GenSight BIOLOGICS

KOL Webcast

78-Week REFLECT Results

July 9, 2021

LUMEVOQ
lenadogene nolparvovec

A LEADING GENE THERAPY BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLOGICS.COM

Moving LUMEVOQ® Towards Commercialization

- **REFLECT confirms LUMEVOQ® efficacy and safety** in a 3rd independent Phase III trial
- **EMA application currently in review**, decision expected in Q2 2022
- **EU Commercial infrastructure** being deployed
- **Pre-BLA meeting with FDA expected Q4 2021** for a BLA filing in Q2 2022
- **Global Early Access in place:**
  - » Temporary Authorization for Use (ATUc) in France at 700kE/patient
  - » Compassionate use currently in Italy, Germany and the US

78-Week REFLECT Results

José-Alain Sahel, MD
University of Pittsburgh School of Medicine

Robert Sergott, MD
Wills Eye Hospital, Philadelphia

REFLECT Design: Double-masked, randomized vs placebo IVT in second affected eye

First affected eye always treated with LUMEVOQ

Placebo: Balanced Sterile Saline Solution (BSS), sterile, apyrogenic solution used for ocular surgery.

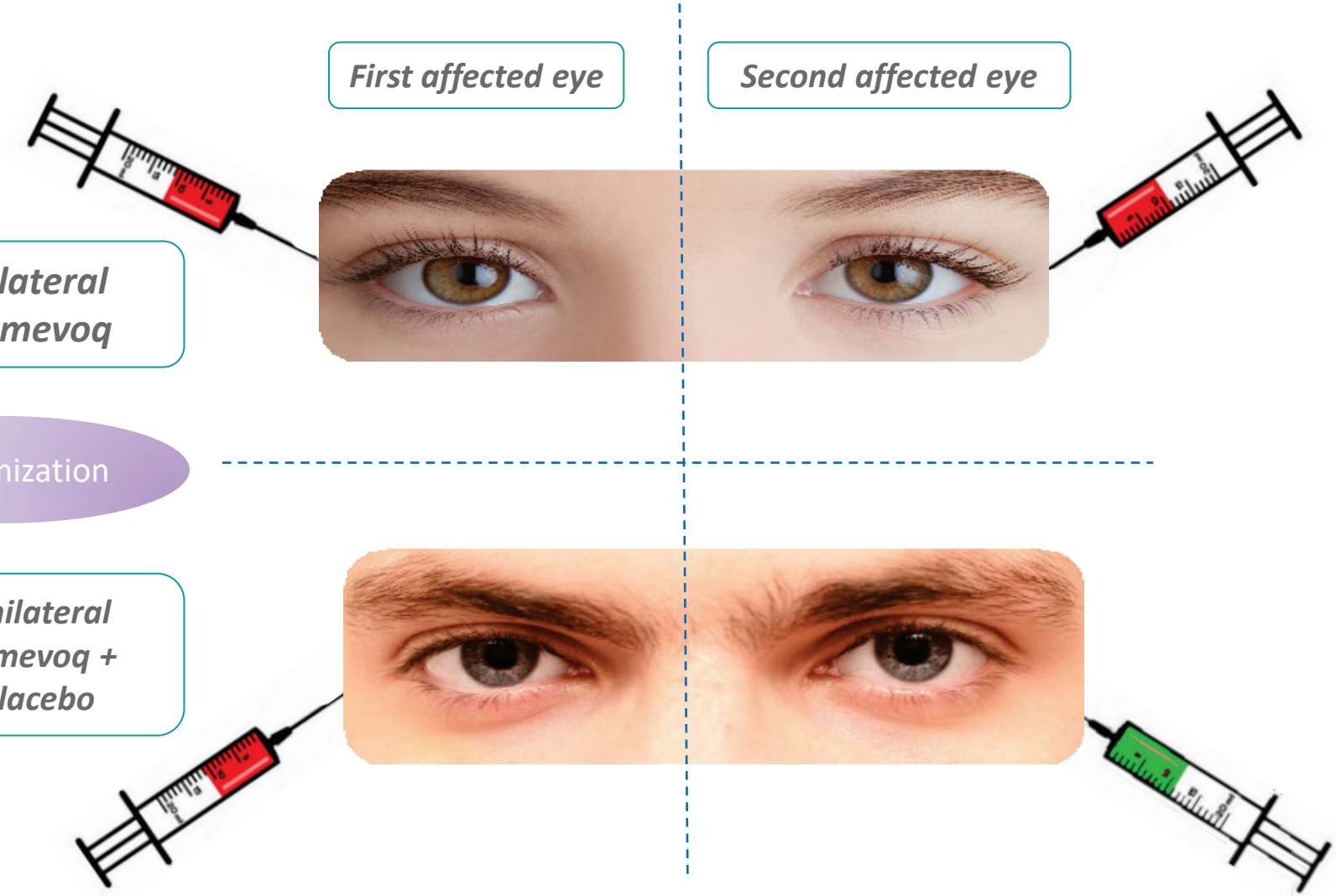
Patient inclusion criteria

- **98 patients** with vision loss ≤ 1 year
- Recruitment 4Q 2017 to July 2019
- 13 centers

Randomization

Bilateral Lumevoq

Unilateral Lumevoq + Placebo



REFLECT Design: Double-masked, randomized vs placebo IVT in second affected eye

First affected eye always treated with LUMEVOQ

Placebo: Balanced Sterile Saline Solution (BSS), sterile, apyrogenic solution used for ocular surgery.

