



Corporate Presentation

May 2022



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



C. RUSSELL TRENARY III
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LAWRENCE KENYON
Chief Financial Officer and Director



JEFF EVANSON
Chief Commercial Officer



TERRY DAGNON
Chief Operating Officer



RANDY THURMAN
Executive Chairman of the Board

MARK HUMAYUN, MD, PhD
Medical Advisor



Investment Highlights

Submitted U.S. FDA BLA of ONS-5010 (bevacizumab-vikg)¹ an Investigational Therapy for the Treatment of Wet AMD

Targeting \$13.1 Billion Global Ophthalmic Anti-VEGF Market²

Differentiated Drug Product

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

Potential for 1st FDA Approved Bevacizumab

- ✓ Compelling pivotal data support U.S. FDA BLA submission;
[filed March 2022](#)
- Launch anticipated Q1 2023
- Provide an economically elegant anti-VEGF solution for patients, payers and doctors

Attractive Market Opportunity

- Over 50% of the U.S. market available for conversion to ONS-5010 representing billions in yearly sales
- 12-years US regulatory exclusivity expected
- Label expansion opportunity into DME and BRVO

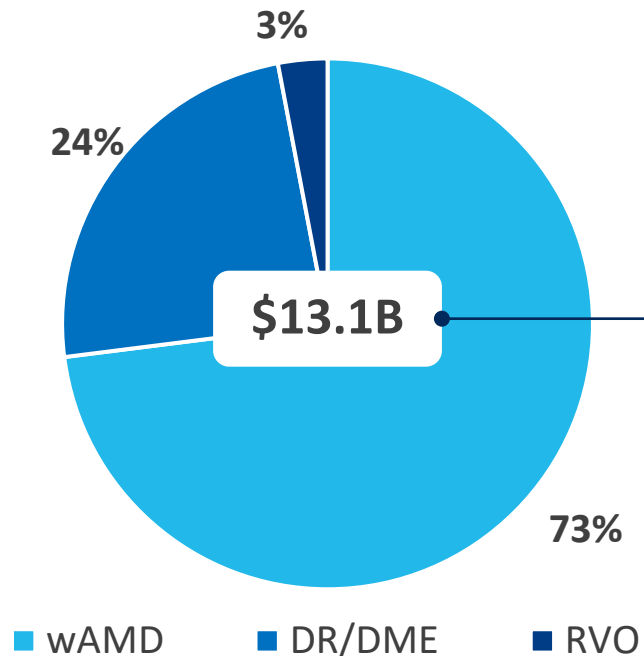
Wet AMD Landscape

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

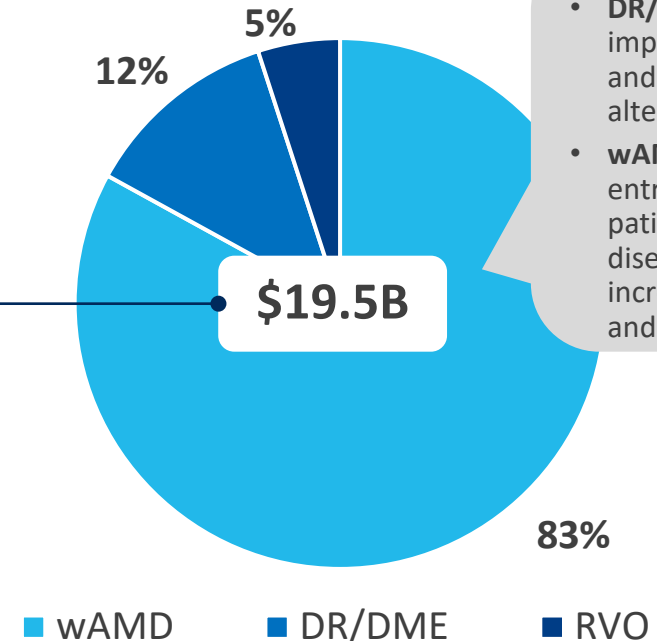
2020 9MM Anti-VEGF Revenue Share (USD)



CAGR

4.1%

2030 9MM Anti-VEGF Revenue Share (USD)



MARKET DRIVERS:

- **DR/DME** is more directly impacted by biosimilars and lower cost alternatives (-2.2% CAGR)
- **wAMD** is buoyed by new entrants targeting patients earlier in the disease cascade, increasing awareness, and earlier diagnosis

Unapproved Bevacizumab Represents 50% of U.S. Wet AMD Market Injections

Anti-VEGF U.S. Market Share in Wet AMD¹



Used Off-Label in Retina from formulation designed for IV use

50%



36%



12%



1%



1%

Expected Drivers to Compete Across All Ophthalmic Anti-VEGF Therapeutics, if Approved by FDA

- 1 Provide cost-effective FDA approved ophthalmic bevacizumab
- 2 Become first-line “step-edit” drug of choice
- 3 12 years market exclusivity
- 4 Penetrate EU and developing markets

