



# Corporate Presentation

February 2023



*Enhancing the standard of care for retinal disorders by working to achieve the first FDA approval for bevacizumab in ophthalmology*

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# Leadership Team: Global Ophthalmic Development and Commercial Launch Excellence



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Chief Financial Officer and Director



**JEFF EVANSON**

Chief Commercial Officer



**TERRY DAGNON**

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**JOEL PRIEVE**

SVP, Commercial Operations



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SVP, Market Access and Marketing



**Surendra Sharma, MD**

SVP, Medical Affairs



**JENNIFER KISSNER**

SVP, Clinical Development



**CHRISTOPHER YONAN**

SVP, Technical Operations



# Investment Highlights

## FDA Market Approval of ONS-5010 (bevacizumab-vikg)<sup>1</sup>, an Investigational Therapy for the Treatment of Wet AMD, Targeted for August 29, 2023 PDUFA Date

### Targeting \$13.1 Billion Global Ophthalmic Anti-VEGF Market<sup>2</sup>

#### Differentiated Drug Product

- Designed to meet robust standards required for FDA ophthalmic approval
- Potential to eliminate risks associated with off-label repackaged bevacizumab, including potential impurities and particulates from compounders re-packaging processes
- Delivery ultimately expected through a convenient pre-filled syringe

#### Potential for 1<sup>st</sup> FDA Approved Ophthalmic Bevacizumab

- **U.S. FDA BLA accepted with target PDUFA action date of August 29, 2023**
- **Potential U.S. launch in Q4 2023**
- **Received validation of Marketing Authorization Application by European Medical Agency**
- Provides an economically elegant anti-VEGF solution for patients, payers and doctors

#### Attractive Market Opportunity

- **Strategic commercialization agreement with AmerisourceBergen**
- Over 50% of the U.S. market estimated to be available for conversion to ONS-5010, representing up to billions in potential yearly sales
- 12-years US regulatory exclusivity expected upon approval
- Label expansion opportunity into DME and BRVO

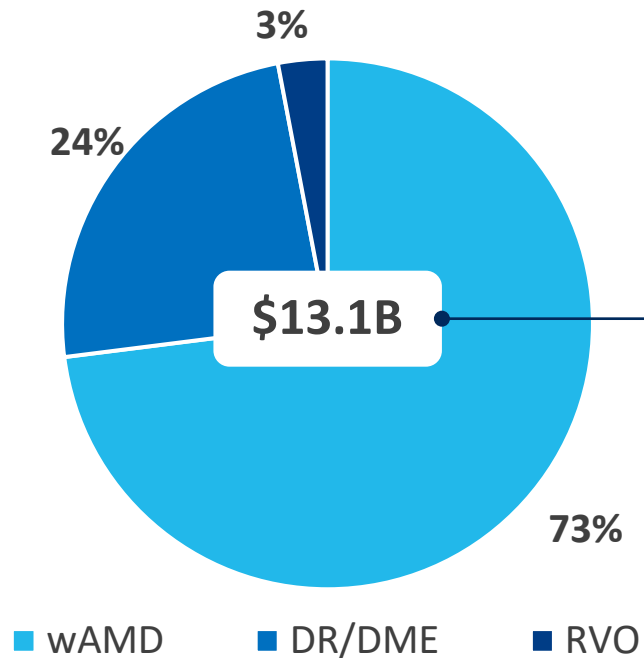
# Wet AMD Landscape

## *Current and Future*

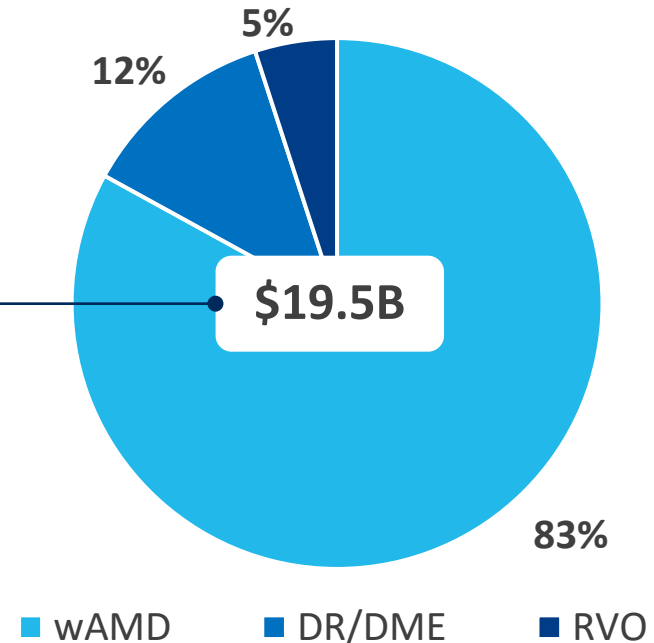
# Targeting Large and Growing Ophthalmic Markets

**ONS-5010, if Approved, will be a Significant Therapy in the Retinal Anti-VEGF Market, Currently Estimated to be in Excess of \$13.1 Billion Worldwide**

2020 9MM Anti-VEGF Revenue Share (USD)



2030 9MM Anti-VEGF Revenue Share (USD)



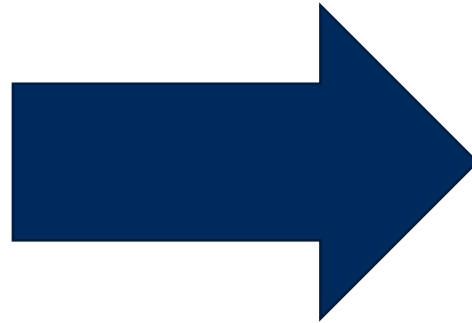
CAGR

4.1%

# The Majority of New Patient Starts are Off-Label Bevacizumab

## New Patient Starts

*66.3% of respondents (n=990) utilize off-label bevacizumab as a first-line agent<sup>1</sup>*



