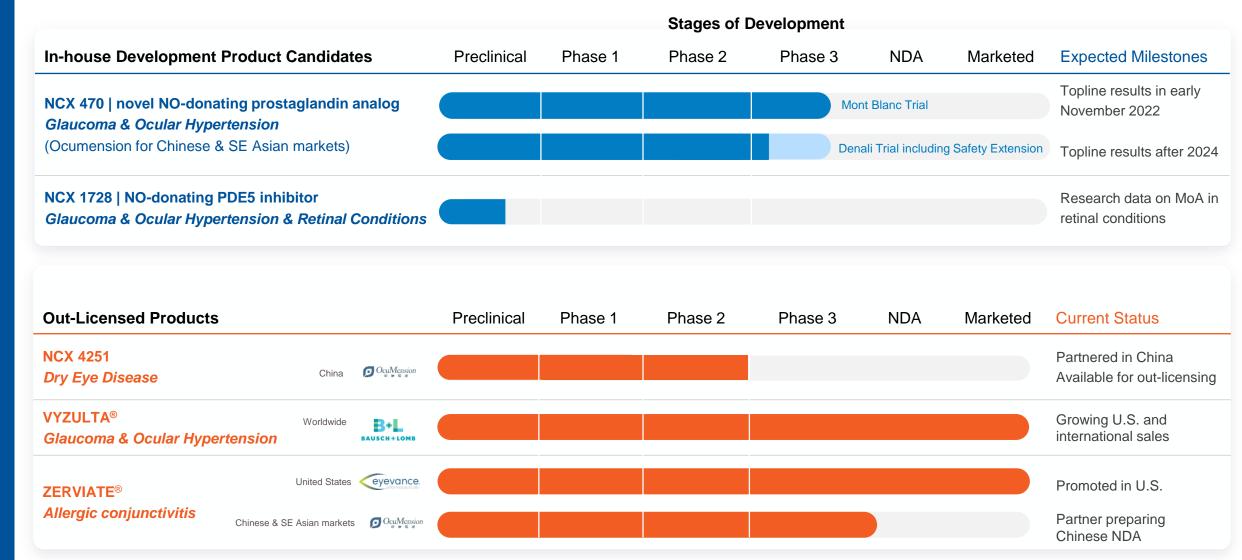
New Chief Executive
Officer, Andreas
Segerros, brings
broad experience and
a strong background
in ophthalmology,
having launched
Xalatan® whilst at
Pharmacia

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





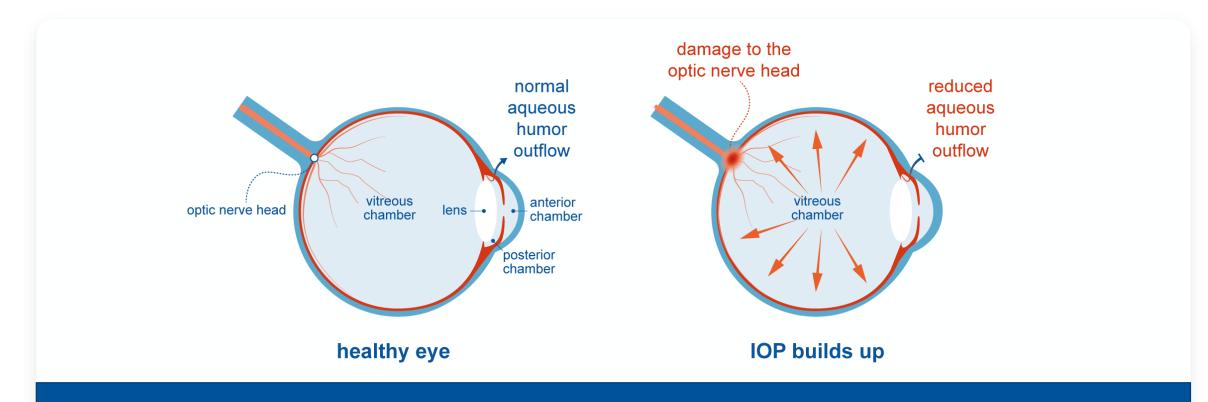






### Glaucoma Snapshot

Elevated intraocular pressure (IOP) contributes to irreversible optic nerve damage, leading to progressive vision loss