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

Variability in Potency¹

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 Events²

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 Events³

 **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.¹
 - **Once a drug or biologic is FDA approved and commercially available compounding is no longer authorized.**^{2,3,4,5}
 - 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.” – FDA⁶**
- “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.” – FDA⁶
- “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.” – FDA⁶
- **“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.” – FDA⁶**

ONS-5010

Submitted U.S. FDA BLA for the
treatment of wet AMD March 2022

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
- Known high affinity to bind to all isoforms of VEGF A

Dosing and Administration

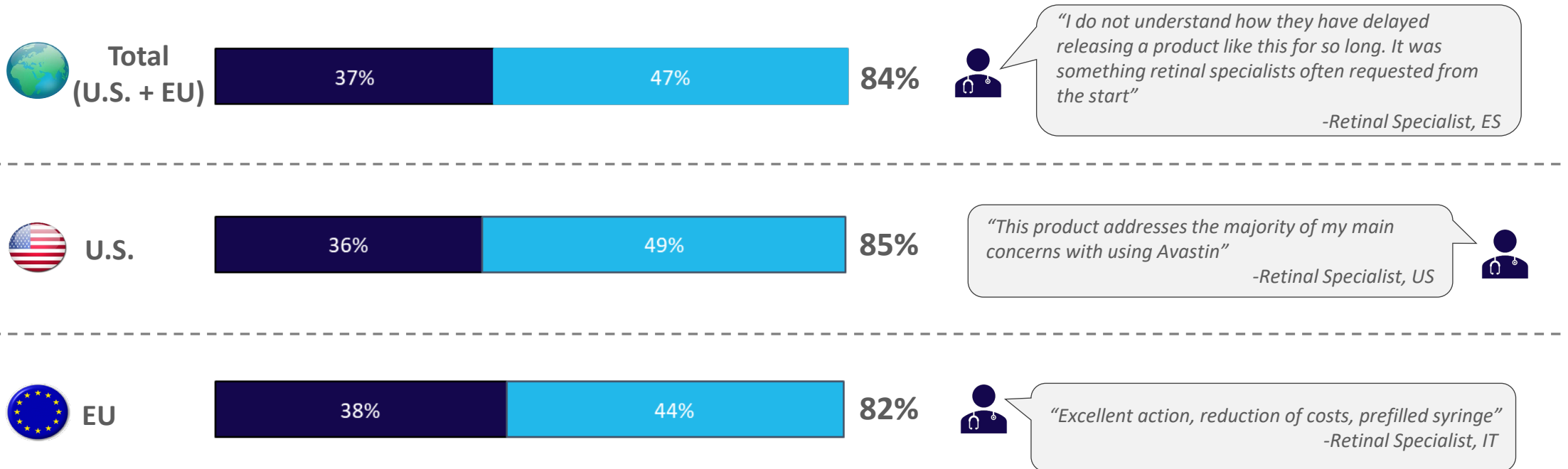
- Supplied either as **pre-filled ophthalmic syringe for intravitreal 1.25 mg injection** administered once monthly, **or in a glass vial**

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.

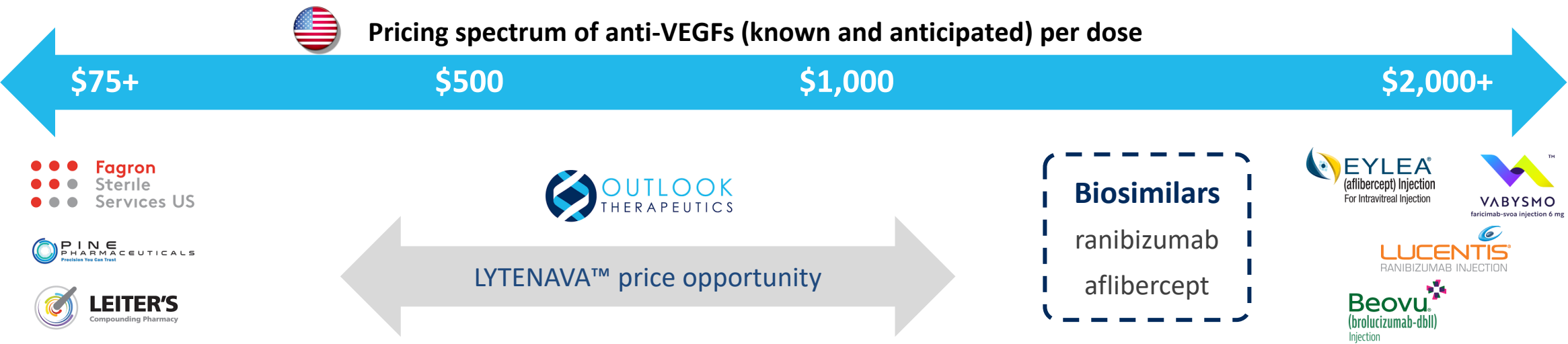
Do Physicians Want an Ophthalmic Approved Bevacizumab?