## Maintenance Therapy

*42.8-50.2% of overall injections continue therapy on off-label<sup>2,3</sup>*

- **Anti-VEGF is the standard-of-care** for the treatment of wAMD, DME and BRVO globally
- **~70% of Retinal Specialists in the US use off-label Avastin first-line for wAMD**
- Despite high usage, Retinal Specialists show **concern for the quality and supply of off-label Avastin**

Source: Navigant Quantitative Survey (n=152), 2019

# Public Health Concern Due To Repackaged and Off-Label Use of Bevacizumab Designed for Other Specialties and Delivery Systems

## Variability in Potency<sup>1</sup>

JAMA Ophthalmology

- 81% of samples had lower protein concentrations than required
- Samples had statistically significant variations in protein concentration among samples

## Safety and Sterility Adverse Events<sup>2</sup>

Warning Letter 

- Unvalidated hold times in syringes
- Patients have lost eyesight due to infections
- Multiple unapproved repackaged IV bevacizumab recalls due to unsterile compounding practices

## Syringe Adverse Events<sup>3</sup>

 **ASRS** American Society of Retina Specialists

- Variability in repackaging can lower quality of syringe products, resulting in adverse events
- Silicone oil droplets may be released from the syringe into the eye

## Not Held to FDA Ophthalmic Quality Standards When Repackaged



400 mg/16 mL, single-use vial;  
100 mg/4 mL, single-use vial



# U.S. Law and FDA Regulations for Compounding and Repackaging

- The Food Drug and Cosmetic Act (FD&CA) and Drug Quality and Security Act of 2013 define what is legal for 503A and 503B Compounding Pharmacies.<sup>1</sup>
  - **Once a drug or biologic is FDA approved and commercially available compounding is no longer authorized.**<sup>2,3,4,5</sup>
    - 503A Compounding pharmacies are regulated by federal regulations and state laws and can only compound or repackage for individual prescriptions in limited quantities and cannot distribute across state lines for > 5% of business.
    - 503B Compounding pharmacies / outsourcing facilities must comply with CGMP regulations, are inspected by FDA and must adhere to reporting requirements.
    - Neither 503A nor 503B pharmacies can compound or repackage commercially available drugs unless they appear on the official FDA drug shortage list.
- **“Compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness, and quality.” – FDA<sup>6</sup>**
- “The restrictions on making drugs that are essentially copies ensure that pharmacists and physicians do not compound drug products under the exemptions for patients who could use a commercially available drug product.” – FDA<sup>6</sup>
- “Such a practice would create significant public health risks because patients would be unnecessarily exposed to drug products that have not been shown to be safe and effective and that may have been prepared under substandard manufacturing conditions.” – FDA<sup>6</sup>
- **“Under the statutory scheme, only very rarely should a compounded drug product that is essentially a copy of a commercially available drug product be offered to a patient.” – FDA<sup>6</sup>**
- On 23 March 2020 FDA announced biological products would no longer be eligible for the exemptions for compounded drugs under sections 503A and 503B of the FD&C Act<sup>7</sup>

# ONS-5010

The Form of Bevacizumab the  
Market Wants

# ONS-5010 Ophthalmic Bevacizumab Target Product Profile

## ONS-5010 (bevacizumab-vikg) Investigational Therapy

### Patient Population

- Patients diagnosed with **wet AMD, DME, or BRVO**

### Description

- Anti-VEGF **bevacizumab designed for ophthalmic indications** wet AMD, DME, and BRVO
- Demonstrated high affinity to bind to all isoforms of VEGF A

### Dosing and Administration

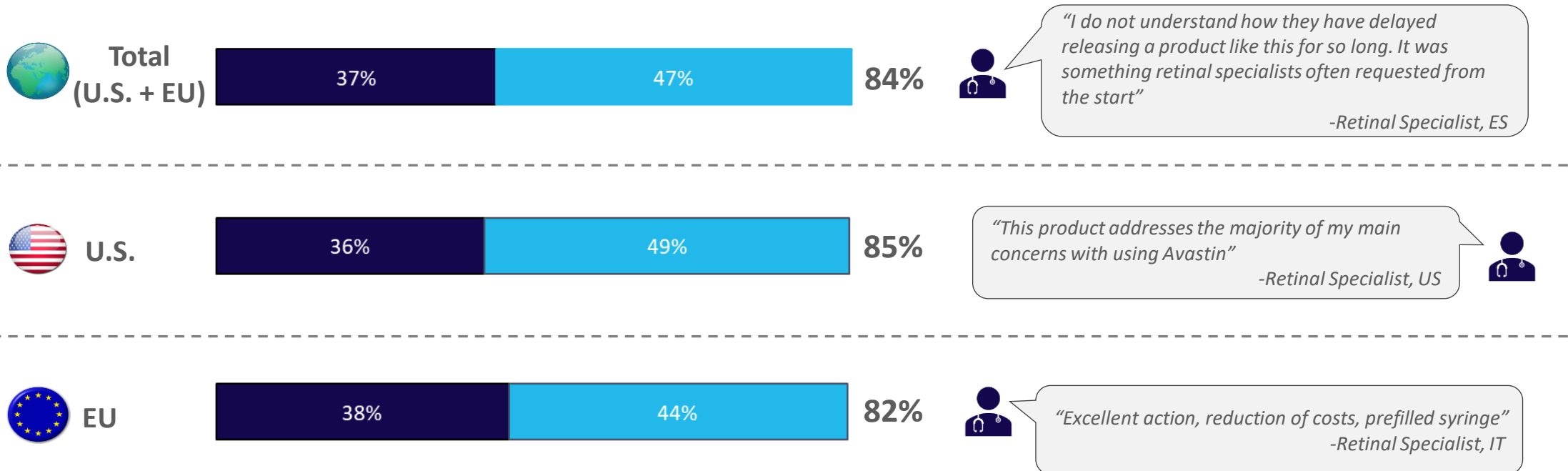
- Supplied either as **pre-filled ophthalmic syringe for intravitreal 1.25 mg injection** administered once monthly, **or in a glass vial**