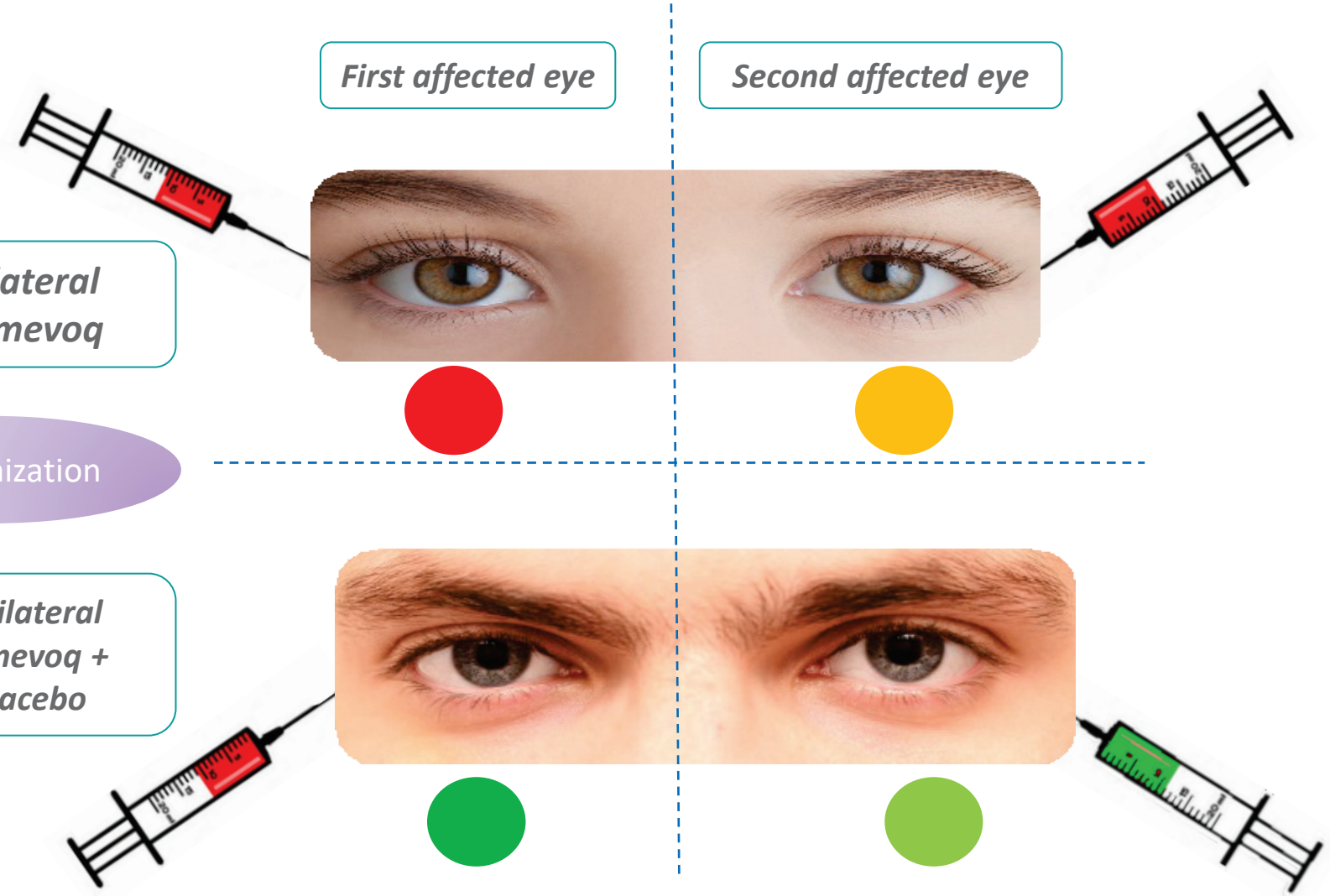
Patient inclusion criteria

- **98 patients** with vision loss ≤ 1 year
- Recruitment 4Q 2017 to July 2019
- 13 centers

Randomization

Bilateral Lumevoq

Unilateral Lumevoq + Placebo



Subjects disposition

	Bilat. GS010 (N=48)	Unilat. GS010 (N=50)	Total (N=108)
Number of subjects enrolled			108
Number of subjects screen failed			10
Number of subjects randomized (ITT population)	48	50	98
Number of patients with available primary endpoint	46	48	94
Number of subjects who discontinued the study before 1.5 year	0	1	1
Reason: Non-compliant to study visits			

Demographic Characteristics

	Bilat. GS010	Unilat. GS010	ALL
N subjects	48	50	98
N males (%)	37 (77.1%)	41 (82.0%)	78 (79.6%)
Age (years) at disease onset			
Mean (SD)	31.7 (14.4)	31.2 (13.4)	31.5 (13.8)
Min ; Max	14 ; 73	14 ; 64	14 ; 73

Baseline Characteristics

Baseline	Bilat. GS010	Unilat. GS010	All
Affected eye status			