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



LYTENAVA™ Pricing Opportunity

If Approved Optimize Uptake: Compounding product prescribers while creating separation from biosimilars and other branded price points



Compounded Avastin (off-label)	LYTENAVA™	Biosimilars to ranibizumab and/or aflibercept	Branded Premium Priced
<p>Cost of compounded Avastin is increasing due to quality issues including syringe failures.</p> <p>Cost per dose could increase to \$100/dose+</p>	<p>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.</p>	<p>Biosimilars, if approved, are likely to price at a 10-30% discount to the branded WAC.</p> <p>Mylan, Coherus and Biogen have thus far discounted ~20-30% from WAC in other biologic areas where they have launched biosimilars.</p>	<p>WAC (list) price for Vabysmo is \$2,200/dose, Lucentis is \$1,950/dose, and both Beovu and Eylea are priced at \$1,850/dose</p> <p>Practice rebates based on volume expected to continue.</p>

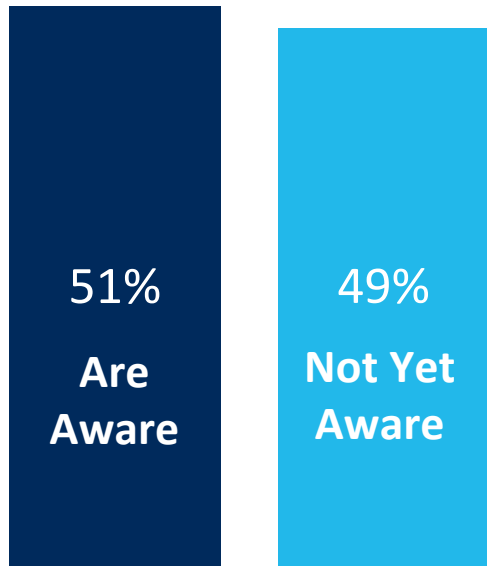
Compounded Bevacizumab Compared to FDA Approved

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

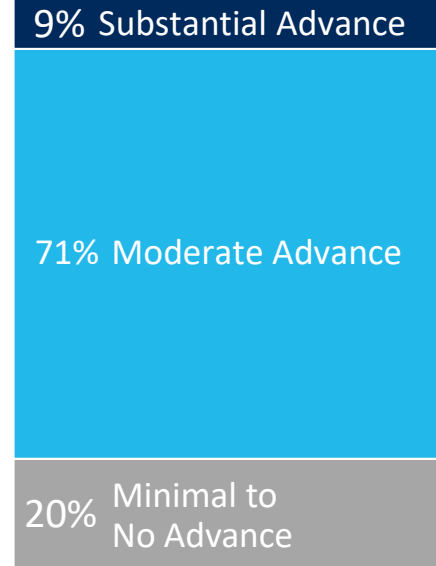
Pre-Commercial Activities Show Growing Awareness Among Ophthalmologists

Ophthalmologists Show Interest In Prescribing ONS-5010 if Approved

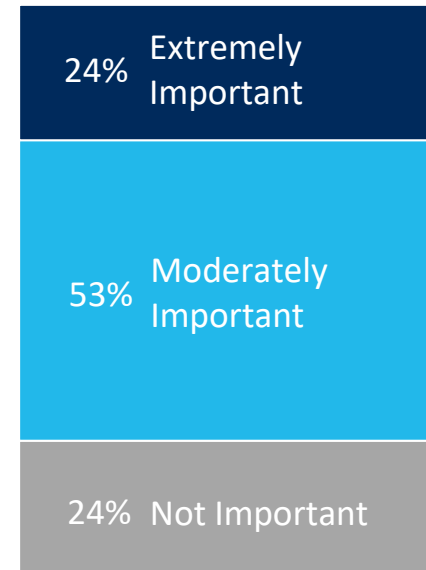
Half of Surveyed Are
Aware of Upcoming BLA
Filing of ONS-5010



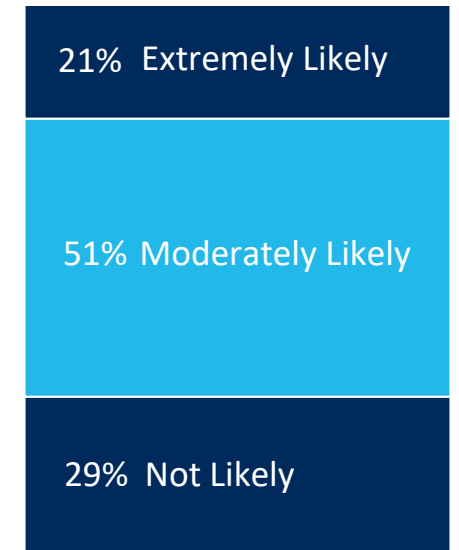
80% of Surveyed Believe
ONS-5010 is an Advancement
Over Other Therapies