### Efficacy, Safety, and AEs

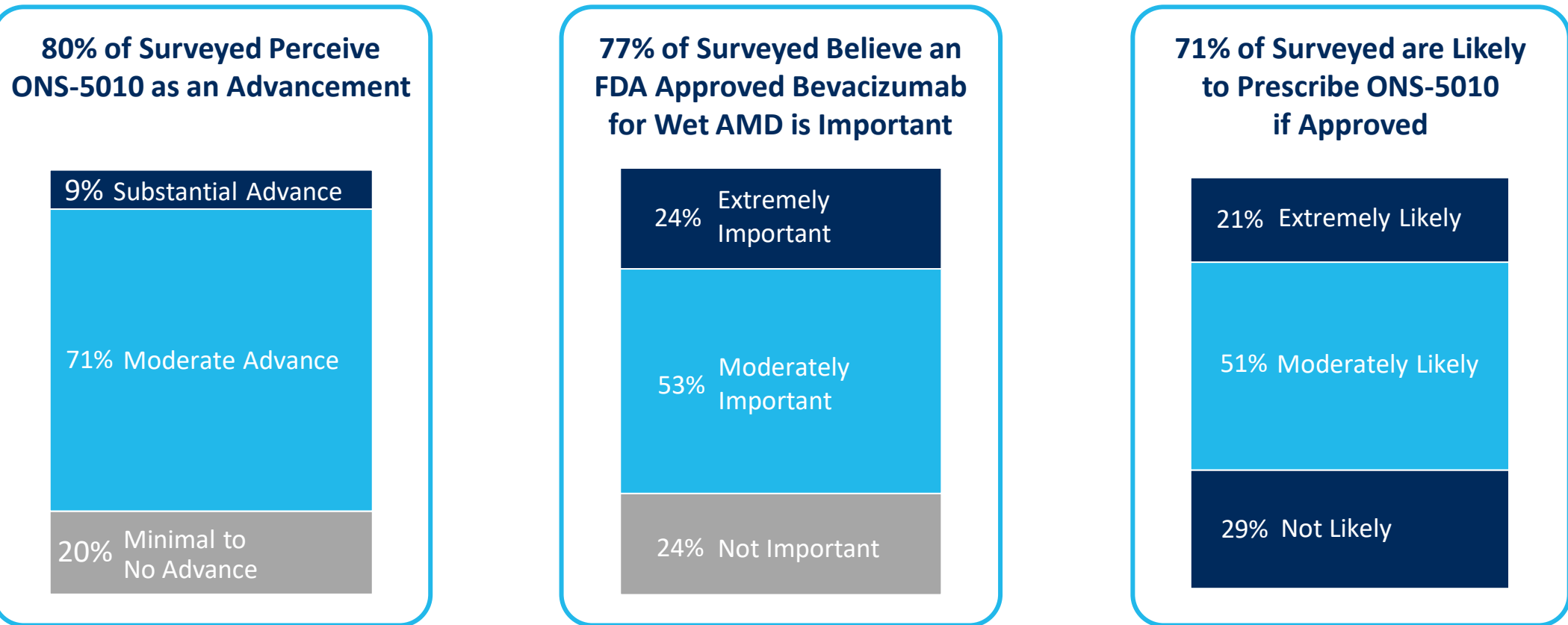
- NORSE TWO demonstrated significant efficacy and safety, and when combined with NORSE ONE and NORSE THREE provides the necessary registration database. These ONS-5010 data when taken as a whole continue to be consistent with previously published results for bevacizumab

# Do Physicians Want an Ophthalmic Approved Bevacizumab?

**>80% of Retinal Specialists Express Interest/High Interest in an FDA-Approved Ophthalmic Bevacizumab to Treat Wet AMD, DME and BRVO**



# Investigational Therapy ONS-5010 Ophthalmologists Survey



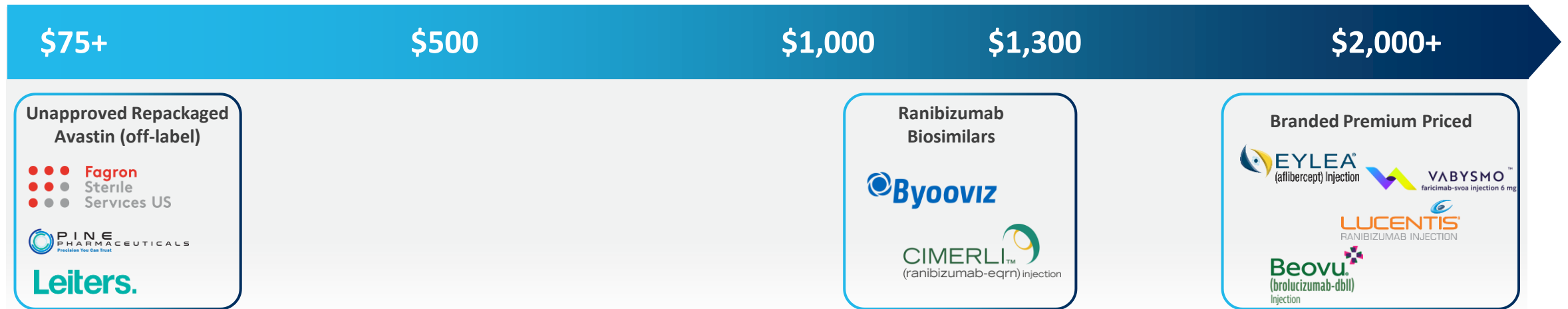
# FDA Approval Requirements vs Compounded Bevacizumab

