

Corporate Presentation

April 4, 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 3rd chapter of the "*Document d'Enregistrement Universel, rapport financier annuel et rapport de gestion 2020*" filed with the French Autorité des Marchés Financiers (AMF) on March 1, 2021 under number D.21-0083 and in the 2nd chapter of the amendment to the "*Document d'Enregistrement Universel, rapport financier annuel et rapport de gestion 2020*" filed with the AMF on December 9, 2021 available on Nicox SA's website (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 to address unmet medical need in dry eye disease

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

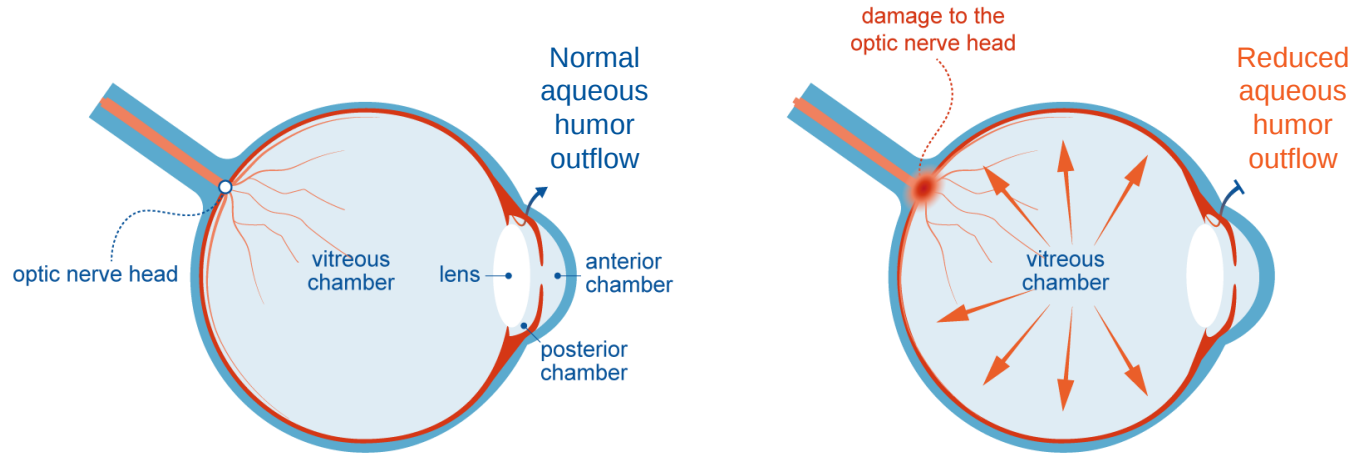
Pipeline

		Stages of Development						Expected milestones
		Preclinical	Phase 1	Phase 2	Phase 3	NDA	Marketed	
NO-Donating Product Candidates Targeting Glaucoma								
NCX 470 novel NO-donating prostaglandin analog <i>Partnered with Ocumension in the Chinese & SE Asian markets</i>		Mont Blanc and Denali trials						Top-line results: - Mont Blanc Q1 2023 - Denali by end 2023
NCX 1728 novel NO-mediated IOP lowering agent								Entry into pre-IND development
Novel Formulation Targeting Dry Eye Disease								
NCX 4251 fluticasone propionate nanocrystal suspension <i>Partnered with Ocumension in the Chinese market</i>								Start of next clinical trial in 2023
Out-Licensed Commercial Products								
VYZULTA® Glaucoma								Revenue growth
ZERVIAE® Allergic conjunctivitis	 United States							Revenue growth
	 Chinese & SE Asian markets							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 glaucoma¹
Unmet medical need: 40% of patients fail to reach IOP goals with first-line therapy²,
prostaglandin analog (PGA) eyedrops

