



# Corporate Presentation

May 3, 2022

# 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's website ([www.nicox.com](http://www.nicox.com)).




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Lead asset NCX 470, Phase 3,  
a potential best-in-class glaucoma treatment

NCX 4251, Phase 2,  
novel treatment with unique mode of application in dry eye disease

Financial strength underpinned by global partnerships and revenue  
generated from out-licensed commercial products

# Pipeline

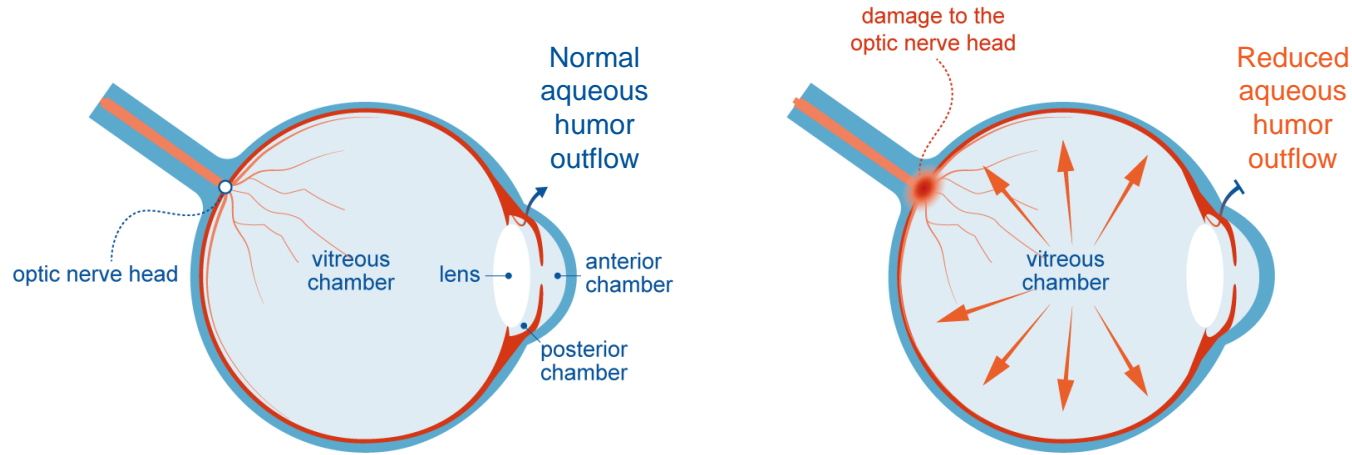
		Stages of Development						Expected milestones
		Preclinical	Phase 1	Phase 2	Phase 3	NDA	Marketed	
Product Candidates								
NCX 470   novel NO-donating prostaglandin analog <i>Glaucoma &amp; Ocular Hypertension</i> <i>Partnered with Ocumension in the Chinese &amp; SE Asian markets</i>		Mont Blanc and Denali trials						Mont Blanc top-line results Q1 2023
NCX 4251   fluticasone propionate nanocrystal suspension <i>Dry Eye Disease</i> <i>Partnered with Ocumension in the Chinese market</i>								CMC preparation for next clinical trial
NCX 1728   NO-donating PDE5 inhibitor <i>Glaucoma &amp; Ocular Hypertension and Retinal Diseases</i>								Entry into pre-IND development
Out-Licensed Commercial Products								
VYZULTA® <i>Glaucoma</i>								Revenue growth
ZERVIAE® <i>Allergic conjunctivitis</i>								Chinese NDA preparation
								



# **NCX 470: Novel Late-Stage Product Candidate in Glaucoma**

**Based on Nicox's NO-Donating Research Platform**

# Glaucoma Results in Progressive and Irreversible Vision Loss



Healthy eye

Intraocular Pressure (IOP) builds up



Typical effect of glaucoma on vision

~3 million patients in the U.S. with open angle glaucoma<sup>1</sup>  
Unmet medical need: 40% of patients fail to reach IOP goals with first-line therapy<sup>2</sup>,  
prostaglandin analog (PGA) eyedrops

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

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

# Every mmHg of IOP Lowering Reduces Risk of Glaucoma Progression

## Results from the Early Manifest Glaucoma Trial (EMGT)<sup>1</sup>

*“In these analyses, each mmHg of decreased IOP was related to an approximately 10% to 20% lowering [of risk of vision loss progression]”*

**~ Prof. Anders Heijl**

## Results from the United Kingdom Glaucoma Treatment Study (UKGTS)<sup>2,3</sup>

*“[...] the risk reduction could be about 19% per mmHg, confirming results from the EMGT and Canadian Glaucoma Study, and showing that intraocular pressure reduction is highly effective, and that every mm of pressure counts.”*