Ophthalmic Solution Requirement	Off-Label Compounded Repackaged IV Solution	FDA Approved Ophthalmic Solution for Intravitreal Injection
Sterile USP <71> <sup>1</sup>	?	Yes
Particulates per USP <789> for ophthalmic solutions <sup>1</sup>	?	Yes
Bacterial endotoxins USP <85> <sup>1</sup>	?	Yes
GMP <sup>2,3</sup>	?	Yes
FDA approved ophthalmic package consistent with USP <771> <sup>1</sup>	No	Yes
FDA reviewed stability data supporting shelf life <sup>2,3</sup>	No	Yes
pH FDA approved and consistent with USP <771> <sup>1,2,3</sup>	No	Yes
Potency FDA approved specifications for shelf life <sup>2,3</sup>	No	Yes
Osmolarity specification for ophthalmic solution <sup>2,3</sup>	No	Yes

# LYTENAVA™ Pricing Opportunity



Pricing spectrum of anti-VEGFs per dose



## LYTENAVA™ Pricing Strategy

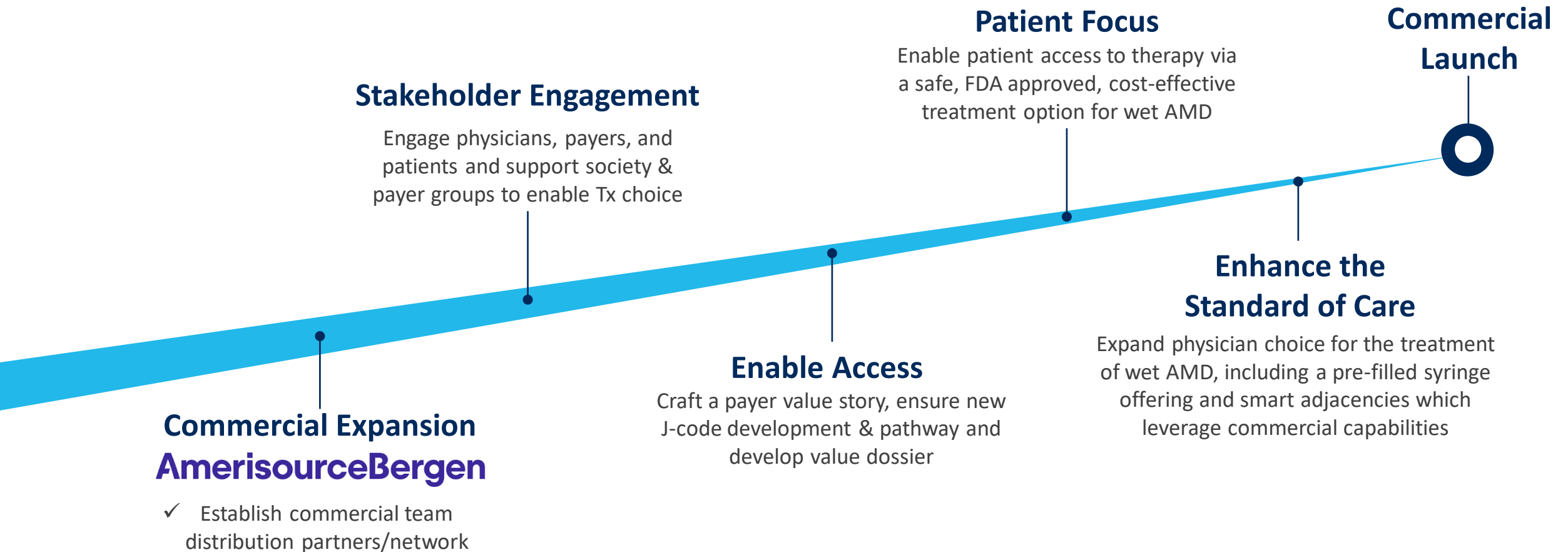
Price low enough to move off-label users to branded LYTENAVA™, while still creating significant margin and value compared to any biosimilar and significantly less than the premium branded products

# ONS-5010

## Commercial Activities

# Charting a Path To a Successful Launch

Focus on Shaping the Market by Creating Awareness and Educating Physicians



# Strategic Commercialization Partnership in U.S. with Preeminent Leader in Specialty Pharma Distribution

## AmerisourceBergen

**Establishes Commercial Depth in Advance of Potential ONS-5010 Commercial Launch**

- ✓ Third-Party Logistics Services and Distribution
- ✓ Medical Information and Pharmacovigilance Services

**Besse Medical is One of the Largest Specialty  
Pharmaceutical Distributors to Retina Specialists**

# ONS-5010

Clinical Data

# Compelling Clinical Data Support Potential FDA Approval in Wet AMD

- ✓ U.S. FDA BLA Accepted with Target PDUFA of August 29, 2023
- ✓ Received Validation of Marketing Authorization Application by European Medical Agency

