Intravitreal Aflibercept Injection 8 mg for DME: 48-Week Results From the Phase 2/3 PHOTON Trial

David M. Brown,[1] on behalf of the PHOTON study investigators

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Note Regarding Forward-Looking Statements*

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* This slide has been added for purposes of posting this presentation on Regeneron’s website.

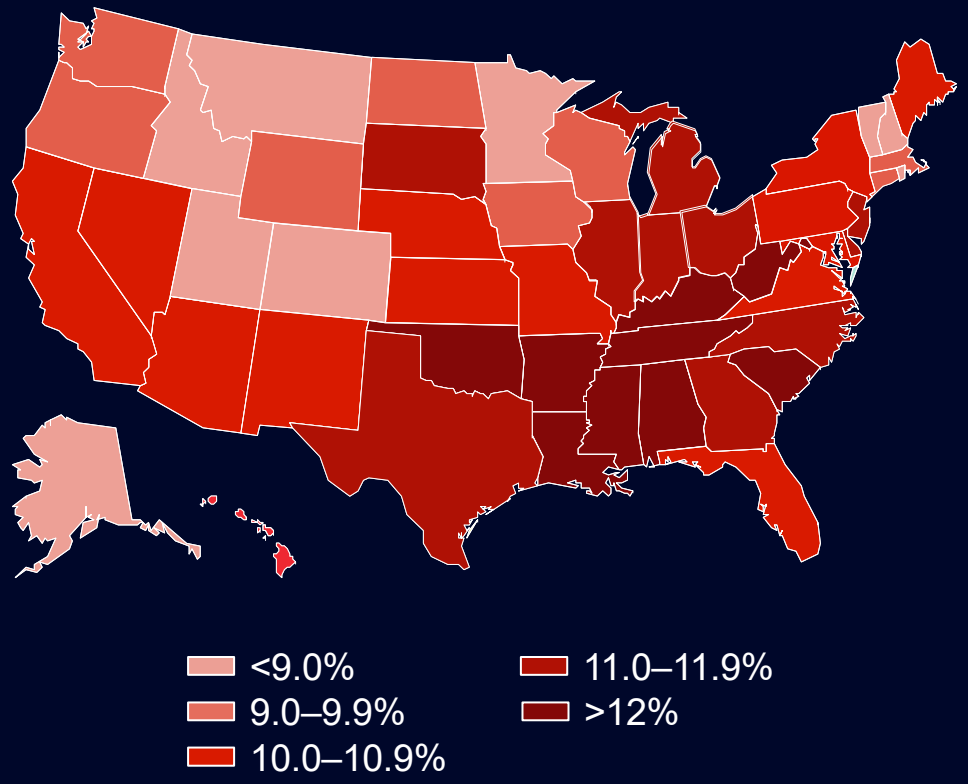
Disclosures

- David M. Brown serves as a scientific advisor for Regeneron/Bayer and Genentech/Roche and as a member of the Regeneron Combination Products Steering Committee
- This study was sponsored by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY) and co-funded by Bayer AG (Leverkusen, Germany). The sponsors participated in the design and conduct of the study, analysis of the data, and preparation of this presentation
- Study disclosures: This study includes research conducted on human patients. Institutional Review Board approval was obtained prior to study initiation

Background

DME

Prevalence of Diabetes in the US (2017)[1,a]



Elevated Anti-VEGF Levels in DR[2]