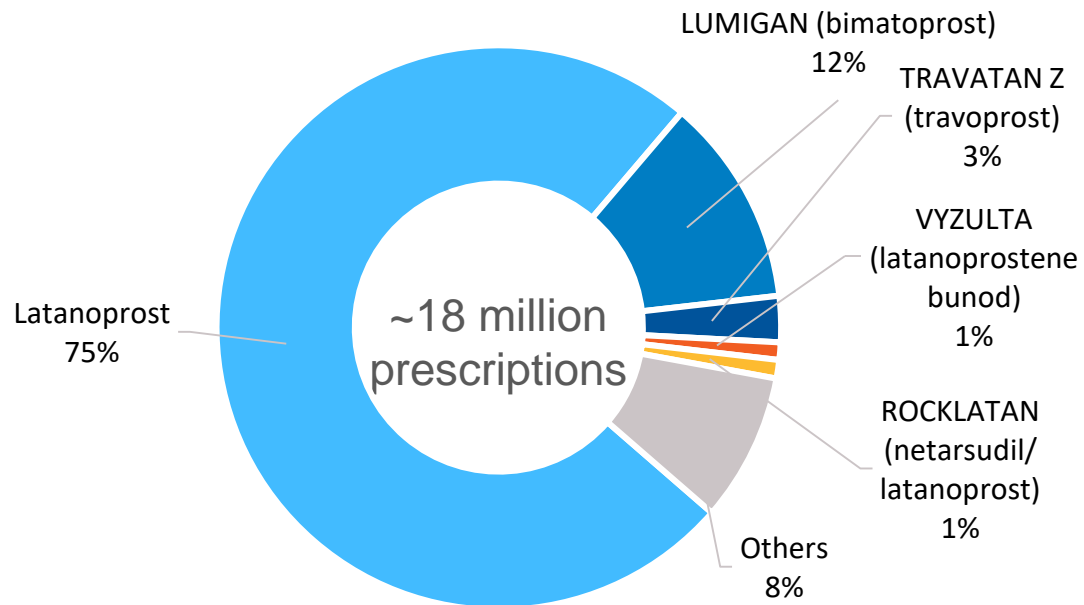
**~ Prof. Anders Heijl**

1. Heijl et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002; 120: 1268-1279
2. Garway Heath et al. Latanoprost for open-angle glaucoma (UKGTS): a randomised, multicentre, placebo-controlled trial. The Lancet 2015; 385: 1295-1304
3. Heijl. Glaucoma treatment: by the highest level of evidence. The Lancet 2015; 385: 1264-1266

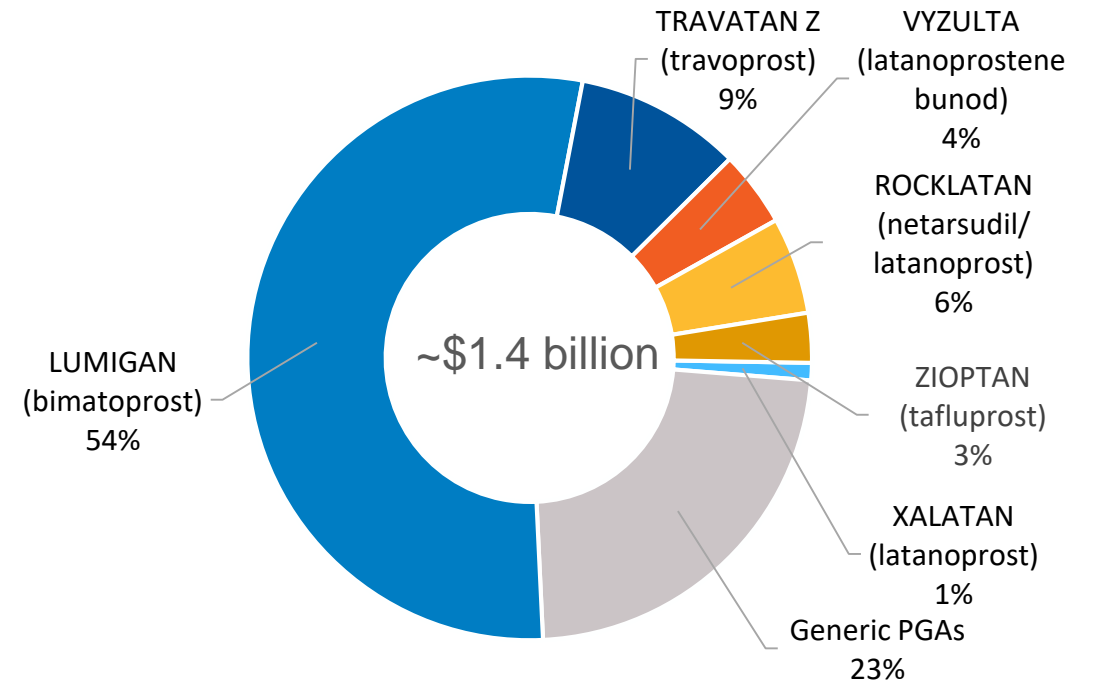
# NCX 470 Targets ~\$1.4 Billion U.S. Glaucoma PGA Market<sup>1</sup>

U.S. Glaucoma Pharmaceuticals Market is ~50% of the Global Market<sup>1</sup>

PGA Prescription Volume<sup>2</sup>



PGA Prescription Value<sup>3</sup>



1. IQVIA™ Analytics Link 2020

2. IQVIA NPA 2020

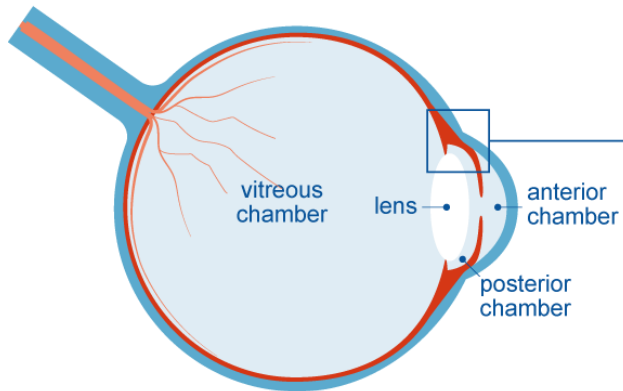
3. IQVIA™ Analytics Link 2020



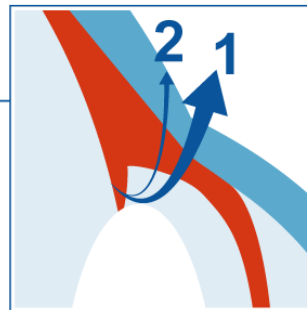
# NCX 470 Targets the Two Key Outflow Pathways for IOP Lowering