## ✓ Positive Signals



Clinical Experience Trial  
1<sup>st</sup> Registration Trial

## ✓ Positive Top-Line Data



Pivotal Trial  
2<sup>nd</sup> Registration Trial

## ✓ Completed



Open-Label Safety Study  
Supports BLA Requirements

# NORSE ONE and NORSE THREE Results



## Clinical Experience Trial

Demonstrated anticipated safety and efficacy signals consistent with previously published results for ophthalmic use of bevacizumab

### Trial Highlights:

- Desired proportion of 3-line visual acuity gainers achieved
- Desired mean gain in visual acuity achieved
- Zero ocular inflammation observed
- Safety was comparable to published bevacizumab studies, such as CATT



## Open-Label Safety Study

Positive safety profile reinforces previously reported safety data for ONS-5010 (bevacizumab-vikg)

### Trial Highlights:

- Provided adequate number of patient exposure required for BLA submission
- No unexpected safety trends
- Zero cases of ocular inflammation



## Pivotal Trial

2<sup>nd</sup> Registration Trial

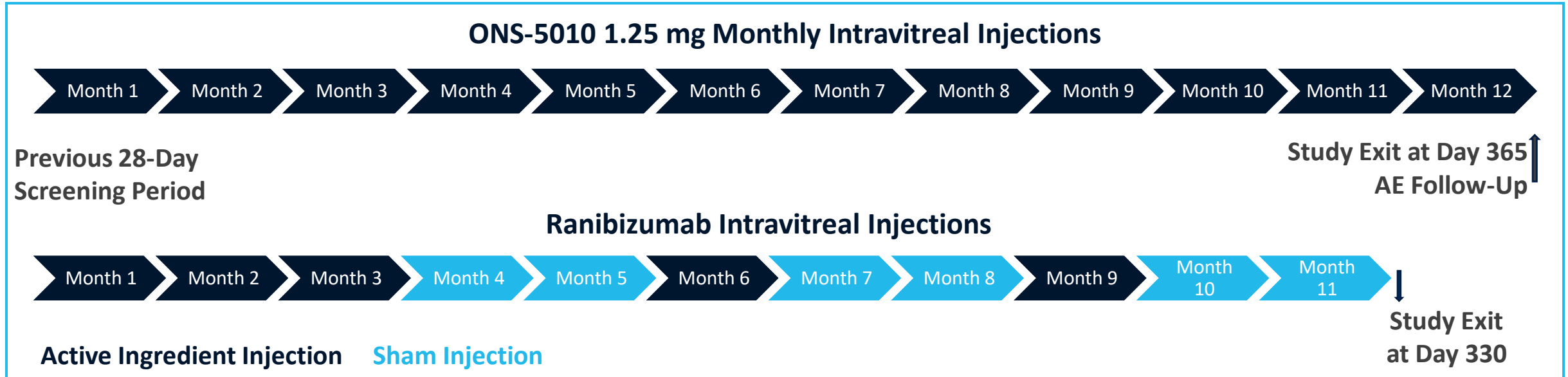


### Trial Highlights:

- Randomized masked controlled trial
- ONS-5010 (bevacizumab-vikg) vs LUCENTIS® (ranibizumab)
- 228 patients enrolled
- Trial conducted in the United States
- Trial arms included >95% treatment-naïve patients

# Phase 3 Pivotal Study Design – Registration Strategy

## 12-Month Study of Safety and Efficacy of ONS-5010 in Subjects with Wet AMD Study Design and Statistical Analysis Plan Agreed to by U.S. FDA