Bilateral	48 (100%)	50 (100%)	98 (100%)
Unilateral*	0	0	0
Duration Vision Loss (Months)**			
Mean (SD)	**8.33 (3.36)**	**8.27 (3.09)**	**8.30 (3.21)**
Median	8.85	8.82	8.85
Q1 - Q3	5.67 - 11.66	5.49 - 11.10	5.49 - 11.60
Range	1.68 - 11.93	2.40 - 11.93	1.68 - 11.93
Time interval of vision loss between first and second eye (days)			
Mean (SD)	56.85 (66.34)	61.88 (54.08)	59.42 (60.14)
Median	33.50	59.50	46.00
Q1 - Q3	0.00 - 88.00	16.00 - 92.00	3.00 - 91.00
Range	0.00 - 266.00	0.00 - 197.00	0.00 - 266.00
LogMAR BCVA first affected eyes			
Mean (SD)	**1.59 (0.47)**	**1.68 (0.43)**	**1.64 (0.45) (Snellen 20/800)**
Median	1.50	1.60	1.60
Q1 - Q3	1.20 - 2.00	1.30 - 2.00	1.30 - 2.00
Range	0.60 - 2.30	0.80 - 2.30	0.60 - 2.30
LogMAR BCVA second/not yet affected eyes			
Mean (SD)	**1.44 (0.51)**	**1.50 (0.46)**	**1.47 (0.48) (Snellen 20/600)**
Median	1.40	1.50	1.40
Q1 - Q3	1.10 - 2.00	1.20 - 2.00	1.20 - 2.00
Range	0.00 - 2.30	0.70 - 2.30	0.00 - 2.30