77% of Surveyed Believe an
FDA Approved Bevacizumab
for Wet AMD is Important

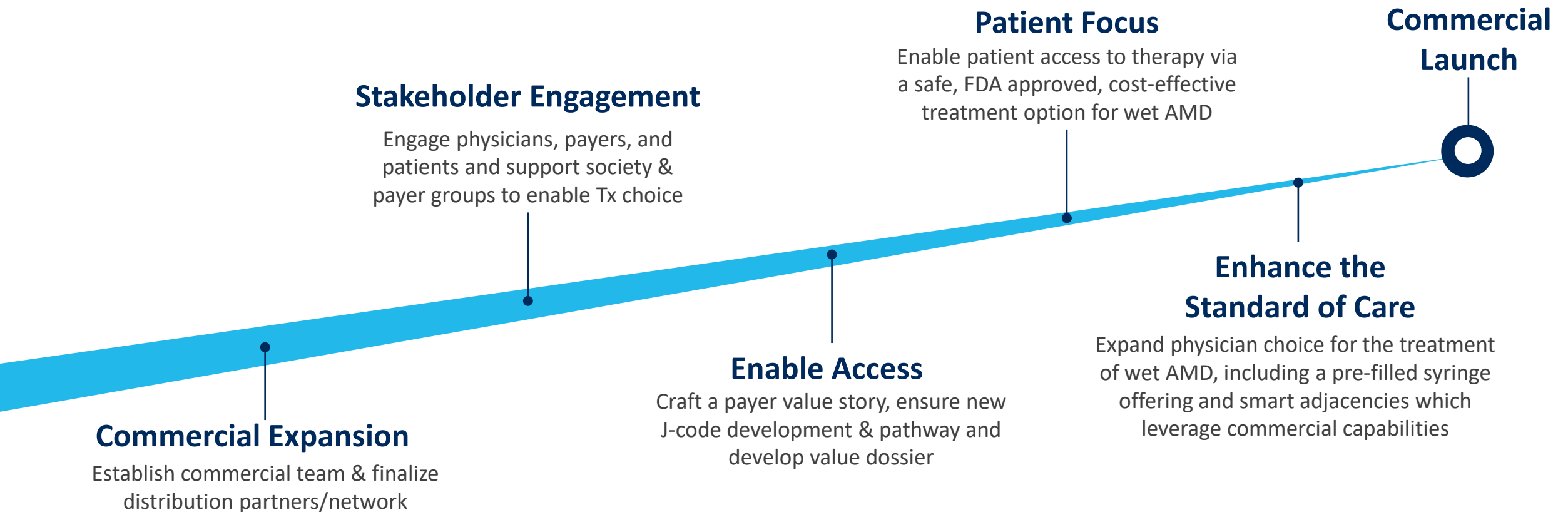


71% of Surveyed Are Likely
to Prescribe ONS-5010
If Approved



Charting a Path To a Successful Launch

Focus on Shaping the Market by Creating Awareness and Educating Physicians



Pathway Towards Potential FDA Approval in Wet AMD

✓ U.S. FDA BLA Submitted March 2022

✓ Positive Signals



Clinical Experience Trial
1st Registration Trial

✓ Positive Top-Line Data



Pivotal Trial
2nd 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

2nd Registration Trial

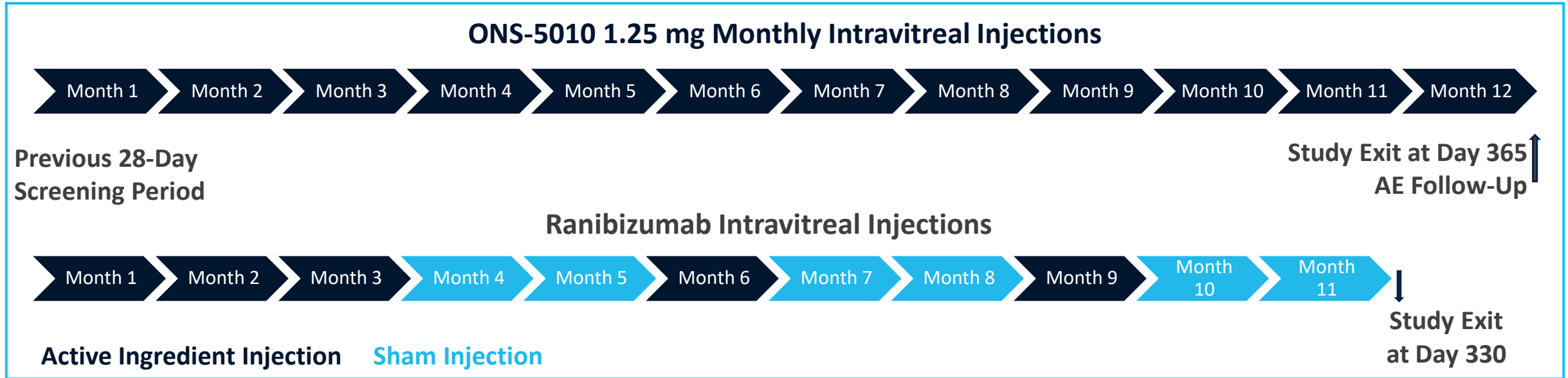


Trial Highlights:

- 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

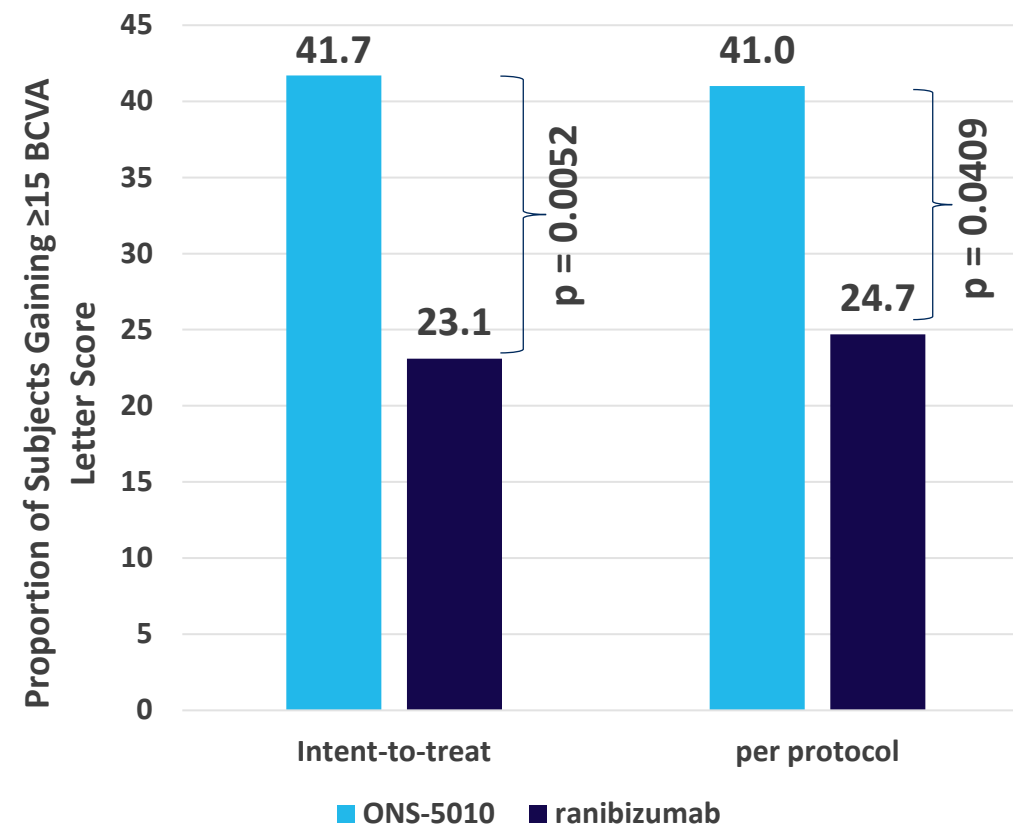
Key Study Outcomes

- Proportion of subjects who gain ≥ 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 Results¹