### Study Eye Characteristics

- Active, primary CNV due to wet AMD
- Treatment-naïve
- BCVA: 20/50 – 20/320

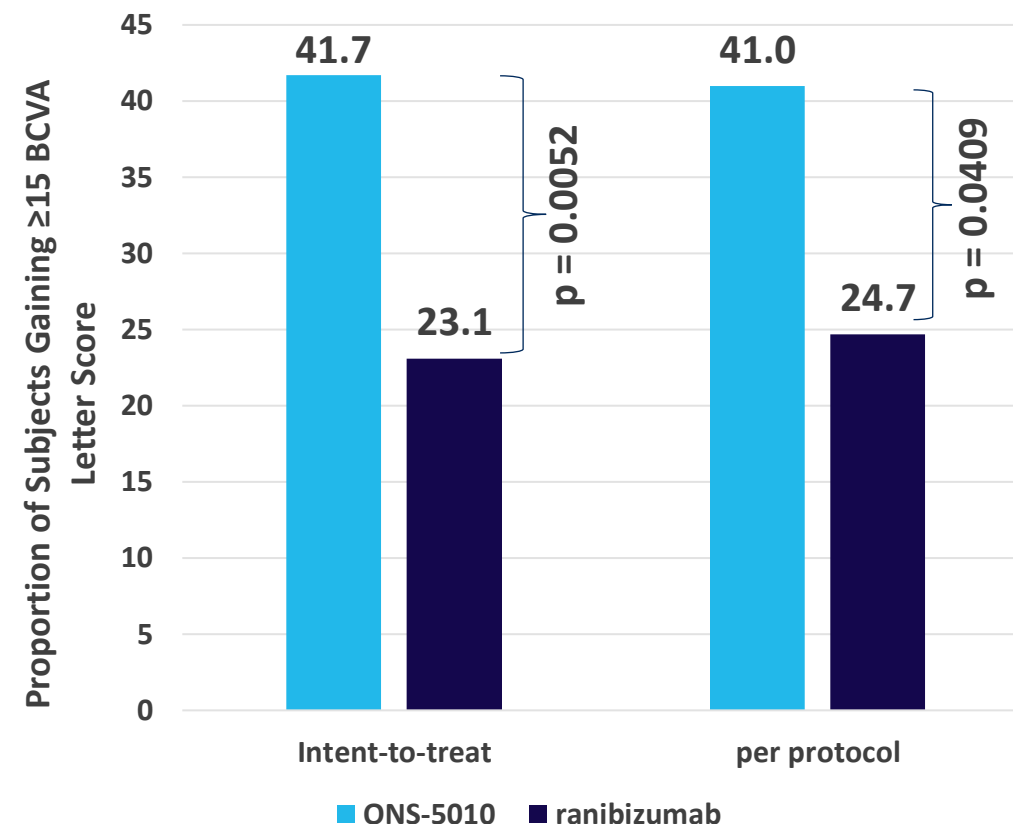
### Key Study Outcomes

- Proportion of subjects who gain  $\geq 15$  letters in BCVA
- Mean change in BCVA from baseline to Month 11
- Frequency and incidence of AEs

# Primary Endpoint Met with Statistically Significant, Clinically Relevant Results<sup>1</sup>

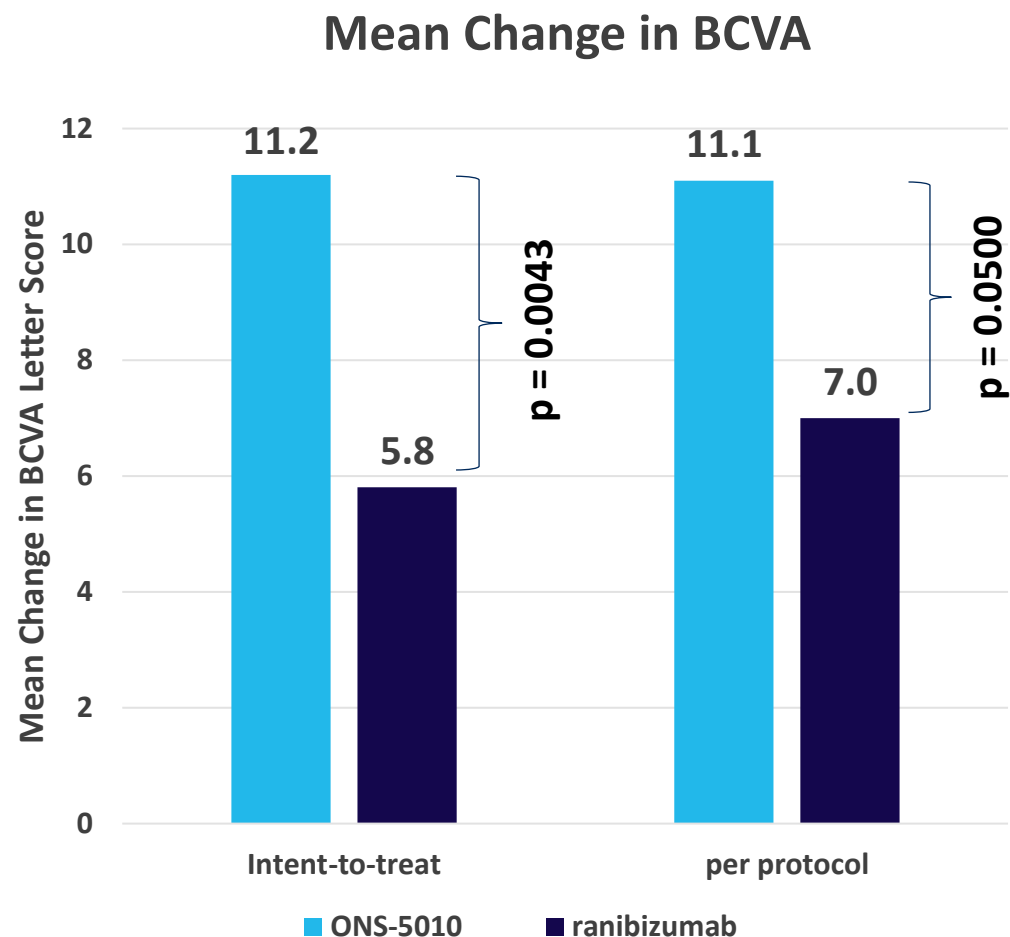
Characteristic	Statistic	ONS-5010 (n=113)	Ranibizumab (n=115)
Intent-to-Treat Pop.			
Number of Subjects	n/N (%)	45/108 (41.7)	24/104 (23.1)
Risk Difference		0.1859	
95% CI		(0.0442,0.3086)	
p-value		0.0052	
Per Protocol Pop.			
Number of Subjects	n/N (%)	34/83 (41.0)	18/73 (24.7)
Risk Difference		0.1631	
95% CI		(0.0120, 0.3083)	
p-value		0.0409	