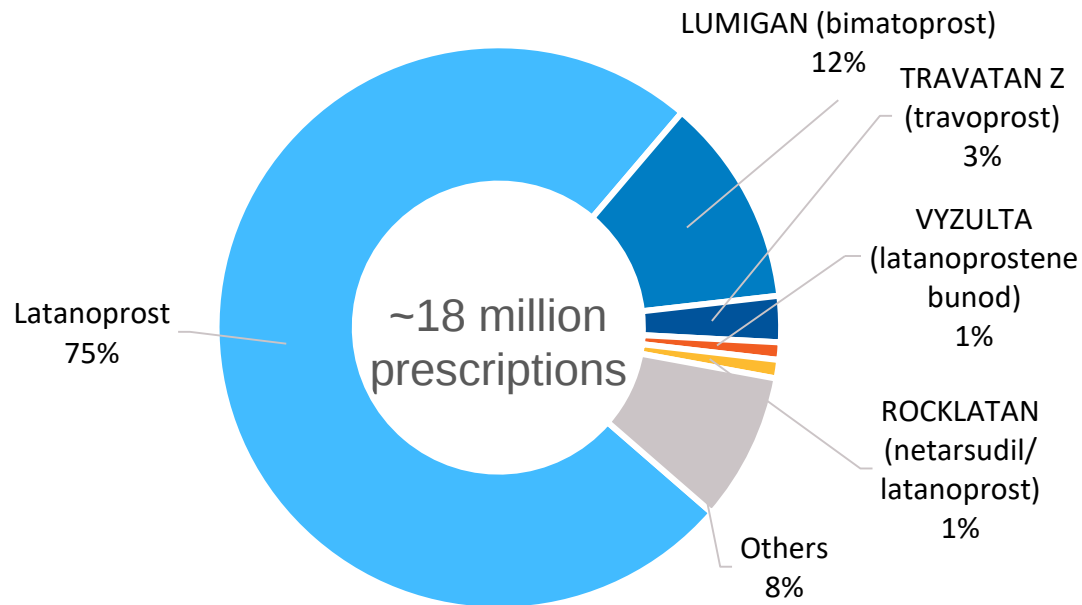
1. <https://www.cdc.gov/features/glaucoma-awareness/index.html>

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

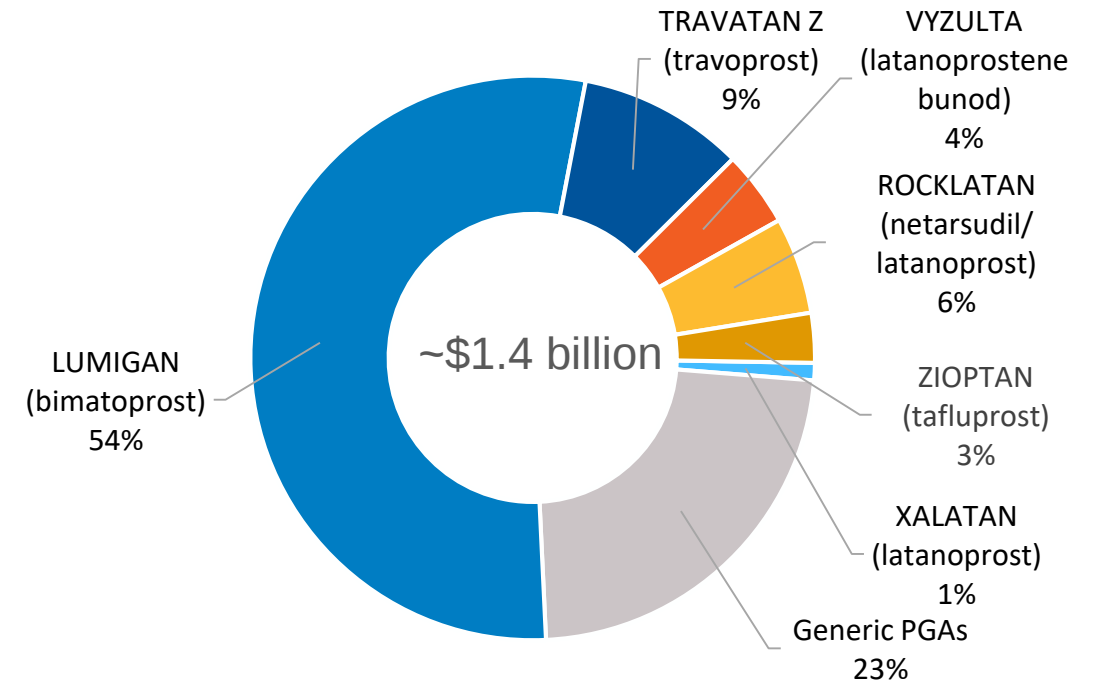
NCX 470 Targets ~\$1.4 Billion U.S. Glaucoma PGA Market¹