### 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 IOPlowering efficacy that is also safe and well tolerated

40% of patients do not achieve their target IOP on existing monotherapies1

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>



2008;246(10):1485-90

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

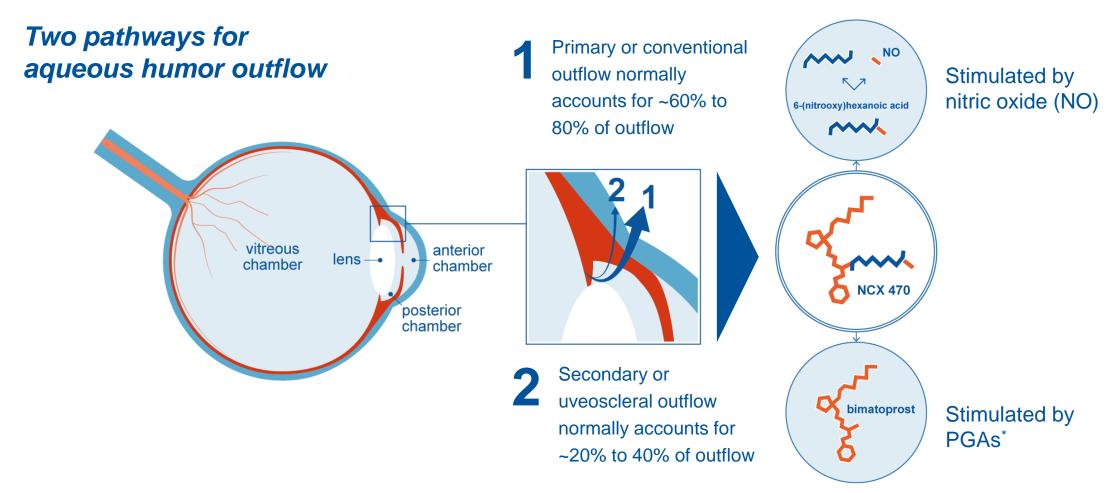
Robin AL et al, Does adjunctive glaucoma treatment therapy affect adherence to the initial primary therapy? Ophthalmology. 2005; 112:863-868

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



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

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







# 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 early November 2022, Denali topline results after 2024



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

<sup>2.</sup> 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 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-inclass IOP-lowering efficacy



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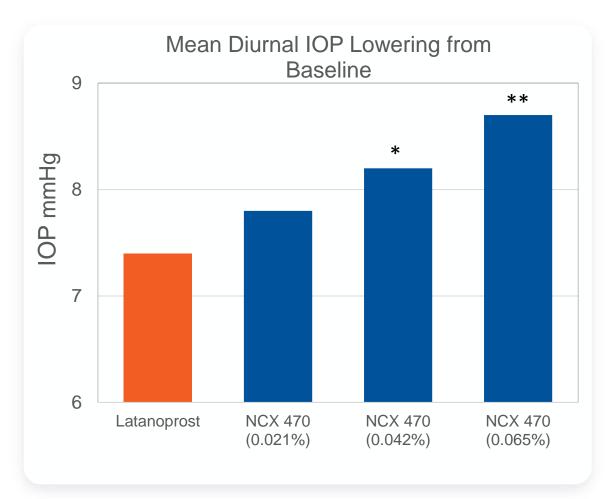
<sup>2.</sup> https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm for Lumigan, Travatan Z, Xalatan

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





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

Mont Blanc topline results due in early 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=691

~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 early 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 Mont Blanc Phase 3 trial due in early November 2022