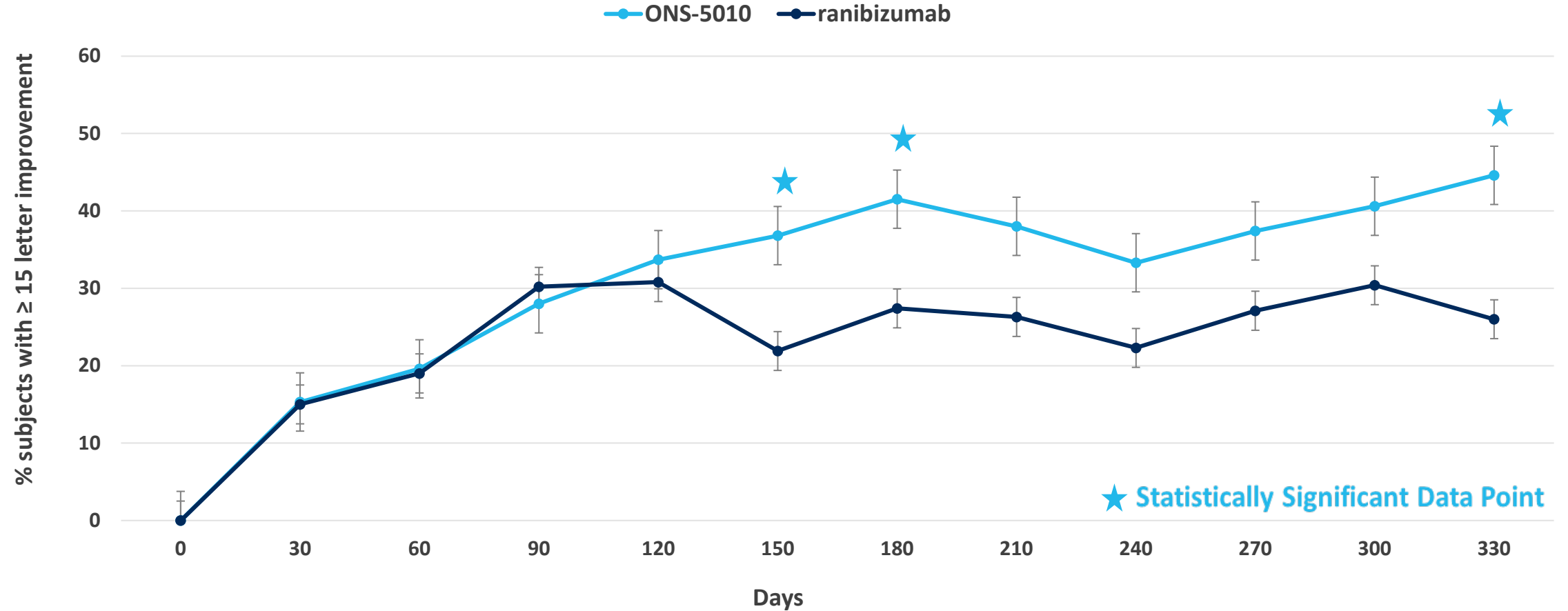
Characteristic	Statistic	ONS-5010 (n=113)	Ranibizumab (n=115)
Intent-to-Treat Pop.			
Number of Subjects	n/N (%)	45/108 (41.7)	24/104 (23.1)
Risk Difference		0.1859	
95% CI		(0.0442,0.3086)	
p-value		0.0052	
Per Protocol Pop.			
Number of Subjects	n/N (%)	34/83 (41.0)	18/73 (24.7)
Risk Difference		0.1631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

Difference in % Subjects Gaining 3 Lines Vision



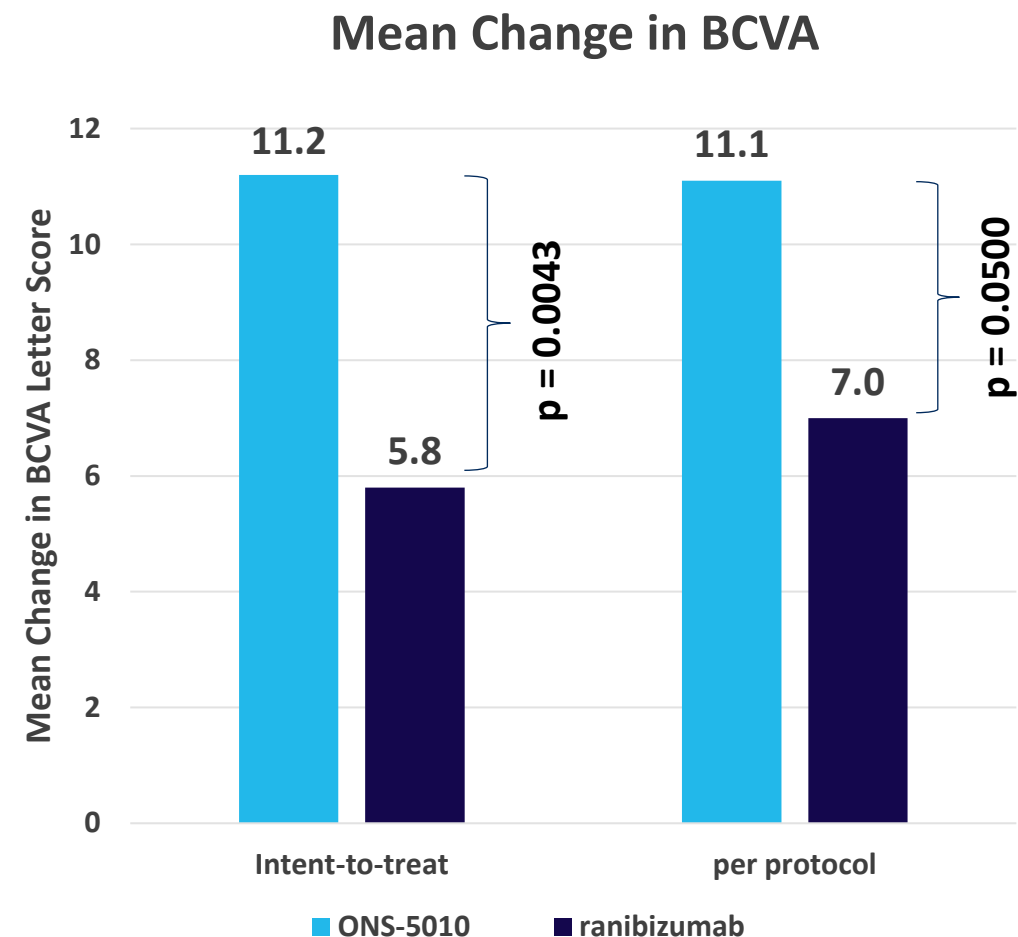
ONS-5010 Rapid Onset of Action with Sustained Significance Over Time