*Two patients in the bilat. GS010 group had only one eye affected at screening, but were then identified as affected at the time of treatment (conversion between screening and baseline)
** REFLECT patients were included with a vision loss of less than one year

Time from treatment administration to primary endpoint

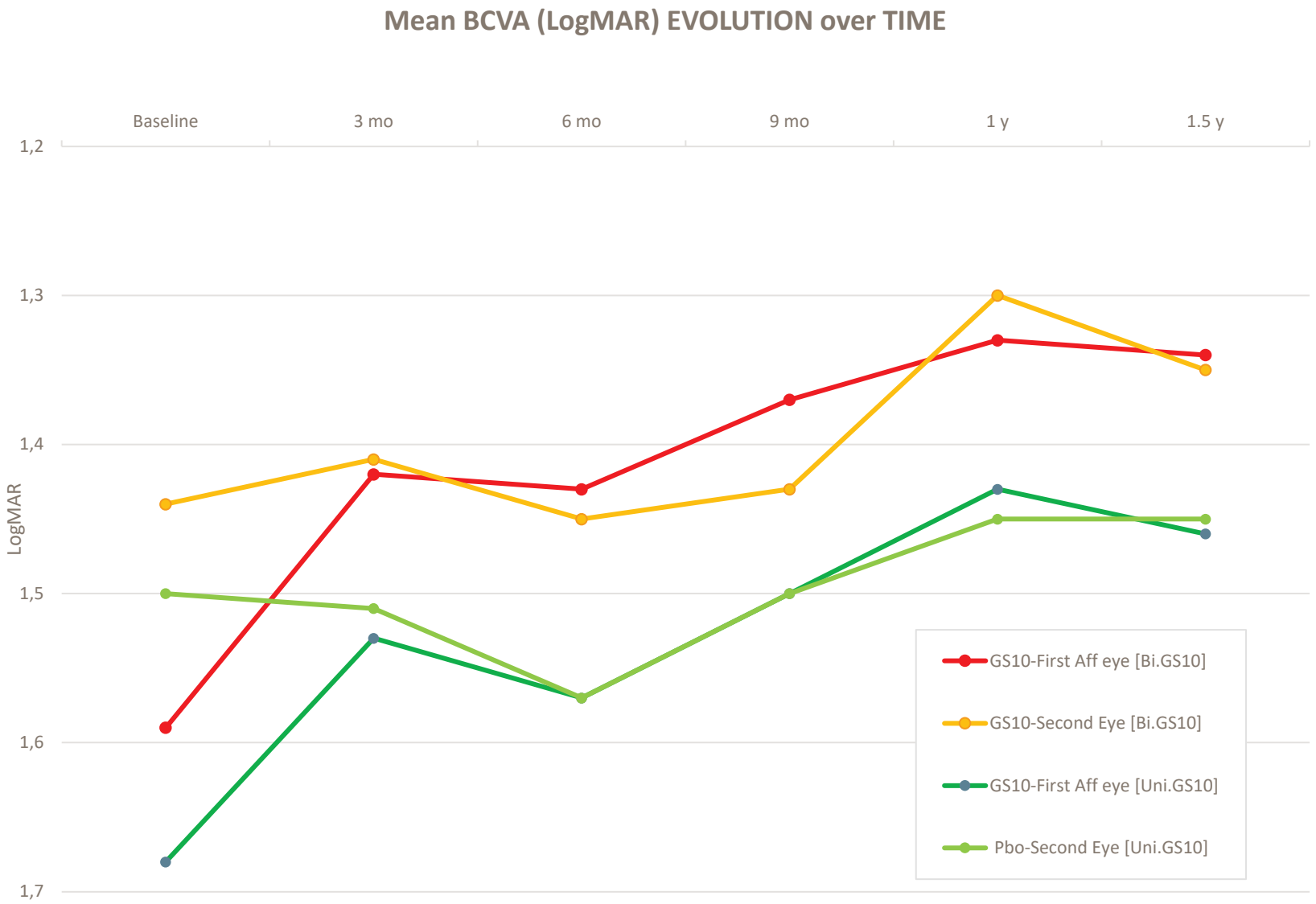
	Bilat. GS010 (N=48)	Unilat. GS010 (N=50)
Time from treatment administration to 1.5 year-endpoint - Months		
Mean (SD)	20.10 (4.01)	19.51 (4.52)
Median	18.60	18.51
Q1 - Q3	17.95 - 22.18	17.97 - 21.62
Range	11.76 - 30.32	2.92 - 30.72