U.S. Glaucoma Pharmaceuticals Market is ~50% of the Global Market¹

PGA Prescription Volume²



PGA Prescription Value³



1. IQVIA™ Analytics Link 2020

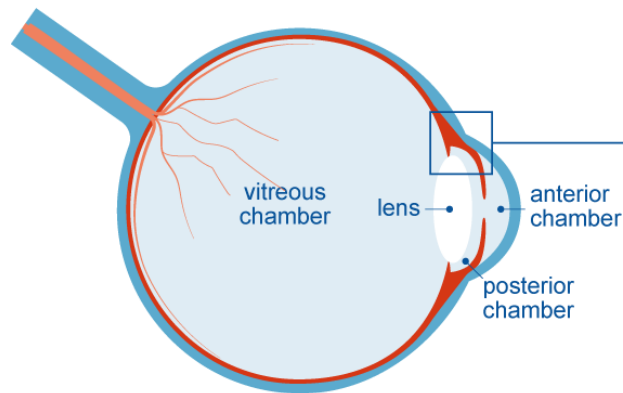
2. IQVIA NPA 2020

3. IQVIA™ Analytics Link 2020

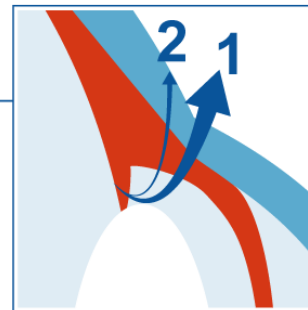
NCX 470 Targets the Two Key Outflow Pathways for Lowering IOP

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

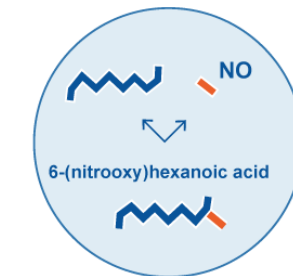
Two pathways for aqueous humor outflow



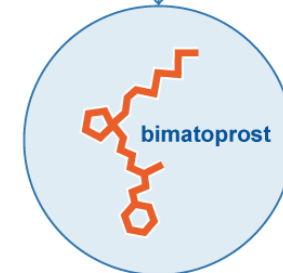
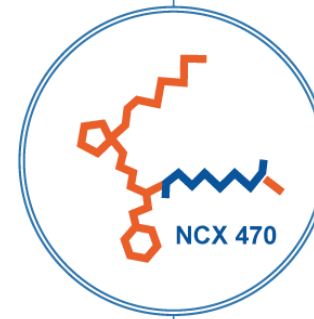
1 Primary or conventional outflow normally accounts for ~60% to 80% of outflow.



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



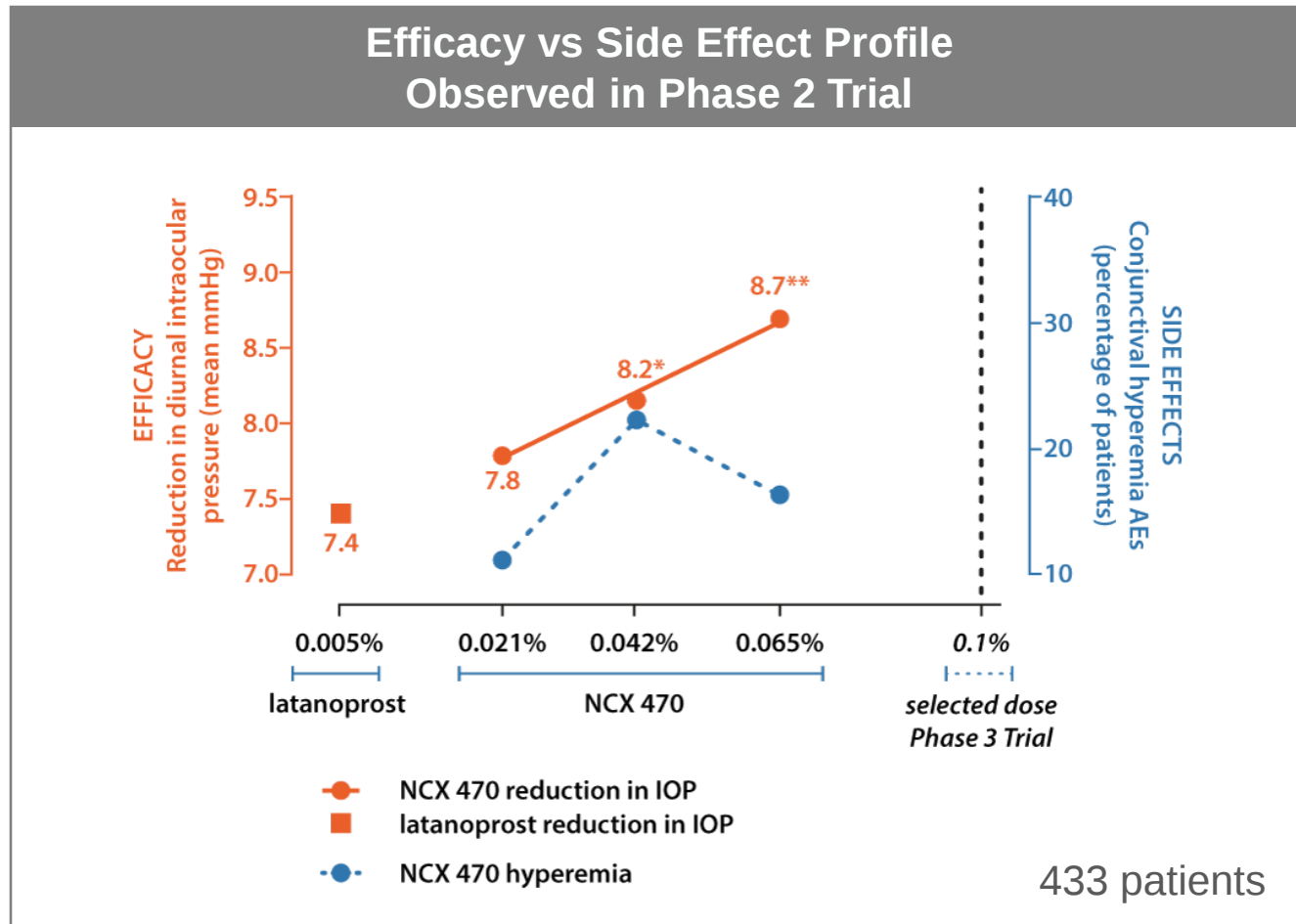
Stimulated by nitric-oxide (NO)