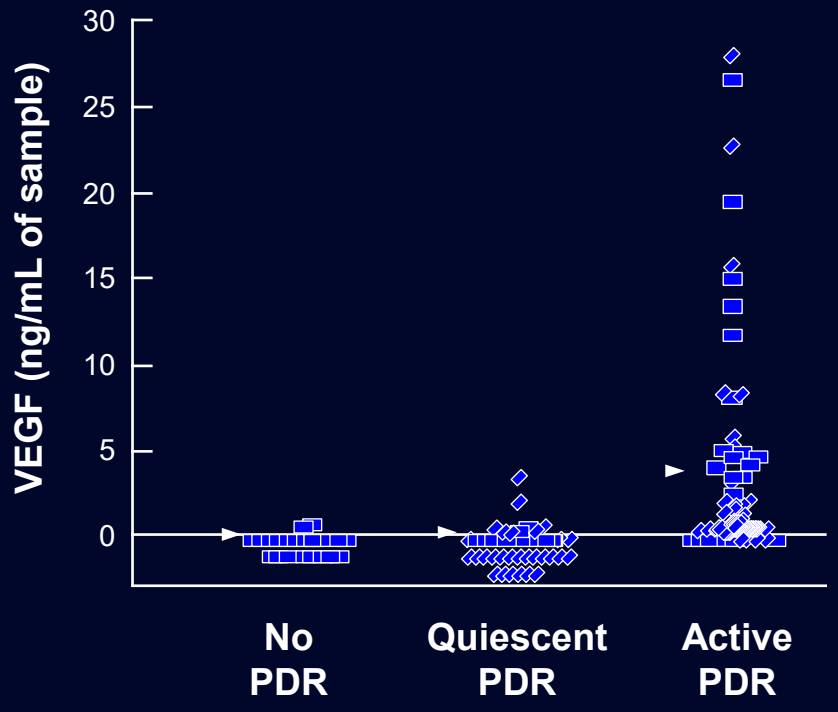


Figure adapted from Aiello et al.[2]

[a]Includes pregnancy-related diabetes, percentages are weighted to reflect population characteristics (e.g., average age)
PDR, proliferative diabetic retinopathy; VEGF, vascular endothelial growth factor.

1. Statista. Where Diabetes is Most Prevalent in the US. Available at: https://www.statista.com/chart/18160/us-states-with-highest-diabetes-rates/. Accessed September 28, 2022. 2. Aiello LP et al. *N Engl J Med.* 1994;331(22):1480-1487.

Characteristics of Aflibercept 8mg

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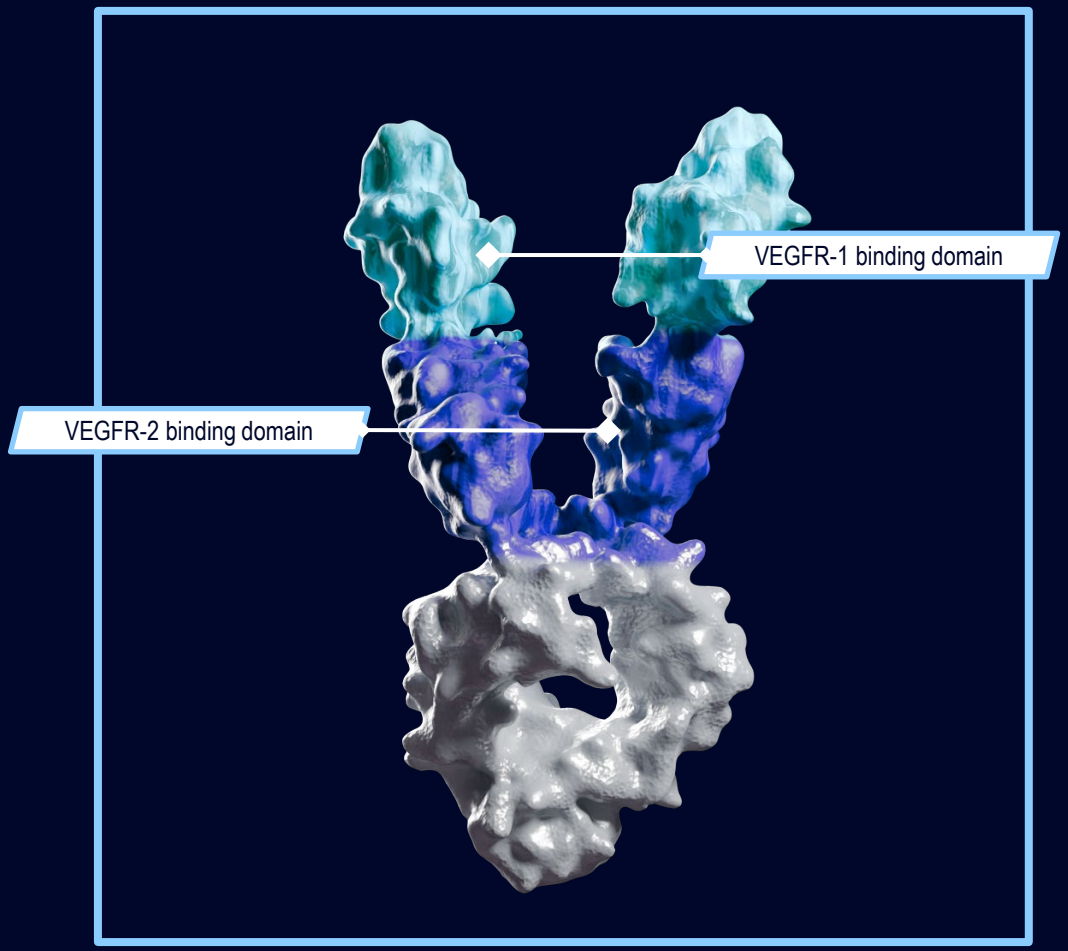
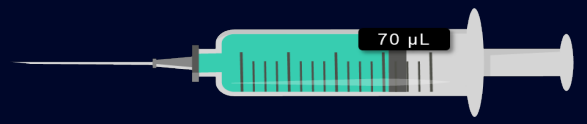
DME