REFLECT patients were included with a vision loss of less than one year

At Month 12 ([9;15[months) post vision loss, all patients (100%) were treated

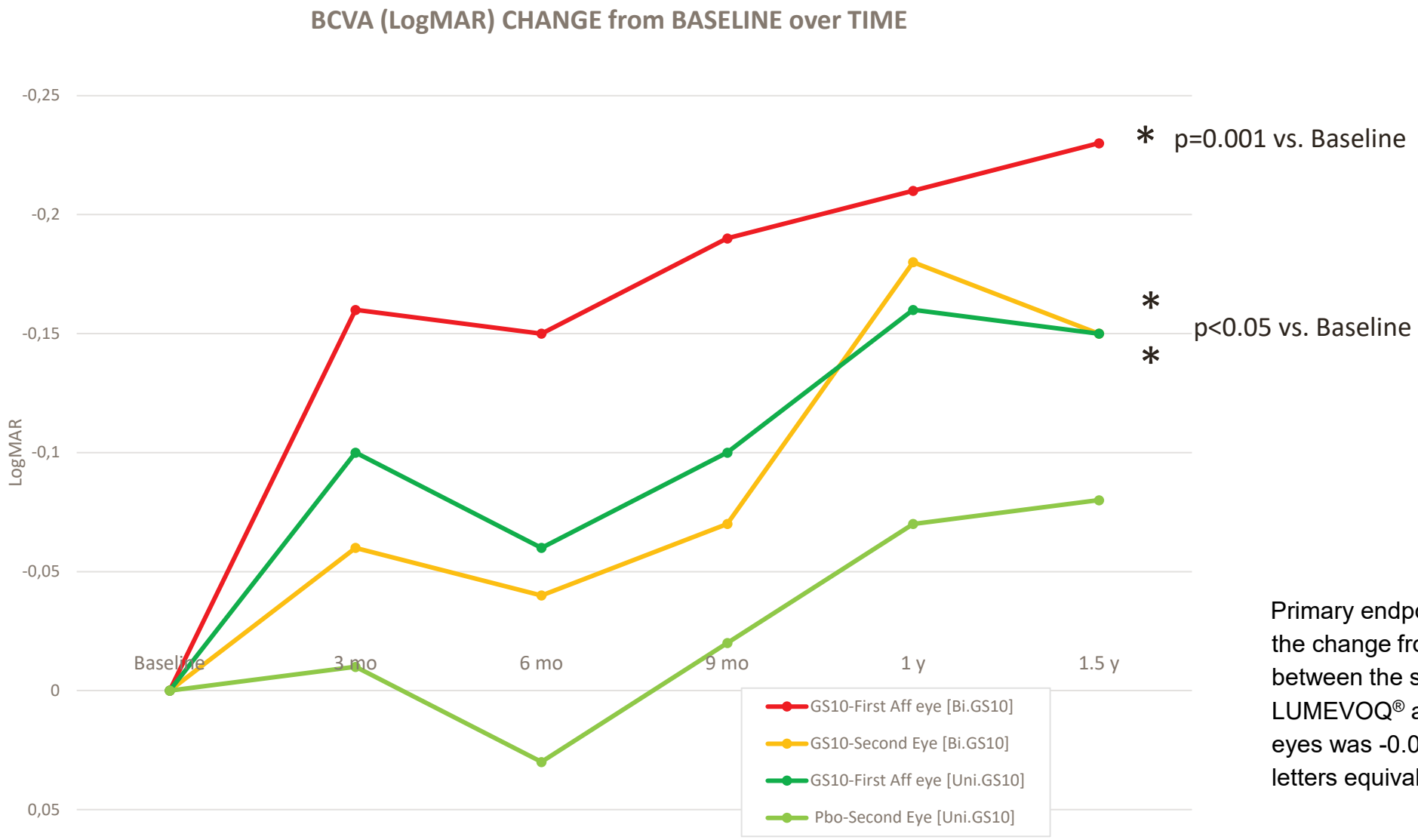
DOSE EFFECT

EVOLUTION of BCVA over Time



Note: Mean LogMAR at each timepoint

Change from Baseline of BCVA over Time



Primary endpoint: The difference of the change from baseline in BCVA between the second affected LUMEVOQ® and placebo-treated eyes was -0.05 LogMAR (+3 ETDRS letters equivalent; p=0.6080).