Stimulated by PGAs

NCX 470: Statistical Superiority to Market Leader in IOP lowering

Linear Dose Response Suggests Potential Higher Efficacy for Phase 3 Dose



* p<0.05, **p=0.0009

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

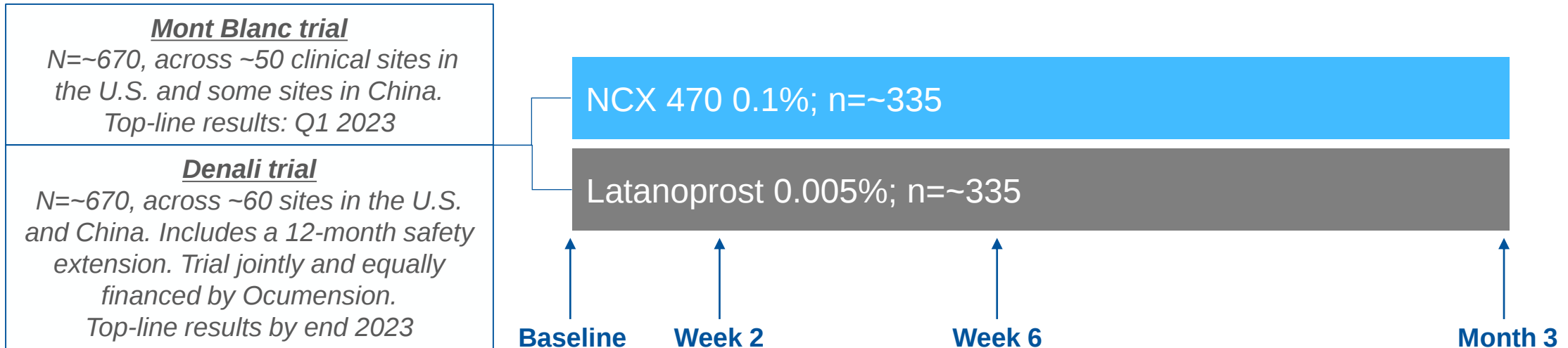
Ongoing Phase 3 Mont Blanc and Denali Trials

- 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 and from Denali by end 2023***

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

Top-line Results Currently Expected in Q1 2023 and by end 2023

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



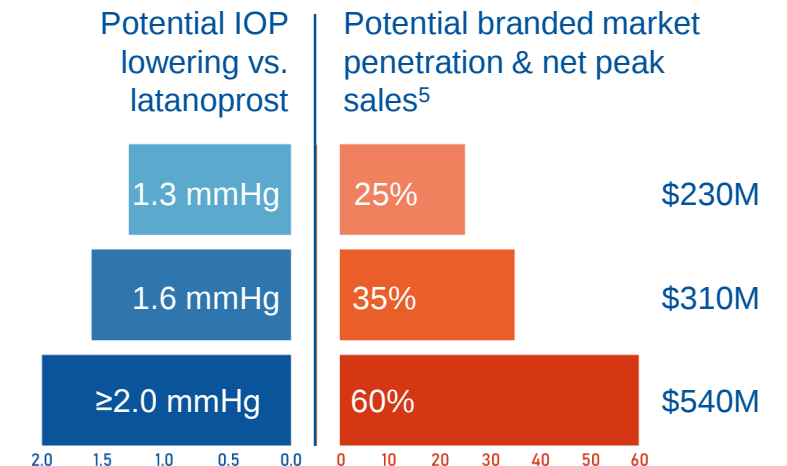
Primary Endpoint: Mean intraocular pressure reduction from time-matched baseline at 8AM and 4PM