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

Combining NO-release with PDE5

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

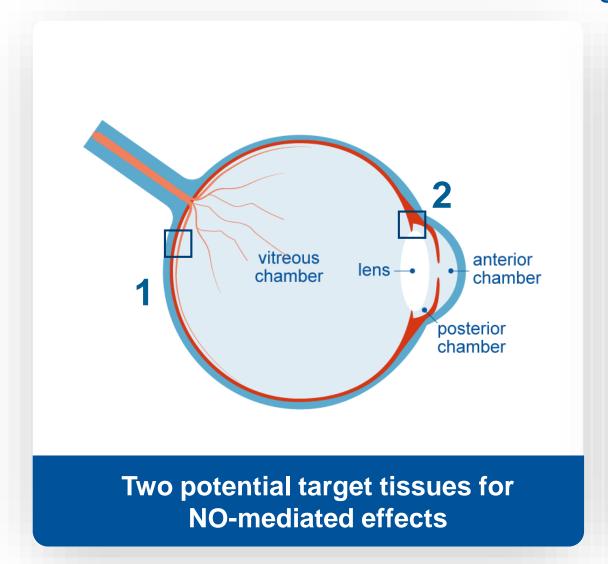
Nonclinical program focused on evaluating MoA

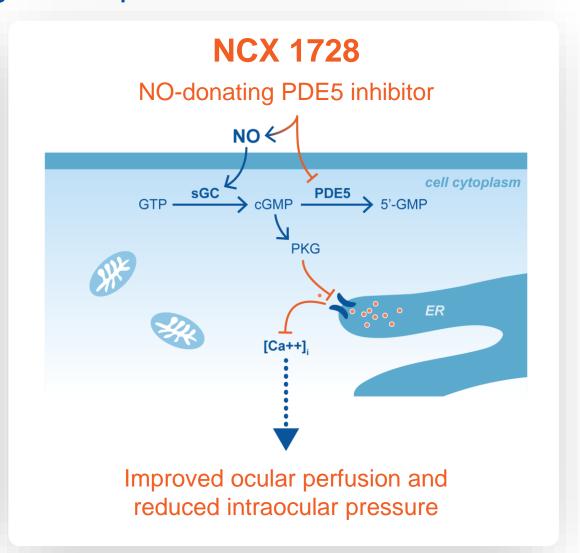
Nonclinical studies underway to evaluate the mechanism of action in models of orphan retinal conditions