Note: Difference from baseline LogMAR. LS means are estimated by mixed models at the eye level, adjusted on baseline, with repeated values for each patient.

Change from Baseline of BCVA at 1.5 Year

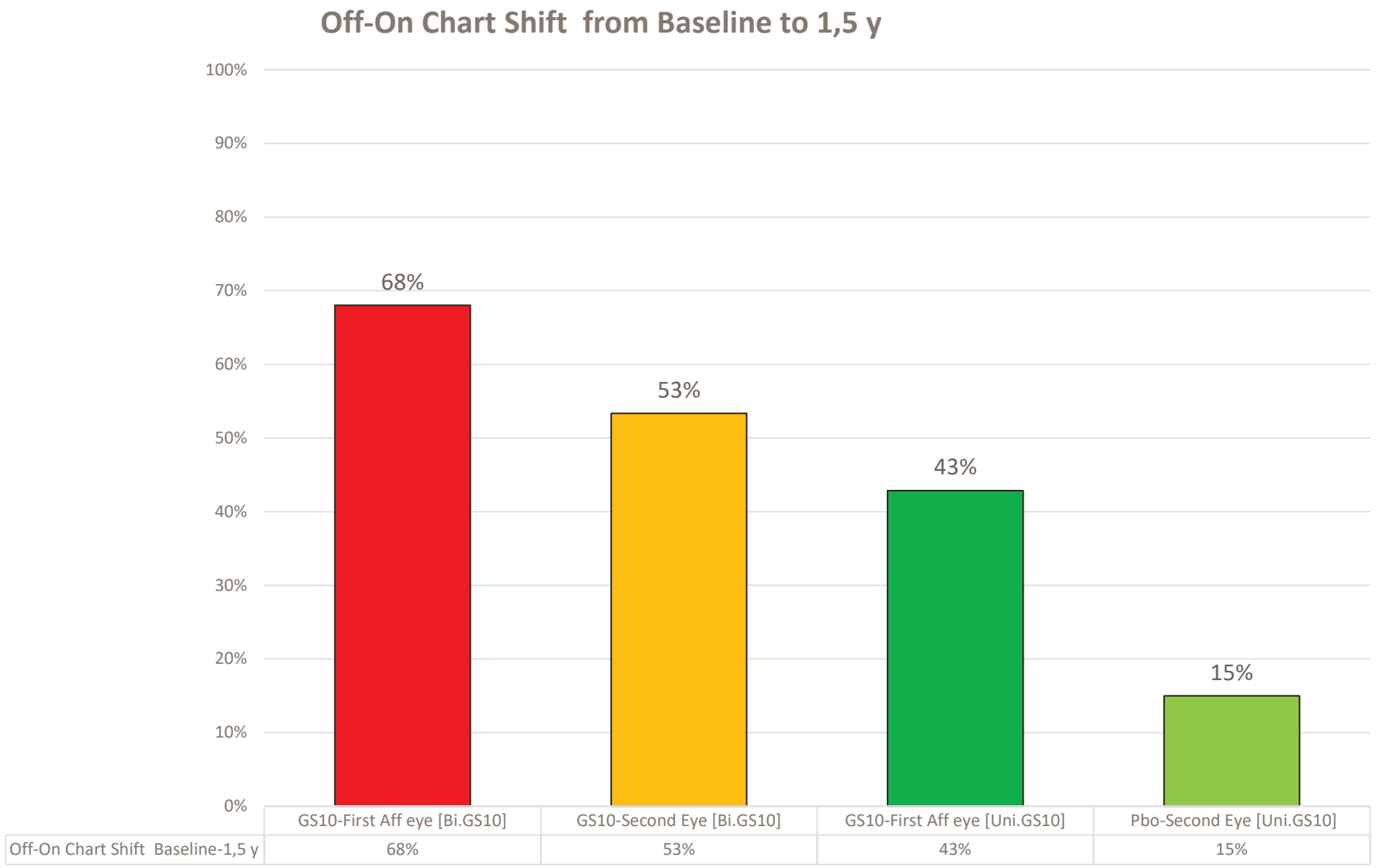
	1st affected eye	2nd affected eye
Subjects bilaterally injected with LUMEVOQ	LUMEVOQ -0,23 LogMAR **+12 ETDRS letters** *p=0.001*	LUMEVOQ -0,15 LogMAR **+8 ETDRS letters** *p<0.05*
Subjects unilaterally injected with LUMEVOQ	LUMEVOQ -0,15 LogMAR **+8 ETDRS letters** *p<0.05*	PLACEBO -0,08 LogMAR **+4 ETDRS letters** *p=NS*