**Difference in % Subjects Gaining 3 Lines Vision**



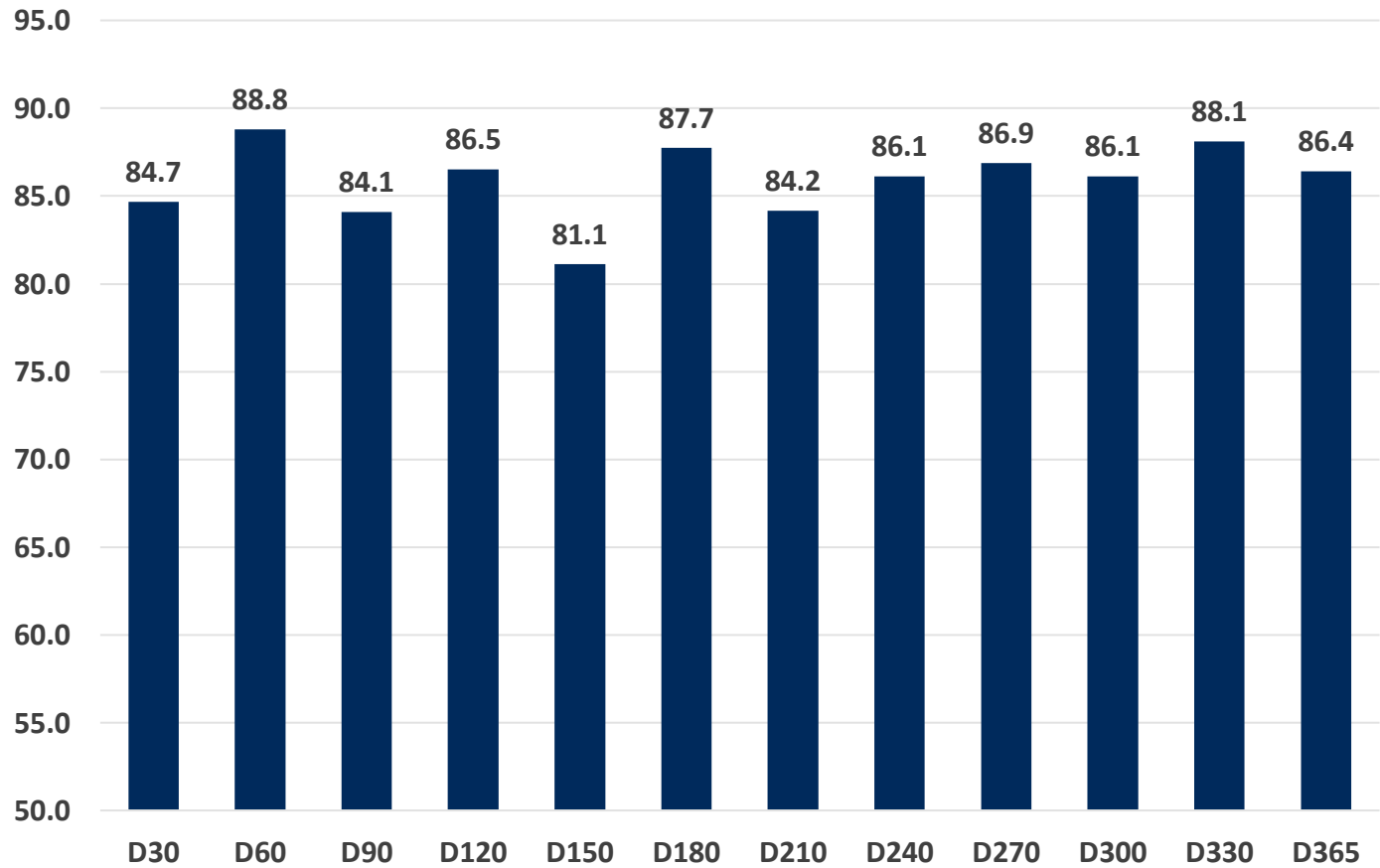
# Key Secondary Endpoints Met with Highly Statistically Significant, Clinically Relevant Results

Characteristic	Statistic	ONS-5010 (n=113)	Ranibizumab (n=115)
BCVA Score Change from Baseline to Month 11 (ITT)	n	104	96
	Mean (SD)	<b>11.2 (12.19)</b>	5.8 (14.80)
p-value		<b>0.0043</b>	
BCVA Score Change from Baseline to Month 11 (PP)	n	80	68
	Mean (SD)	11.1 (12.77)	7.0 (14.56)
p-value		<b>0.0500</b>	



# NORSE TWO - BCVA

Proportion of Subjects Who Maintained or Gained BCVA by Visit



The **majority** of subjects maintained or gained BCVA during the study (defined as change from baseline in BCVA  $\geq 0$ )

- $\geq 80\%$  of subjects maintained BCVA each month
- At 1 year, **86.4%** of subjects had maintained or gained BCVA, supporting the sustained positive effect of ONS-5010