Potential for Best-in-Class Efficacy with Novel Dual Mechanism of Action

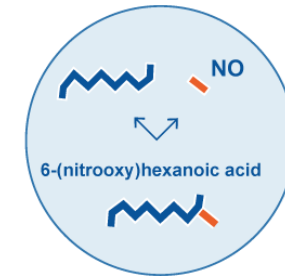
***Two pathways for aqueous humor outflow***



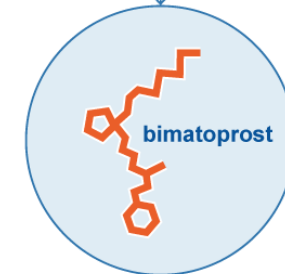
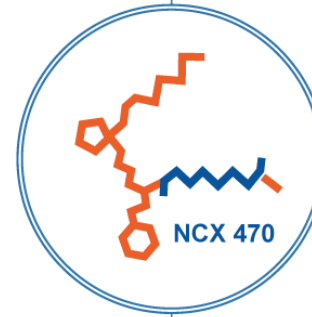
**1** Primary or conventional outflow normally accounts for ~60% to 80% of outflow.



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



Stimulated by nitric-oxide (NO)

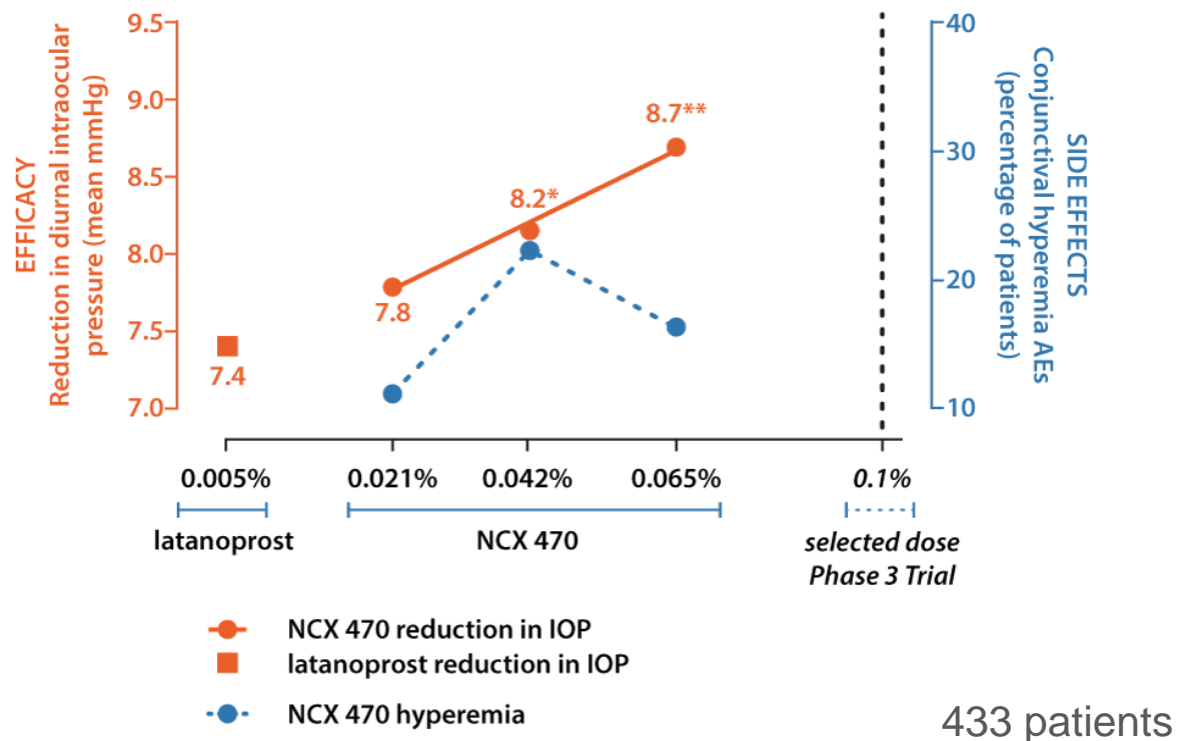


Stimulated by PGAs

# NCX 470: Statistical Superiority to Market Leader in IOP Lowering

## Linear Dose Response Suggests Potential Higher Efficacy for Phase 3 Dose

### Efficacy vs Side Effect Profile Observed in Phase 2 Trial



### Summary Phase 2 Dolomites Trial Results

- Large Phase 2 trial achieved statistical superiority to market leader, with comparable safety and no serious adverse events
- Conjunctival hyperemia plateaued