Change from Nadir of BCVA at 1.5 Year

	1st affected eye	2nd affected eye
Subjects bilaterally injected with LUMEVOQ	LUMEVOQ -0.37 LogMAR **+ 19 ETDRS letters** *p<0.0001*	LUMEVOQ -0.31 LogMAR **+16 ETDRS letters** *p<0.0001*
Subjects unilaterally injected with LUMEVOQ	LUMEVOQ -0.37 LogMAR **+19 ETDRS letters** *p<0.0001*	PLACEBO -0.25 LogMAR **+13 ETDRS letters** *p<0.0001*

RESPONDERS

Off-On Chart Switch from Baseline and 1.5 year – Eye groups



	GS10-First Aff eye [Bi.GS10]	GS10-Second Eye [Bi.GS10]	GS10-First Aff eye [Uni.GS10]	Pbo-Second Eye [Uni.GS10]
Off-On Chart Shift Baseline-1,5 y	68%	53%	43%	15%

Responder rate (eyes and subjects): Clinically Relevant Recovery (CRR) from nadir – At 1.5 years

	Responder definition: CRR from nadir					
	First GS010 eyes (bilat. GS010)	**Second GS010 eyes (bilat. GS010)**	**First GS010 eyes (unilat. GS010)**	**Second placebo eyes (unilat. GS010)**	**Bilat. GS010 Subjects (response one or both eyes)**	**Unilat. GS010 Subjects (response one or both eyes)**
Eyes/Subjects numbers	48	48	50	50	48	50
Responders	30 (63%)	26 (54%)	29 (58%)	25 (50%)	33 (69%)	31 (62%)
Odd Ratio [CI]					1.31 [0.56;3.03]	

Responder rate (eyes and subjects): Improvement of at least 0.3 LogMAR from nadir – At 1.5 years

Responder definition: Improvement of at least 0.3 LogMAR from nadir						
	First GS010 eyes (bilat. GS010)	**Second GS010 eyes (bilat. GS010)**	**First GS010 eyes (unilat. GS010)**	**Second placebo eyes (unilat. GS010)**	**Bilat. GS010 Subjects (response one or both eyes)**	**Unilat. GS010 Subjects (response one or both eyes)**
Eyes/Subjects numbers	48	48	50	50	48	50
Responders	30 (63%)	26 (54%)	27 (54%)	23 (46%)	33 (69%)	32 (64%)
Odd Ratio [CI]					1.28 [0.55;2.97]	

Responder rate (eyes and subjects) – Being on-chart: BCVA ≤ LogMAR 1.6 (on-chart) – At 1.5 years