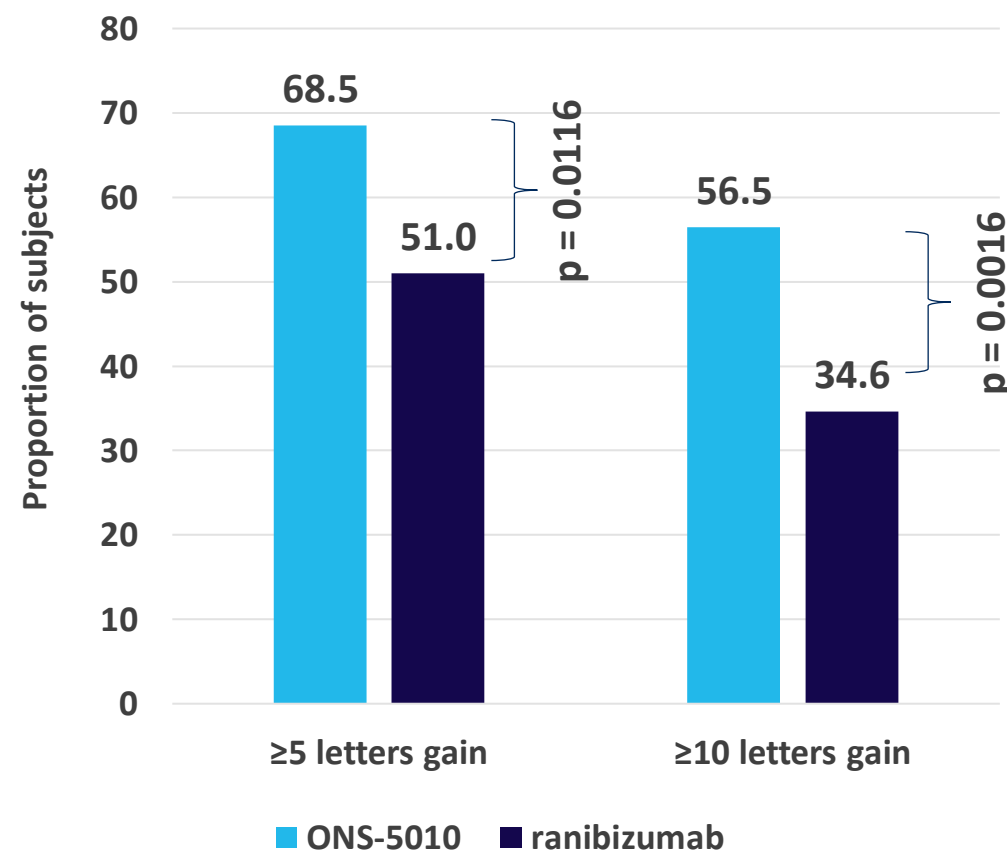


# Statistically Significant, Clinically Relevant Secondary Endpoints

Characteristic	Statistic	ONS-5010 (n=113)	Ranibizumab (n=115)
Subjects Gaining ≥5 letters			
Number of Subjects	n/N (%)	74/108 (68.5)	53/104 (51.0)
Risk Difference		0.1756	
95% CI		(0.0315,0.3052)	
p-value		0.0116	
Subjects Gaining ≥10 letters			
Number of Subjects	n/N (%)	61/108 (56.5)	36/104 (34.6)
Risk Difference		0.2187	
95% CI		(0.0726,0.3487)	
p-value		0.0016	

68.5% (p = 0.0116) ONS-5010 subjects gained ≥ 5 letters of vision  
 56.5% (p = 0.0016) ONS-5010 subjects gained ≥ 10 letters of vision  
 41.7% (p = 0.0052) ONS-5010 subjects gained ≥ **15 letters of vision**

## Responder Analysis



# Safety Results: Consistent with Previously Reported Results from NORSE ONE and NORSE THREE

## Only One ONS-5010 Ocular Inflammation AE Reported in NORSE TWO (Iritis)

Characteristic	Statistic	ONS-5010 (n=113)	Ranibizumab (n=115)	Overall (n=228)
<b>≥ 1 Adverse Event</b>	<b>n (%)</b>	<b>85 (75.2)</b>	<b>85 (73.9)</b>	<b>170 (74.6)</b>
≥ 1 ocular Adverse Event	n (%)	59 (52.2)	61 (53.0)	120 (52.6)
≥ 1 non-ocular Adverse Event	n (%)	56 (49.6)	52 (45.2)	108 (47.4)
<b>≥ 1 Serious Adverse Event</b>	<b>n (%)</b>	<b>14 (12.4)</b>	<b>16 (13.9)</b>	<b>30 (13.2)</b>
≥ 1 ocular Serious Adverse Event	n (%)	1 (0.9)	0	1 (0.4)
≥ 1 non-ocular Serious Adverse Event	n (%)	13 (11.5)	16 (13.9)	29 (12.7)

# NORSE SEVEN

## Pre-Filled Syringe

Vials Versus  
Pre-Filled Syringe



### Trial Highlights:

- 3-month study to compare the safety of ONS-5010 in vials versus Outlook Therapeutics investigational pre-filled syringe
  - Vial arm (n= has been fully enrolled and is now complete)
- Enrolling ~120 subjects with visual impairment due to retinal disorders
  - Wet AMD
  - BRVO
  - DME

# Financial Highlights

NASDAQ: OTLK

**Closed ~\$54 Million in Net Proceeds from Financings on December 28, 2022**

**\$52.3M**

Cash Balance<sup>1</sup>

**~\$324M**

Market Cap<sup>2</sup>

**~257M**

Shares Outstanding<sup>3</sup>

**~494K**

Average Volume<sup>2</sup>

**Sufficient Capital to Support Operations Past Anticipated FDA Approval of ONS-5010 in the Third Quarter of Calendar 2023 and into the Fourth Calendar Quarter of 2023<sup>4</sup>**



## Company Summary

- **Targeting \$13.1 billion global ophthalmic anti-VEGF market<sup>1</sup>**
  - *Initial U.S. target segment worth up to billions in potential yearly revenue served by compounding pharmacies which by law should be converted to Outlook Therapeutics' LYTENAVA, if FDA approved*
- **Potential FDA approval August 29, 2023 as the first FDA approved ophthalmic formulation of bevacizumab**
- **Received validation of Marketing Authorization Application by European Medical Agency**
- **Current capital expected to fund operations through anticipated FDA approval of ONS-5010 in the third calendar quarter of 2023<sup>2</sup>**
- **Management team with proven ophthalmic commercial launch expertise**
  - *Leveraging strategic commercialization agreement with AmerisourceBergen to preserve capital and enhance commercial reach*