### Ongoing Phase 3 Mont Blanc and Denali Trials

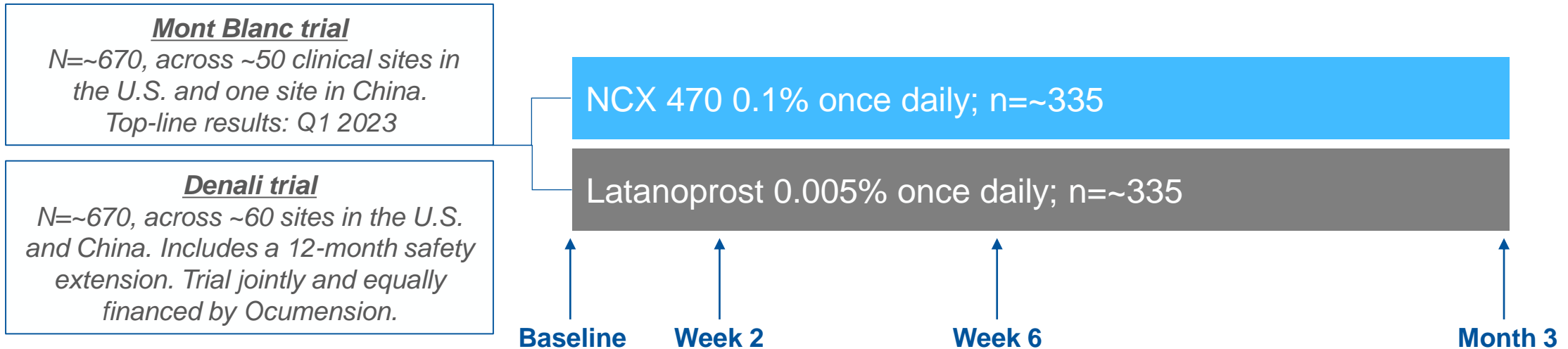
- Two multi-regional Phase 3 glaucoma trials at 0.1% dose ongoing in 670 patients each; designed for U.S. and China NDA submissions
- **Top-line results from Mont Blanc expected in Q1 2023**

\* p<0.05, \*\*p=0.0009

# NCX 470: 2 Phase 3 trials Support U.S. & China NDA Submissions

Mont Blanc Top-line Results Currently Expected in Q1 2023

Randomized, double-masked in patients with open angle glaucoma or ocular hypertension



*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 Potential Peak Sales in U.S. First-Line Glaucoma Market

	EXISTING MARKET: ~\$1.4 billion <sup>1</sup>		
Current therapies	Traditional <sup>2</sup> PGAs	VYZULTA (latanoprostene bunod ophthalmic solution), 0.024% <sup>3</sup>	ROCKLATAN (fixed dose combination of netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% <sup>2</sup>
	Latanoprost: >70% of PGA prescriptions		
	Available for over 20 years	Launched December 2017	Launched May 2019
IOP lowering	6 mmHg to 8 mmHg	7 mmHg to 9 mmHg	6.8 mmHg to 9.2 mmHg
Regulatory Phase 3	Compared with timolol	Compared with timolol	Compared with latanoprost
Comparison	No label data vs. PGAs	No label data vs. PGAs Phase 2 showed ~1.3 mmHg better vs latanoprost	1.58 mmHg greater reduction than latanoprost at 3 months <sup>4</sup>
Hyperemia	8% to 50%	6%	59% plus additional side effects not seen with PGAs

## NCX 470

***Two market research studies have estimated U.S. peak sales for NCX 470 0.1% of between \$200 million and \$300 million if NCX 470 demonstrates superiority in IOP lowering of 1.5 to 1.7 mmHg<sup>6</sup> in Phase 3 compared to latanoprost 0.005%***

1. IQVIA™ Analytics Link 2020

2. Indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension

3. Indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension

4. See Section 14, Clinical trials, Figure 1 and 2 of ROCKLATAN package insert for diurnal IOP at Day 90 for ROCKLATAN vs. latanoprost including both Mercury-1 and Mercury-2 IOP values (1.5; 1.7; 1.3; 1.5;2.0; and 1.5 mmHg)

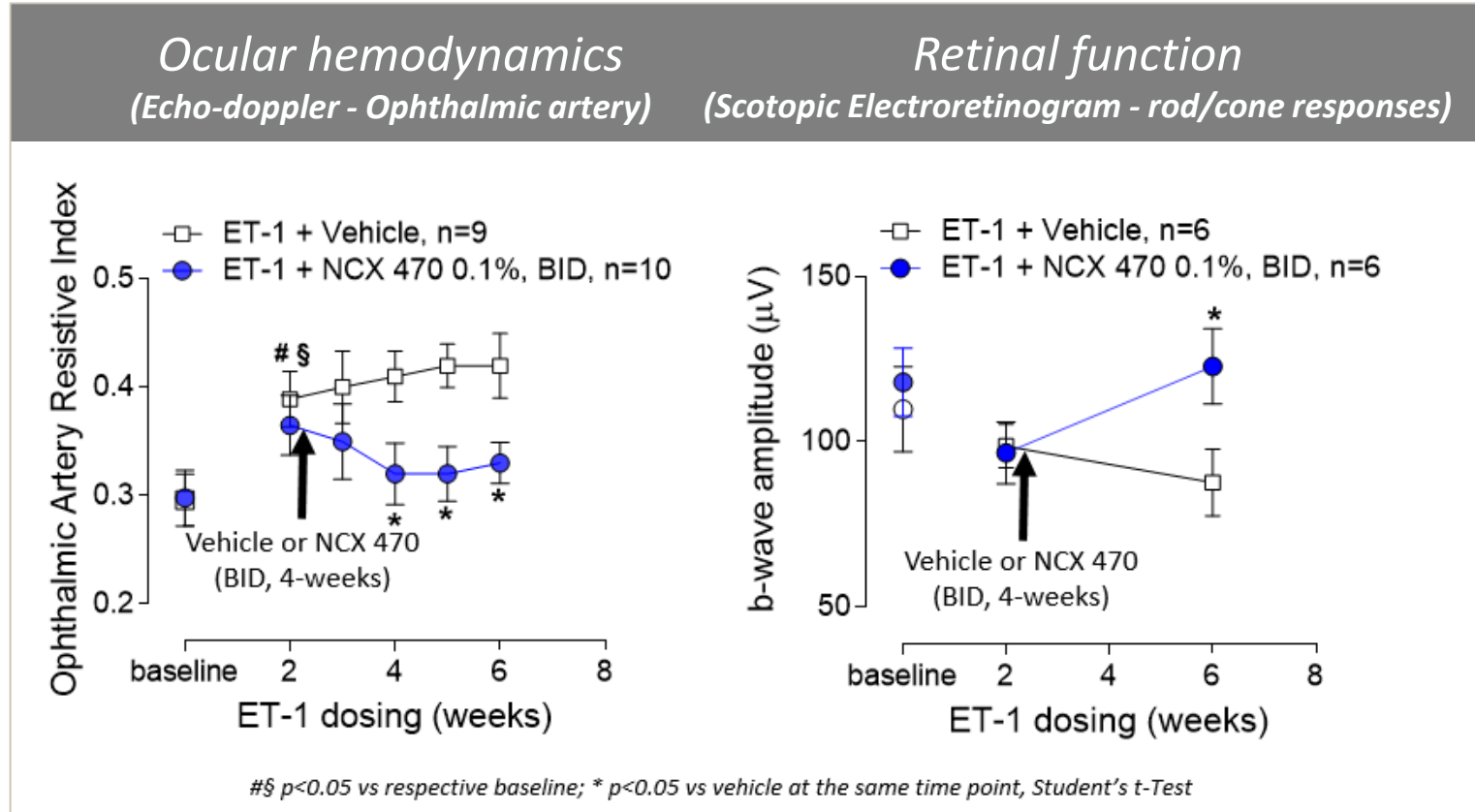
5. Nicox internal market research, 2019 and 2021