≥ 15 Letter Gainers (± SE) Over Time



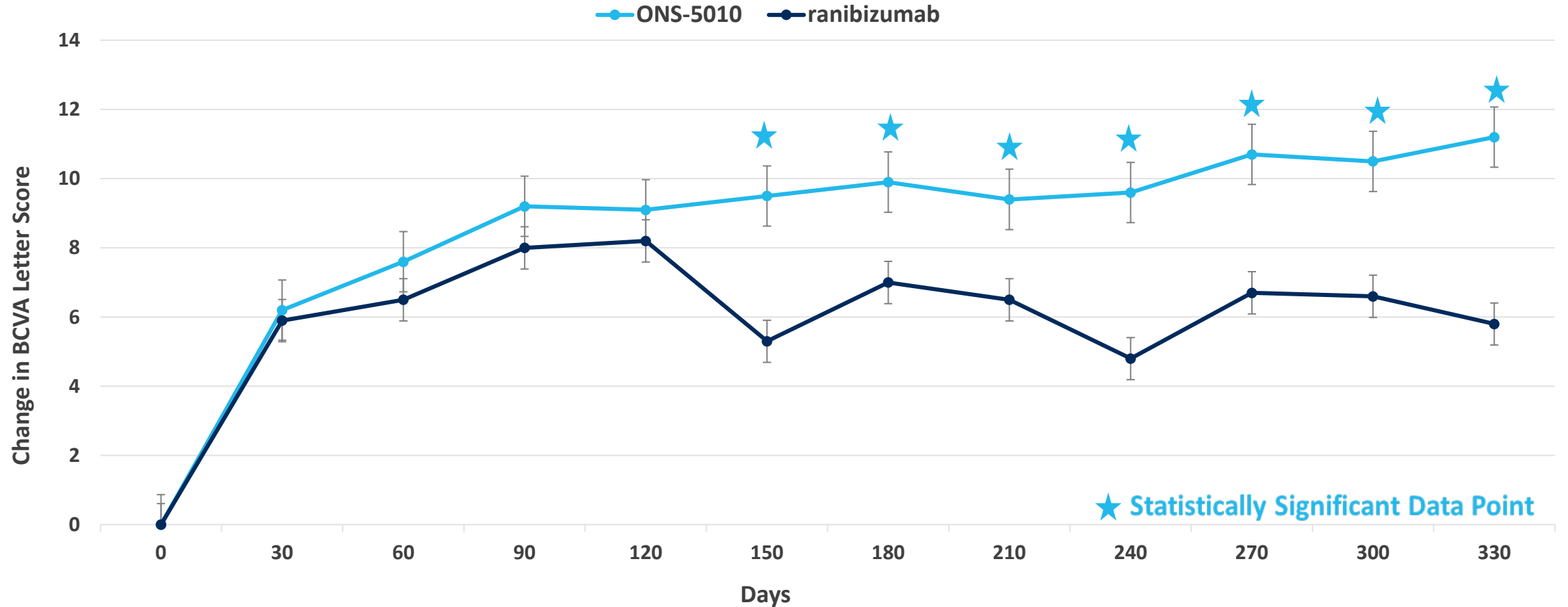
Key Secondary Endpoints Met with Highly Statistically Significant, Clinically Relevant Results