NCX 470 Potential Peak Sales in U.S. First-Line Glaucoma Market

Current therapies	EXISTING MARKET: ~\$1.4 billion ¹		
	Traditional ² PGAs	VYZULTA (latanoprostene bunod ophthalmic solution), 0.024% ³	ROCKLATAN (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% ²
	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 ⁴
Hyperemia	8% to 50%	6%	59% plus additional side effects not seen with PGAs

NCX 470

NCX 470 potential superiority in IOP lowering in Phase 3 compared to latanoprost 0.005%

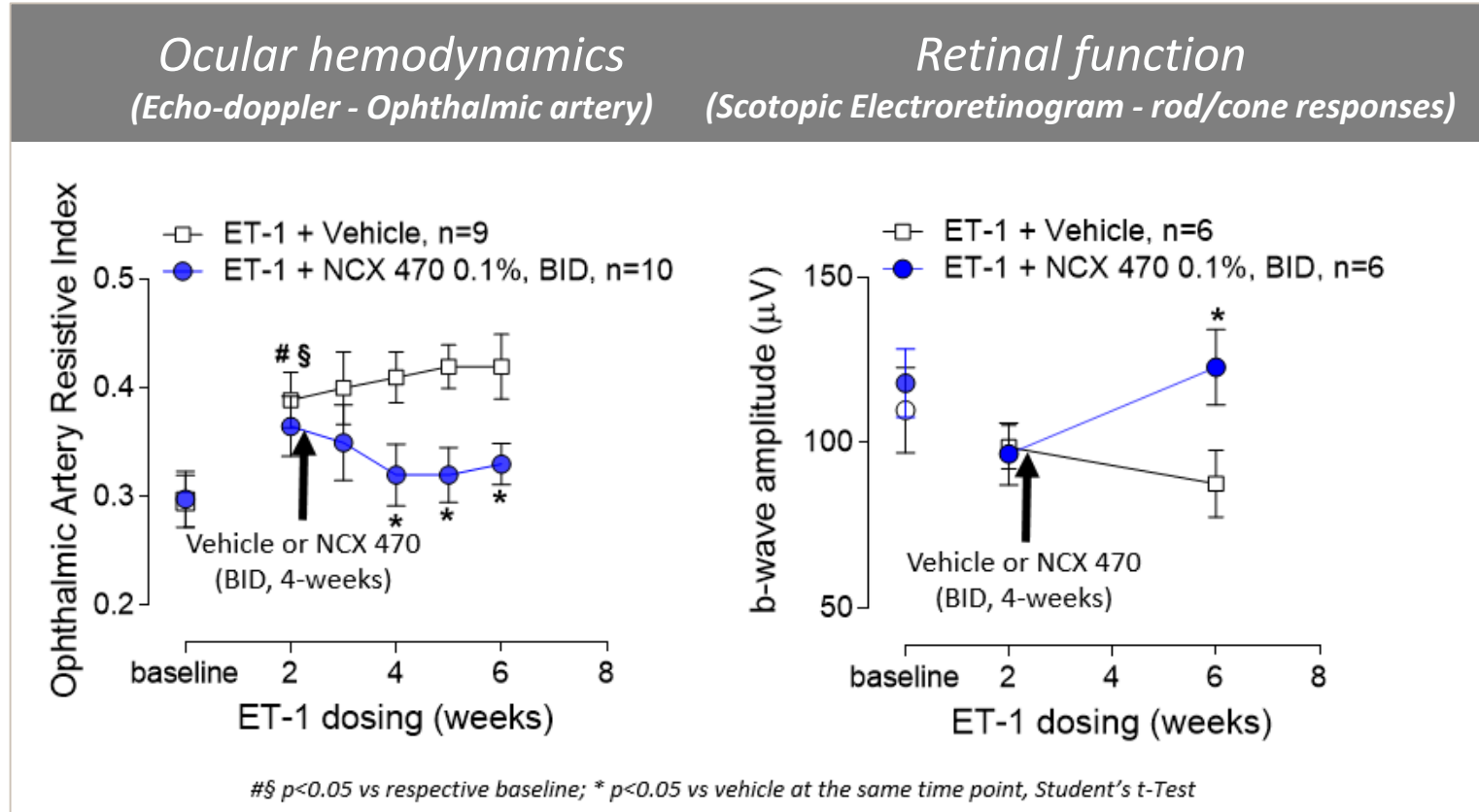


1. IQVIA™ Analytics Link 2020
2. Indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension
3. Indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension
4. See Section 14, Clinical trials, 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

NCX 470 Shows Retinal Cell Protection in a Non-Clinical Model¹

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. Nicox internal data in a model of ischemia/reperfusion injury to the optic nerve in rabbits induced by ET-1. ET-1 alone was administered twice-weekly for two weeks, followed by concomitant dosing with NCX 470 or vehicle for a further 4 weeks.