6. Approved label claim

# NCX 470 Shows Retinal Cell Protection in a Non-Clinical Model<sup>1</sup>

Improved ocular perfusion and retinal function in damaged eyes

Potential therapeutic properties beyond IOP lowering



- Detrimental effect of ET-1 on ophthalmic artery hemodynamics was **significantly reversed** in eyes receiving NCX 470 0.1% bid ( $p<0.05$  vs. vehicle at week 6)
- Photoreceptor response decline induced by ET-1 was **almost completely reversed** in eyes treated with NCX 470 0.1% bid ( $p<0.05$  vs. vehicle at week 6)

1. Bastia et al., NCX 470 restores ocular hemodynamic and retinal cell physiology after ET-1-induced ischemia/reperfusion injury of optic nerve and retina in rabbits. Journal of Ocular Pharmacology and Therapeutics 2022; in press



# NCX 4251: Novel Treatment With Unique Mode of Application in Dry Eye Disease

# NCX 4251 and Dry Eye Disease

An Innovative Potential Therapy for Treatment of Dry Eye Disease

## Product



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

## Prevalence



**34 million**  
Americans estimated to have dry  
eye disease<sup>1</sup>

## Market

**Over \$5bn**  
sales  
worldwide<sup>2</sup>

NCX 4251 is a novel, patented, ophthalmic suspension of fluticasone propionate nanocrystals

1. Paulsen et al, Dry Eye in the Beaver Dam Offspring Study: Prevalence, Risk Factors, and Health-Related Quality of Life. Am J Ophthalmol. 2014 April ; 157(4): 799–806.
2. Fortune Business Insights, Dry Eye Syndrome Market Size, Share & Industry Analysis, By Product (Anti-inflammatory and Artificial Tears & Lubricants), By Distribution Channel (Hospital Pharmacies, Retail Pharmacies, Online Pharmacies, and Others), and Regional Forecast, 2020-2027.

# NCX 4251: Mississippi Phase 2b Clinical Trial and Next Steps

## Targeting Future Development in Dry Eye Disease

### Design

Mississippi was a 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

- 224 patients with blepharitis across multiple centers in the U.S.
- Evaluation visits at days 4 (blepharitis evaluation only), 8, 11 and 15 with follow-up at day 29

### Results

Whilst not meeting the primary efficacy endpoint in blepharitis (*complete cure in the composite score of eyelid redness, eyelid discomfort and eyelid debris*), the results showed:

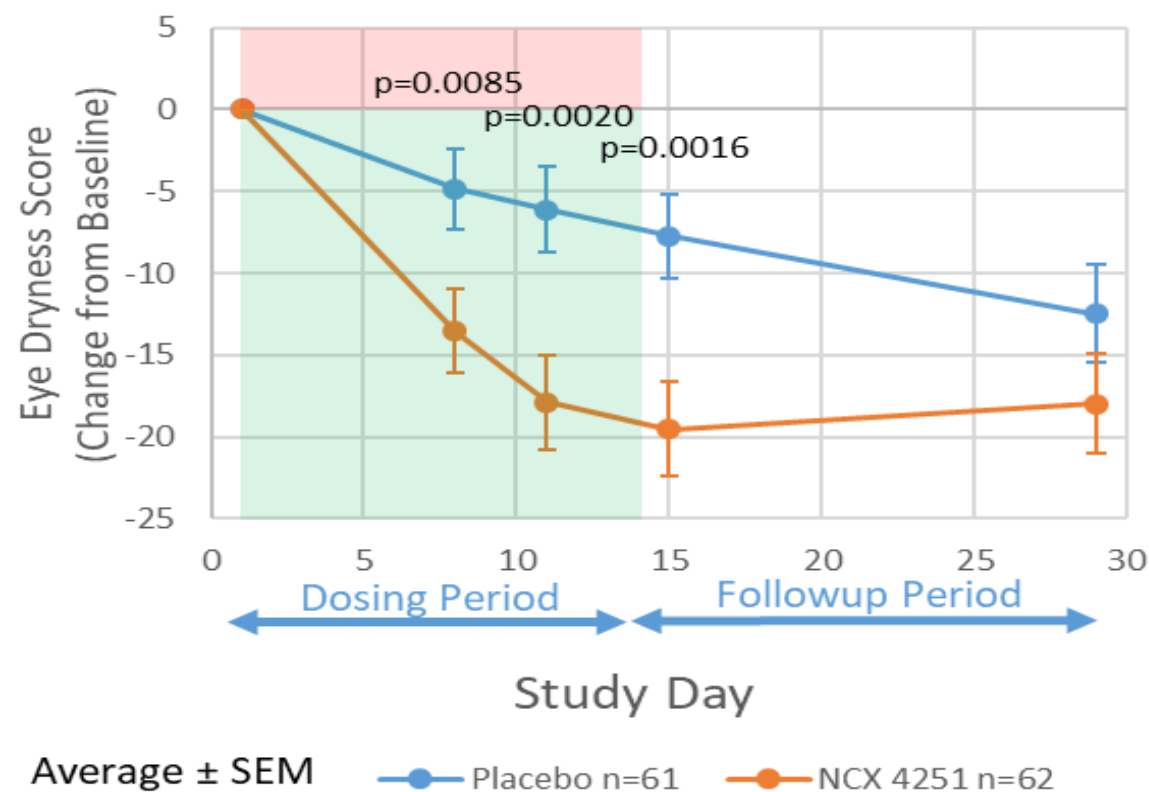
- *Statistical significance in change from baseline for the composite score of eyelid redness, eyelid discomfort and eyelid debris between active and placebo groups*
- **Statistically significant and clinically relevant effect over placebo in a number of dry eye symptoms in a subgroup of patients, in a post hoc analysis.** 70%-80% of blepharitis sufferers also have dry eye
- NCX 4251 was found to be safe and well-tolerated after 14 days administration

### Next Steps

- Clear path forward identified for dry eye disease following positive meeting with the U.S. FDA in early 2022
- Exploring how to best advance the development of NCX 4251 in dry eye disease

# NCX 4251: Efficacy in Reducing Signs & Symptoms of Dry Eye Disease<sup>1</sup>

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



## Post hoc subset analysis

- 123 of the overall 224 patients had inferior corneal fluorescein staining scores  $\geq 2$  on a scale of 0 (none) to 4 (severe)
- In this subset, patients had **statistically significant difference against placebo for change from baseline in eye dryness scores**
- Statistically significant differences against placebo were also observed in other symptoms of dry eye disease (photophobia, blurred vision, burning/stinging, foreign body sensation, ocular itching, pain) at all timepoints during treatment. In some symptoms the effects of treatment persisted up to two weeks after the end of dosing treatment
- Treatment group differences in change from baseline in inferior corneal fluorescein staining approached significance and could potentially reach that with a larger sample size