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



ONS-5010 Rapid Onset of Action with Sustained Significance Over Time

Mean (\pm SE) Change in BCVA Over Time

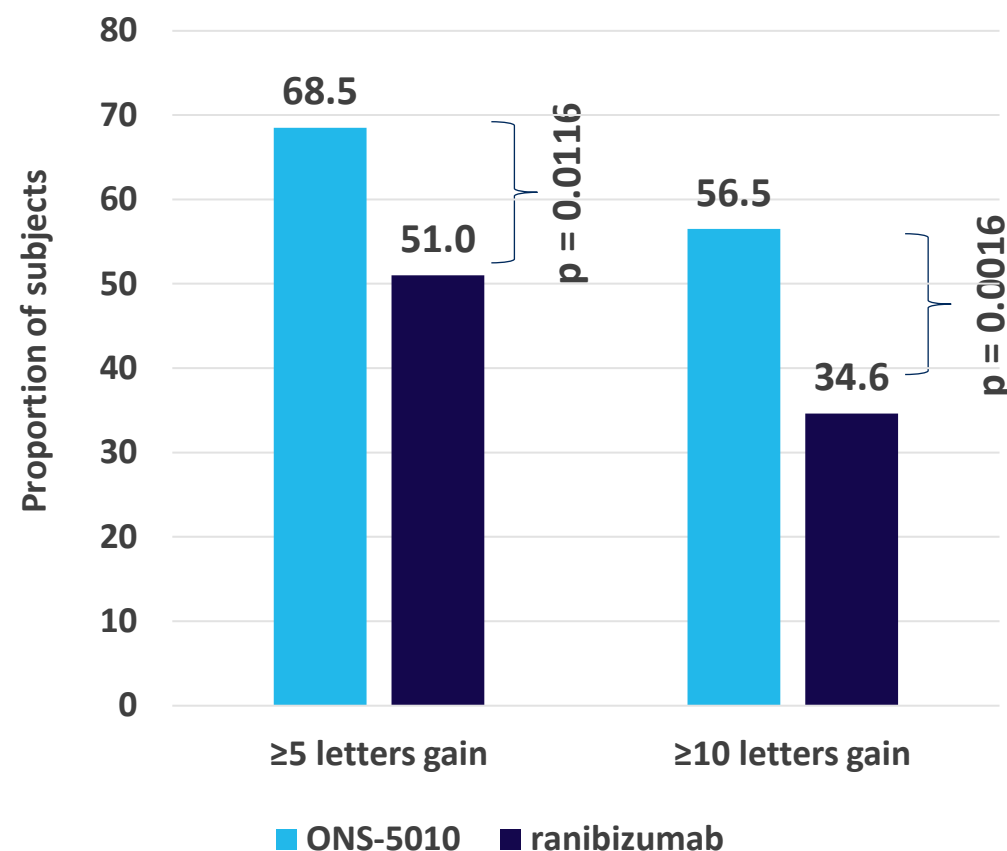


Statistically Significant, Clinically Relevant Secondary Endpoints

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)
≥ 1 Adverse Event	n (%)	85 (75.2)	85 (73.9)	170 (74.6)
≥ 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)
≥ 1 Serious Adverse Event	n (%)	14 (12.4)	16 (13.9)	30 (13.2)
≥ 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)

Safety Results: Frequency and Incidence of Ocular AEs $\geq 3\%$

Low Incidence of Ocular AEs, Despite More Injections in ONS-5010 Arm

Characteristic	Statistic	ONS-5010 (n=113)	Ranibizumab (n=115)	Overall (n=228)
≥ 1 Ocular TEAE in Study Eye	n (%)	51 (45.1)	48 (41.7)	99 (43.4)
Cataract	n (%)	6 (5.3)	3 (2.6)	9 (3.9)
Conjunctival hemorrhage	n (%)	10 (8.8)	3 (2.6)	13 (5.7)
Corneal abrasion	n (%)	4 (3.5)	1 (0.9)	5 (2.2)
Dry eye	n (%)	2 (1.8)	5 (4.3)	7 (3.1)
Intraocular pressure increased	n (%)	7 (6.2)	1 (0.9)	8 (3.5)
Neovascular AMD	n (%)	0	4 (3.5)	4 (1.8)
Retinal hemorrhage	n (%)	4 (3.5)	6 (5.2)	10 (4.4)
Subretinal fluid	n (%)	3 (2.7)	4 (3.5)	7 (3.1)
Visual acuity reduced	n (%)	4 (3.5)	14 (12.2)	18 (7.9)
Vitreous detachment	n (%)	4 (3.5)	2 (1.7)	6 (2.6)
Vitreous floaters	n (%)	4 (3.5)	1 (0.9)	5 (2.2)

Only One ONS-5010 Ocular Inflammation AE Reported in All Three ONS-5010 Studies

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 pre-filled syringe
 - Vial arm has been fully enrolled and is now complete
- Enrolling ~120 subjects with visual impairment due to retinal disorders
 - Wet AMD
 - BRVO
 - DME
- Data expected to support sBLA submission in 2023

Financial Highlights

NASDAQ: OTLK

**Sufficient capital through the anticipated approval of the ONS-5010 BLA
expected in the first calendar quarter of 2023¹**

\$70.2M

Cash Balance²

~\$388M

Market Cap³

~224M

Shares Outstanding²

~1.3M

Average Volume³



Company Summary

- **Targeting \$13.1 billion global ophthalmic anti-VEGF market¹**
 - *Initial U.S. target segment worth potentially billions in yearly revenue are served by compounding pharmacies which by law should be converted to Outlook Therapeutics' LYTENAVA, if FDA approved*
- **Potential for first FDA approved ophthalmic formulation of bevacizumab**
- **U.S. FDA BLA submitted March 2022 with anticipated approval to follow 9-12 months later**
- **Sufficient capital through the anticipated approval of the ONS-5010 BLA**
- **Management team with proven ophthalmic commercial launch expertise**