NCX 1728: Lead Compound in a New Class of IOP Lowering Agents

Molecules in this new class showed robust IOP lowering in a non-human primate model of ocular hypertension¹

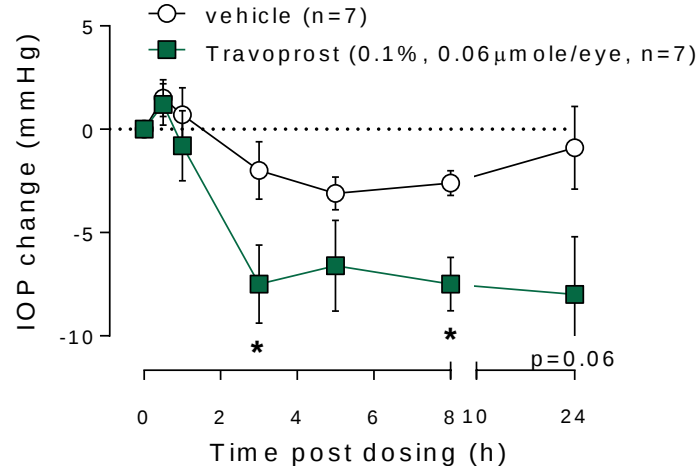
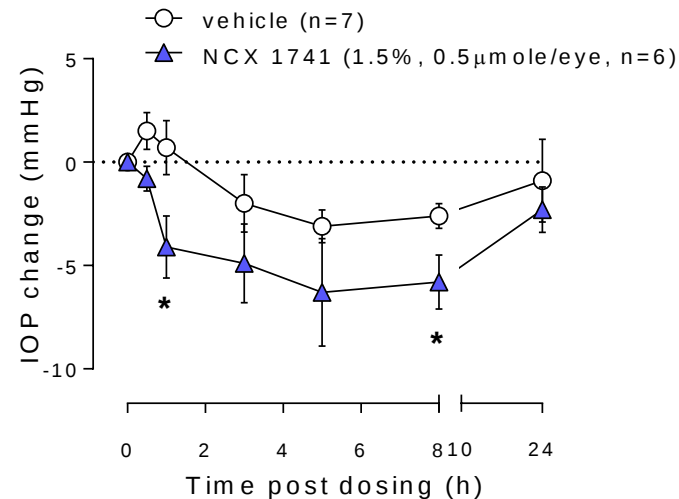
- Lead in a new class of compounds (non-PGA related) with **NO-mediated IOP lowering effects** enhanced and prolonged by **concomitant PDE5 inhibition** within the same molecule
- Molecules in this class demonstrated **IOP lowering similar to travoprost** in animal models of ocular hypertension and glaucoma¹
- Molecules in this new class have potential as **monotherapy**, as **adjunctive therapy** or in **fixed-dose combinations**¹ with PGAs for IOP lowering in patients with open-angle glaucoma or ocular hypertension
- **Optimization of ophthalmic formulations** of NCX 1728 underway prior to initiating nonclinical testing required for the filing of an Investigational New Drug (IND) application

1. Bastia E. et al., J. Ocul. Pharmacol. Ther. 2021, 15 Feb DOI: 10.1089/JOP.2020.0126

NCX 1741, an Analog of NCX 1728, Lowers IOP in Ocular Hypertensive Non-human Primates

Potential as monotherapy, as adjunctive therapy or in fixed-dose combinations with PGAs for IOP lowering

Intraocular pressure (IOP)-lowering



* $p < 0.05$ vs. vehicle at the respective time-point, Multiple t-test

- NCX 1741 is an analog of NCX 1728
- In non-human primates, NCX 1741 had faster onset of action and similar IOP-lowering efficacy as travoprost 0.1% for up to 8h post-dosing^{1,2}

1. Impagnatiello F. et al., *Investigative Ophthalmology & Visual Science* 2020, Vol.61, 2786.

2. Bastia E. et al., NCX 1741, a Novel Nitric Oxide-Donating Phosphodiesterase-5 Inhibitor, Exerts Rapid and Long-Lasting Intraocular Pressure-Lowering in Cynomolgus Monkeys, *J Ocul Pharmacol Ther* 2021 May;37(4):215-222

NCX 4251: Novel Treatment to Address Unmet Medical Need in Dry Eye Disease

Dry Eye Disease – Existing Market with Unmet Medical Need

NCX 4251: 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 disease¹

Market

**Over \$5bn
sales
worldwide²**

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:

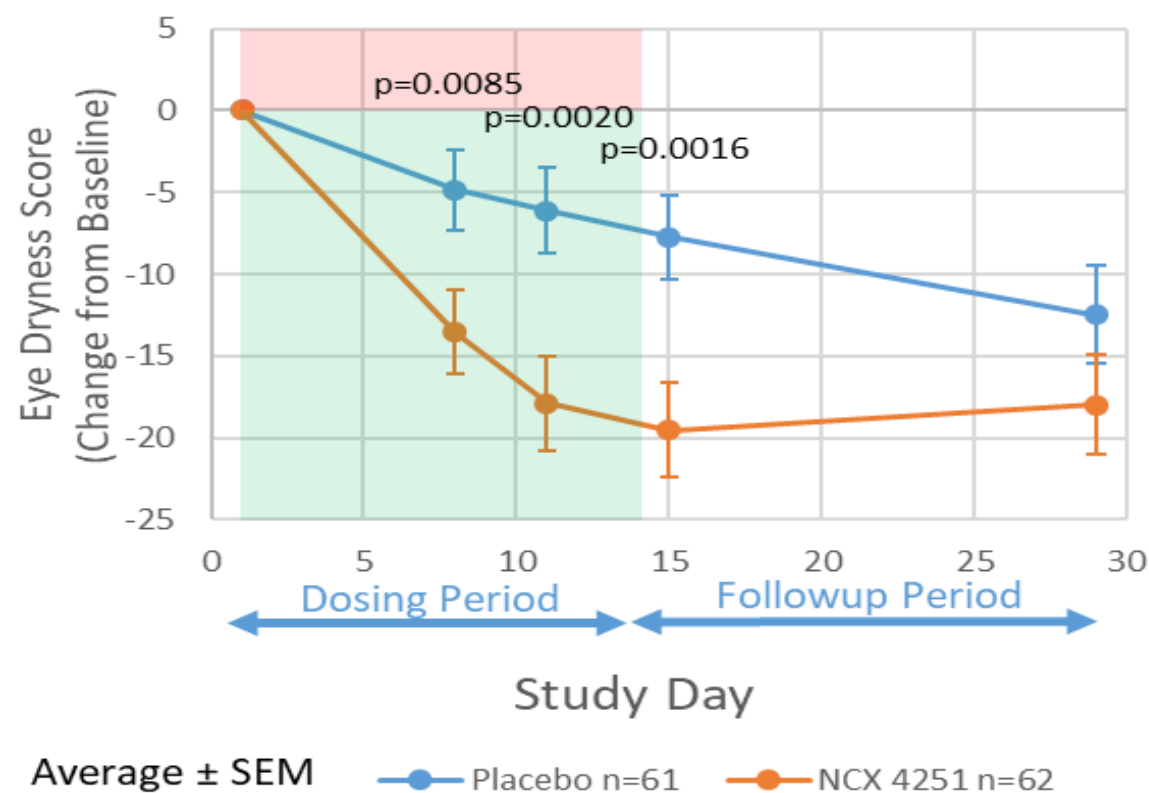
- *Statistical significance in change from baseline for the composite score of eyelid redness, eyelid discomfort and eyelid debris between active and placebo groups*
- **Statistically significant and clinically relevant effect over placebo in a number of dry eye symptoms in a subgroup of patients, in 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
- Design of next clinical trial being discussed with clinical advisors

NCX 4251: Efficacy in Reducing Signs & Symptoms of Dry Eye Disease¹

Reduction from baseline in eye dryness score²
in patients with inferior corneal fluorescein staining score of ≥ 2



Post hoc subset analysis

- 123 of the overall 224 patients had inferior corneal fluorescein staining scores ≥ 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

Corporate

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

Key Commercial Partnerships

VYZULTA

Partnered with Bausch + Lomb worldwide

- First eye drop approved in 20 years with a novel approach to reduce IOP
- Commercialized in U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine; approved in 9 additional markets
- **\$20 million** milestone at \$100 million net sales¹
- **6% to 12%** net² royalties on global sales

ZERVIAE

Partnered with Eyevance in the U.S.