# **NCX 1728: NO-Donating PDE5 Inhibitor in Glaucoma & IOP-Lowering and Certain Retinal Diseases**

**Based on Nicox's NO-Donating Research Platform**

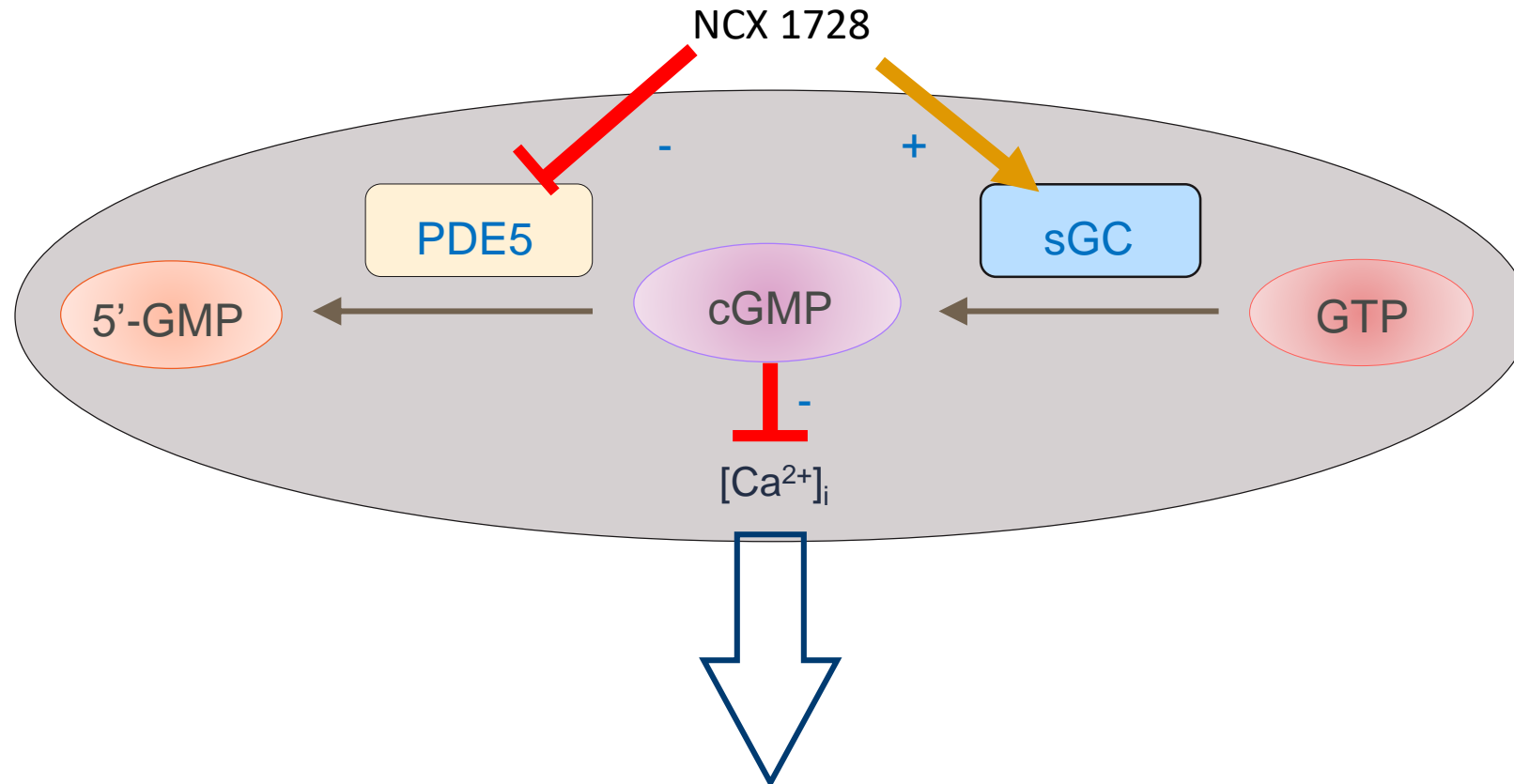


## NCX 1728: NO-donating PDE5 inhibitor

- Lead in a new class of compounds (non-PGA related) with **NO-mediated IOP lowering effects** enhanced and prolonged by **concomitant PDE5 inhibition** within the same molecule
- Class of molecules is being evaluated for development in **glaucoma & IOP lowering** and in certain **retinal diseases**
- **Optimization of ophthalmic formulations** of NCX 1728 underway prior to initiating nonclinical testing required for the filing of an Investigational New Drug (IND) application

# NCX 1728 Mechanism of action

Enhancing and prolonging the activity of NO



Improved ocular perfusion and reduced intraocular pressure

## Corporate

- Key Partnerships
- Financial Highlights
- Anticipated Value-Creating Milestones

# Key Partnerships

## OCUMENSION

NCX 470, ZERVIAE, NCX 4251

- Exclusive rights<sup>1</sup> in China and certain Southeast Asian markets on three key assets
- NCX 470: received €18 million; **6% to 12%** net royalties on sales; funding 50% of Phase 3 Denali clinical trial
- ZERVIAE: Up to **\$17.2 million** in sales milestones plus **5% to 9%** royalties on net sales. Phase 3 trial for Chinese NDA successfully completed
- NCX 4251: Up to **\$11.3 million** in milestones plus **5% to 10%** royalties on sales

## VYZULTA

Partnered with Bausch + Lomb worldwide

- First eye drop approved in 20 years with a novel approach to reduce IOP
- Commercialized in 7 territories including the U.S., approved in 9 additional markets
- **\$20 million** milestone at \$100 million net sales<sup>2</sup>
- **6% to 12%** net<sup>3</sup> royalties on global sales

## ZERVIAE

- First and only eye drop formulation of cetirizine
- Commercialized in the U.S. by Eyevance, a wholly-owned subsidiary of Santen Pharmaceutical Co., Ltd, Japan
- Licensed to other partners in the Chinese market, Korea, Gulf and Arab markets, South East Asia, Mexico

1. Includes SE Asian markets for NCX 470 and ZERVIAE, and Korea for NCX 470

2. \$15 million of this is payable to Pfizer per the terms of the contract signed with Pfizer in August 2009 by which Nicox recovered the rights to latanoprostene bunod

3. Net of royalties payable to Pfizer, per the terms of the contract signed with Pfizer in August 2009 by which Nicox recovered the rights to latanoprostene bunod

# Partnership with Fera on Naproxcinod in Sickle Cell Disease

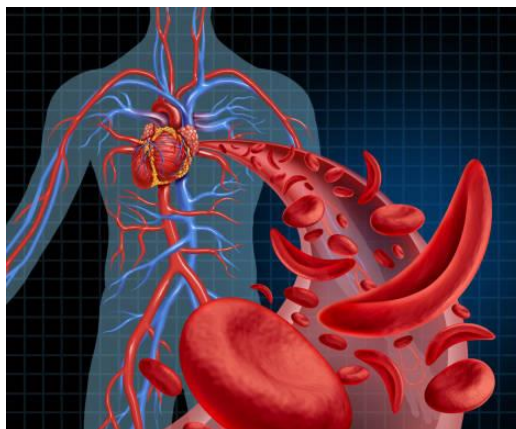
## Developing Naproxcinod for an Inherited Orphan Disease

### Disease



***Faulty version of hemoglobin causes normally oval-shaped red blood cells to assume a sickle-like shape***

### Prevalence



**100,000**

Americans estimated to suffer from sickle cell disease

### Status

- Naproxcinod is a **COX-Inhibiting Nitric Oxide Donor (CINOD)**
- **Orphan Drug Designation** granted by the U.S. FDA for sickle cell disease
- Fera has an **exclusive license for the United States**
- Naproxcinod already **tested on 2,700 patients** in another indication, providing a significant clinical safety database for the development in sickle cell disease
- Strong scientific rationale on the **role of NO in sickle cell disease**