- Novel intravitreal formulation delivers aflibercept 8mg in 70 µL injection (114.3 mg/mL)



- 4-times higher molar dose compared to aflibercept 2mg is hypothesized to provide longer effective vitreal concentration and enable more sustained effect on VEGF signaling

The ongoing pivotal PHOTON trial evaluates the efficacy and safety of aflibercept 8mg vs 2mg in patients with DME

VEGFR, vascular endothelial growth factor receptor

PHOTON Study Design

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DME

Multi-center, randomized, double-masked study in patients with DME*
Randomized 1 (2q8) : 2 (8q12) : 1 (8q16)
Note: 2mg arm received 5 initial monthly injections versus 8mg arms, which received only 3 initial monthly injections

2q8
Aflibercept 2mg every 8 weeks after 5 initial monthly injections
n=167

8q12
8mg every 12 weeks after 3 initial monthly injections
n=328

8q16
8mg every 16 weeks after 3 initial monthly injections
n=163

Primary EP at Week 48
Mean change in BCVA (Non-inferiority)

*Treatment naïve and previously treated
BCVA, best corrected visual acuity; EP, endpoint

PHOTON: Dosing Schedule

DME
Primary Endpoint

Year 1:

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48
2q8	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16	X	X	X	o	o	o	X	o	o	o	X	o	o

Note: 2mg arm received 5 initial monthly injections versus 8mg arms, which received only 3 initial monthly injections

Dose Regimen Modifications (DRM) in Year 1

- At Weeks 16 or 20, 8q12 and 8q16 patients meeting DRM criteria will be shortened to Q8
- At Week 24, 8q16 patients meeting DRM criteria will be shortened to Q12
- At subsequent dosing visits, 8mg patients meeting DRM criteria will be shortened by 4 weeks
- Minimum interval for all patients is Q8

DRM Criteria for Shortening Dosing Interval:

>10-letter loss in BCVA from Week 12
due to persistent or worsening DME

AND

>50-micron increase in CRT from Week 12

Stippled boxes = initial treatment phase; X=active injection; o=sham injections
Note: Figure does not reflect all dosing options once a patient is shortened. No extension of interval was allowed in the first year

PHOTON: Dosing Schedule

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DME
Primary Endpoint

Year 1:

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48
2q8	X	X	X	X	X	o	X	o	X	o	X	o	X
8q12	X	X	X	o	o	X	o	o	X	o	o	X	o
8q16	X	X	X	o	o	o	X	o	o	o	X	o	o

Note: 2mg arm received 5 initial monthly injections versus 8mg arms, which received only 3 initial monthly injections

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Patient Disposition at Week 48

DME

	2q8	8q12	8q16	Total
# Randomized	167	329	164	660
# Completing Week 48	94.0%	91.2%	95.1%	92.9%
# Discontinued before Week 48	6.0%	8.8%	4.9%	7.1%