Responder definition: BCVA ≤ LogMAR 1.6 (on-chart)						
	First GS010 eyes (bilat. GS010)	**Second GS010 eyes (bilat. GS010)**	**First GS010/Second placebo eyes (unilat. GS010)**	**Second placebo eyes (unilat. GS010)**	**Bilat. GS010 Subjects (response one or both eyes)**	**Unilat. GS010 Subjects (response one or both eyes)**
Eyes/Subjects numbers	48	48	50	50	48	50
Responders	39 (81%)	35 (73%)	34 (68%)	34 (68%)	41 (85%)	36 (72%)
Odd Ratio [CI]					2.24 [0.78;6.47]	

SAFETY

Ocular Adverse Events During Post-Treatment up to 1.5 Years (Safety Population)
Favorable safety profile of LUMEVOQ confirmed

Eyes with	First Eye GS010 n (%) n* (bilat. N=49)	Eye GS010 n (%) n* (bilat. N=49)	Eye GS010 n (%) n* (bilat. N=49)	Eye Placebo n (%) n* (bilat. N=49)	Total (N=196) n (%) n*
At least one ocular TEAE	44 (89.8) 145	43 (87.8) 147	38 (77.6) 137	27 (55.1) 50	152 (77.6) 479
At least one ocular TEAE by severity					
Mild	42 (85.7) 132	41 (83.7) 130	37 (75.5) 123	26 (53.1) 48	146 (74.5) 433
Moderate	6 (12.2) 11	6 (12.2) 15	9 (18.4) 14	2 (4.1) 2	23 (11.7) 42
Severe	1 (2.0) 2	1 (2.0) 2	0	0	2 (1.0) 4
At least one ocular TEAE leading to study discontinuation	0	0	0	0	0
At least one ocular serious TEAE	0	0	0	0	0

No ocular or systemic AE leading to study discontinuation
No serious ocular adverse event
Most ocular adverse events are mild

The good safety profile is comparable in unilaterally and bilaterally treated subjects.

n* = number of events

Intraocular Inflammation During Post-Treat. up to 1.5 Years (Safety Population)
Favorable safety profile of LUMEVOQ® confirmed

Eyes with	Statistic	First Eye GS010 n (%) (bilat. N=49)	Second Eye GS010 n (%) (bilat. N=49)	First Eye GS010 n (%) (unilat. N=49)	Second Eye Placebo n (%) (unilat. N=49)	Total (N=196)
At least one intraocular inflammation TEAE	n (%)	35 (71.4)	35 (71.4)	34 (69.4)	5 (10.2)	109 (55.6)
At least one anterior inflammation TEAE	n (%)	26 (53.1)	26 (53.1)	29 (59.2)	3 (6.1)	84 (42.9)
At least one intermediate inflammation TEAE	n (%)	27 (55.1)	26 (53.1)	28 (57.1)	2 (4.1)	83 (42.3)
At least one posterior inflammation TEAE	n (%)	0	0	0	0	0
At least one non-specific eye inflammation TEAE	n (%)	0	0	0	0	0

No severe intraocular inflammation
No serious intraocular inflammation

The main ocular adverse event is intraocular inflammation, mostly mild, and responsive to conventional treatment.

n* = number of events

CONCLUSION

1. **REFLECT Phase III pivotal study confirms Lumevoq efficacy**
   - Statistically significant visual acuity improvement from baseline in LUMEVOQ®-treated eyes
   - Statistically significant visual acuity improvement from nadir in all eyes
   - Contralateral effect on the placebo eyes confirmed, as in REVERSE and RESCUE Phase III pivotal studies

2. **Dose effect - A bilateral treatment with Lumevoq is more beneficial than a unilateral treatment**
   - Bilaterally treated patients have better improvement of visual acuity than unilaterally treated patients

3. **Safety**
   - Favorable safety profile of LUMEVOQ® confirmed
   - Comparable safety profile in unilaterally and bilaterally treated subjects

Q&A Session

José-Alain Sahel, MD
University of Pittsburgh School of Medicine

Robert Sergott, MD
Wills Eye Hospital, Philadelphia

Bernard Gilly, PhD
Co-Founder & Chief Executive Officer

Magali Taiel, MD
Chief Medical Officer