*Nicox is eligible to potentially receive a single \$40 million sales-based milestone if naproxcinod reaches \$1 billion yearly sales (for any indication) in the U.S. as well as royalties of 7% on future net sales of naproxcinod in the U.S., and retains all rights to naproxcinod outside the U.S., subject to the payment of royalties to Fera, if intellectual property developed under the agreement is used outside the U.S.*



# Financial Highlights

Estimated Financial Position as of March 31, 2022 <sup>1</sup>	
Cash, Cash Equivalents	€35.1 million
Debt <sup>2</sup>	€20.5 million
Cash runway	Q4 2023

Outstanding Shares <sup>3</sup>	43.2 million
Management and Employees Ownership	1.9%
Key Institutional Investor	HBM Partners 7.0%

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

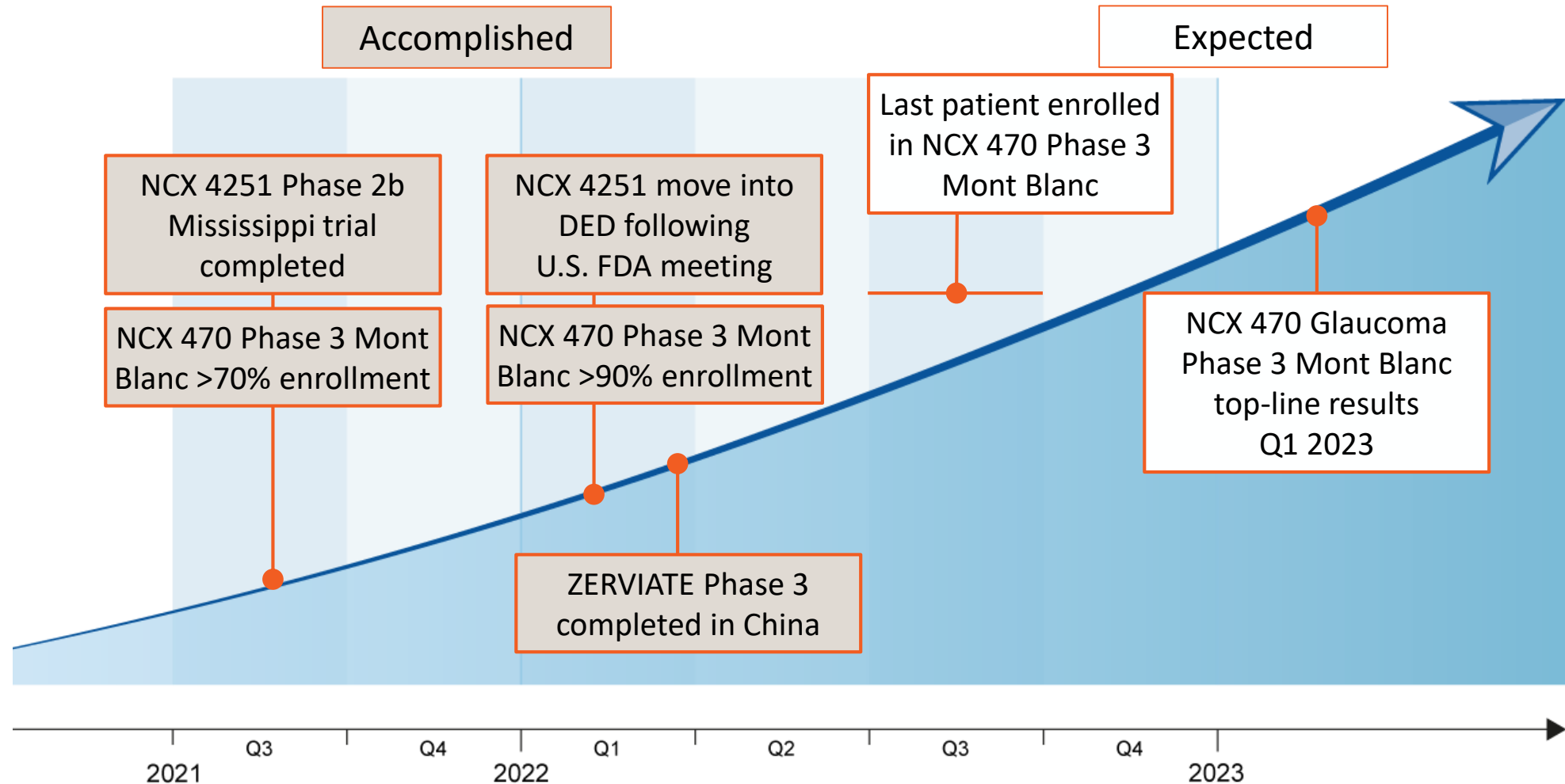
1. Unaudited figure

2. From a bond financing agreement with Kreos Capital, for €18.5 million, a non-dilutive €2 million loan facility credit agreement guaranteed by the French state in the context of the COVID-19 pandemic

3. Existing outstanding shares as of March 31, 2022

# Value-Creating Milestones

## Building Our Late-Stage Ophthalmic Portfolio for Commercialization



Lead asset NCX 470, Phase 3,  
a potential best-in-class glaucoma treatment

NCX 4251, Phase 2,  
novel treatment with unique mode of application in dry eye disease

Financial strength underpinned by global partnerships and revenue  
generated from out-licensed commercial products

# Innovative Solutions to Help Maintain Vision and Improve Ocular Health

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