- First and only eye drop formulation of cetirizine
- Eyevance is a wholly-owned subsidiary of Santen Pharmaceutical Co., Ltd
- Up to **\$37.5 million** in potential future sales milestones
- **8% to 15%** royalties³ on U.S. net sales
- Licensed to other partners in Chinese market, Korea, Gulf and Arab markets, South East Asia, Mexico

OCUMENSION PARTNERSHIP

- Exclusive rights⁴ 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

1. \$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

2. 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

3. Nicox committed to pay to Eyevance certain manufacturing costs, which will be deducted from these royalty payments, reducing the effective royalty initially to 5% net until such costs are paid

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

Partnership with Fera on Naproxcinod in Sick 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 December 31, 2021 ¹	
Cash, Cash Equivalents	€41.9 million
Debt ²	€18.3 million
Cash runway	Q4 2023

Outstanding Shares ³	43.2 million
Management and Employees Ownership	1.9%
Key Institutional Investors	HBM Partners 7.0%
	Armistice Capital 4.0%

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

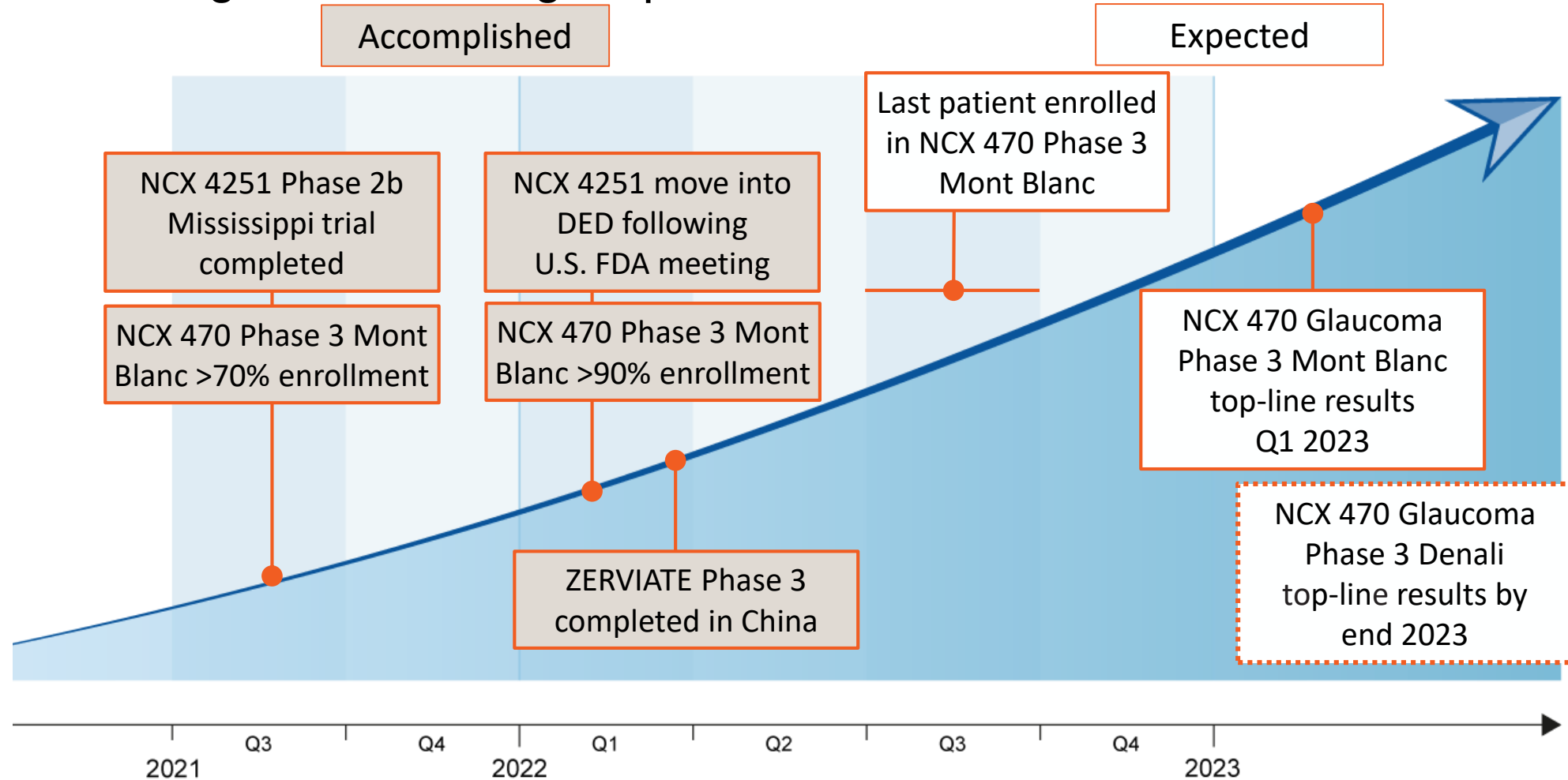
1. Unaudited figure

2. From a bond financing agreement with Kreos Capital, for €16.3 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 January 27, 2022

Value-Creating Milestones

Building Our Late-Stage Ophthalmic Portfolio for Commercialization



Innovative Solutions to Help Maintain Vision and Improve Ocular Health

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