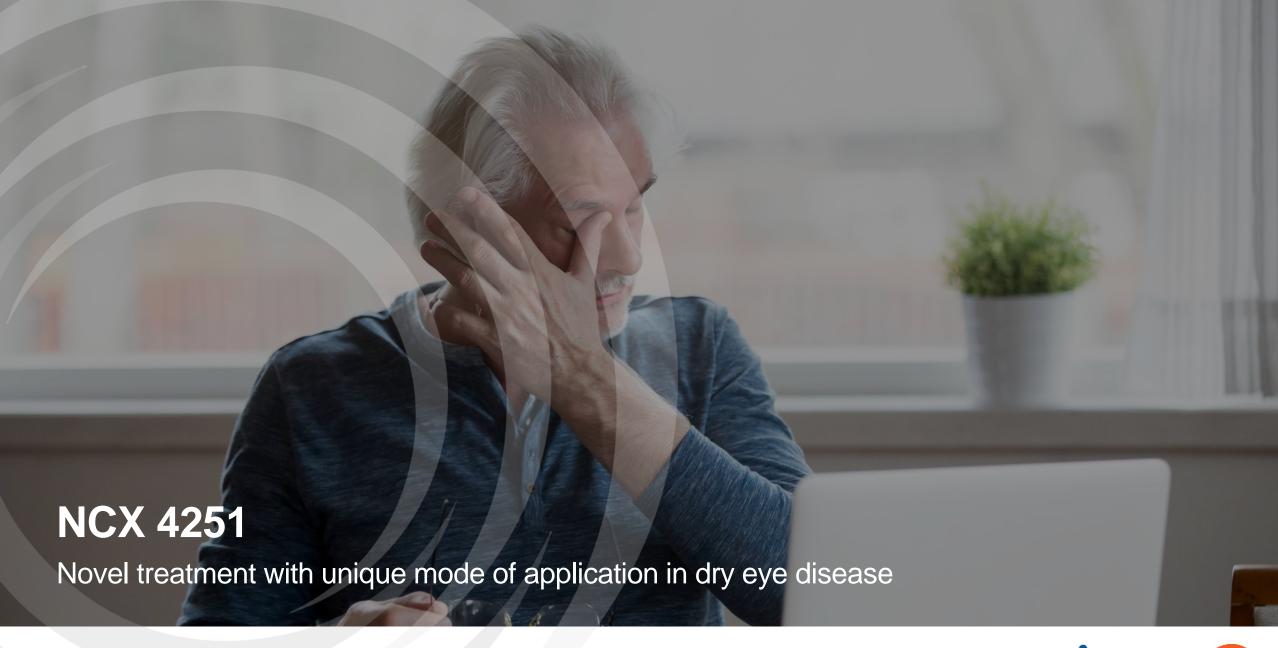


# NCX 1728: NO-Mediated IOP Lowering and Improved Ocular Perfusion













# 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 sideeffects

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

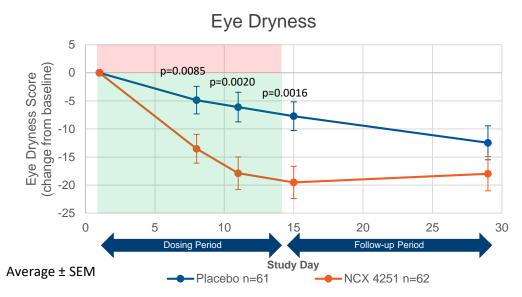




# Mississippi: Post-Hoc Results Puts Dry Eye Disease in Sight



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



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

#### 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 ≥ 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)



Eye dryness measured on a visual analog scale (0 to 100)

<sup>2.</sup> 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







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

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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 OcuMension

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



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







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 Eyevance (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. Ocumnesion has rights in Chinese markets





# Financial Highlights

Cash balance expected to support current operations through November 30, 2023

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

Cash, Cash Equivalents	€25.6 million
Debt <sup>2</sup>	€20.6 million
Cash runway <sup>3</sup>	November 30, 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

<sup>.</sup> Unaudited results



<sup>2.</sup> 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

The cash runway is calculated assuming the development of NCX 470 alone. The Company estimates that it is financed until 31 October 31, 2023, and until 30 November 30, 2023 assuming the extension of 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

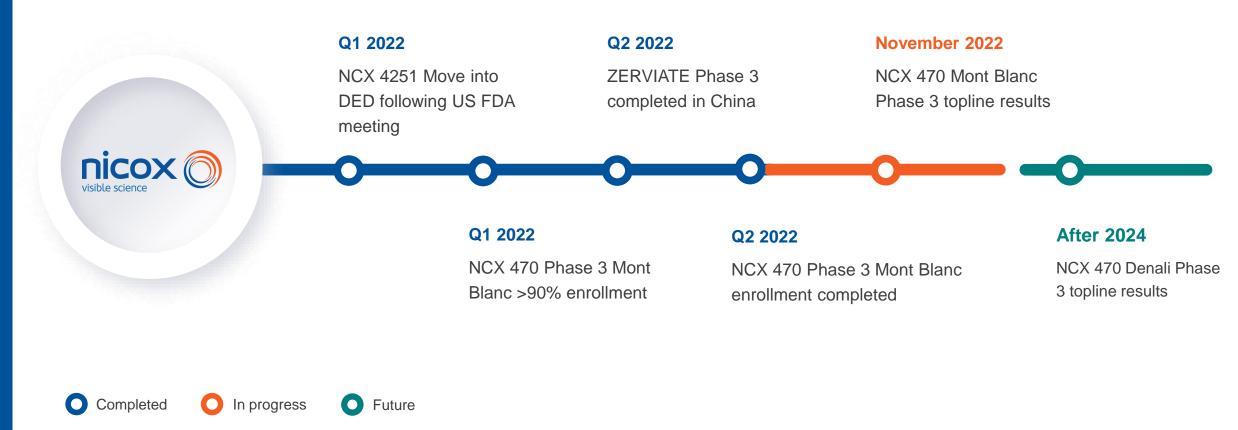
Existing outstanding shares as of September 14, 2022

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



## Value-Creating Milestones

#### Building a high-value ophthalmology pipeline







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