Baseline Demographics

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DME

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
Age (years)	63.0 (9.8)	62.1 (11.1)	61.9 (9.5)	62.3 (10.4)
Female (%)	44.9%	36.0%	39.3%	39.1%
Race (%)				
White	67.1%	70.4%	78.5%	71.6%
Black or African American	10.8%	10.7%	5.5%	9.4%
Asian	18.0%	14.6%	14.1%	15.3%
Other	2.4%	3.0%	0.6%	2.4%
Not reported	1.8%	1.2%	1.2%	1.4%
Hispanic or Latino (%)	18.6%	16.5%	20.9%	18.1%
Duration of diabetes (years)	15.9 (10.0)	15.1 (10.0)	15.7 (10.7)	15.5 (10.2)
Hemoglobin A1C (%)	8.1 (1.5)	7.9 (1.5)	7.8 (1.5)	8.0 (1.5)
BMI (kg/m^2)	29.9 (6.5)	30.4 (6.2)	31.0 (6.1)	30.5 (6.2)

Data are mean (SD) unless otherwise indicated
BMI, body mass index; FAS, full analysis set; SAF, safety analysis set; SD, standard deviation

Baseline Characteristics of the Study Eye

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DME

	2q8	8q12	8q16	Total
N (FAS/SAF)	167	328	163	658
BCVA (ETDRS letters)	61.5 (11.2)	63.6 (10.1)	61.4 (11.8)	62.5 (10.9)
Snellen Equivalent	20/63	20/50	20/63	20/63
20/32 (>73 to 78 letters)	12.0%	18.0%	14.1%	15.5%
20/40 or worse (≤73 letters)	88.0%	82.0%	85.9%	84.5%
CRT (μm)	457.2 (144.0)	449.1 (127.4)	460.3 (117.8)	454.0 (129.5)
Prior treatment for DME (%)	44.3%	43.6%	43.6%	43.8%
DRSS categories (%)				
Better or equal to Level 43	62.9%	60.1%	65.6%	62.2%
Level 47 or worse	31.7%	34.5%	28.2%	32.4%
Missing/Ungradable	5.4%	5.5%	6.1%	5.6%

Data are mean (SD) unless otherwise indicated
DRSS, Diabetic Retinopathy Severity Score; ETDRS, Early Treatment of Diabetic Retinopathy Study

PHOTON: 48-Week BCVA
Primary Endpoint Met in Both 8mg Groups

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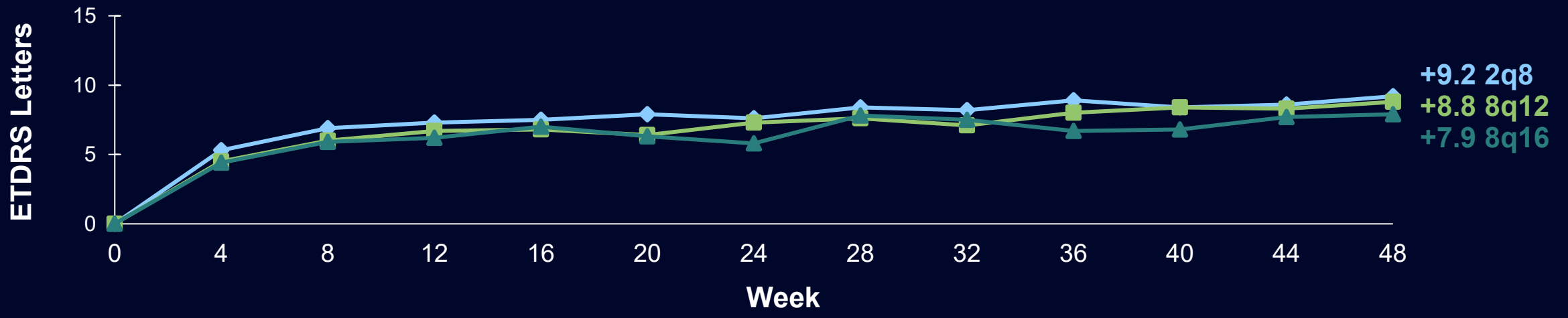
DME

BCVA Change from Baseline



	LS mean change from BL at Week 48 (MMRM)	Diff. in LS means vs. 2q8	2-sided 95% CI	1-sided test for non-inferiority at 4-letter margin
2q8	8.7			
8q12	8.1	-0.57	-2.26, 1.13	p <0.0001
8q16	7.2	-1.44	-3.27, 0.39	p = 0.0031

Observed values (censoring data post intercurrent event [ICE]); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline)

Large Majority of 8mg Patients Maintained Randomized Intervals Through Week 48

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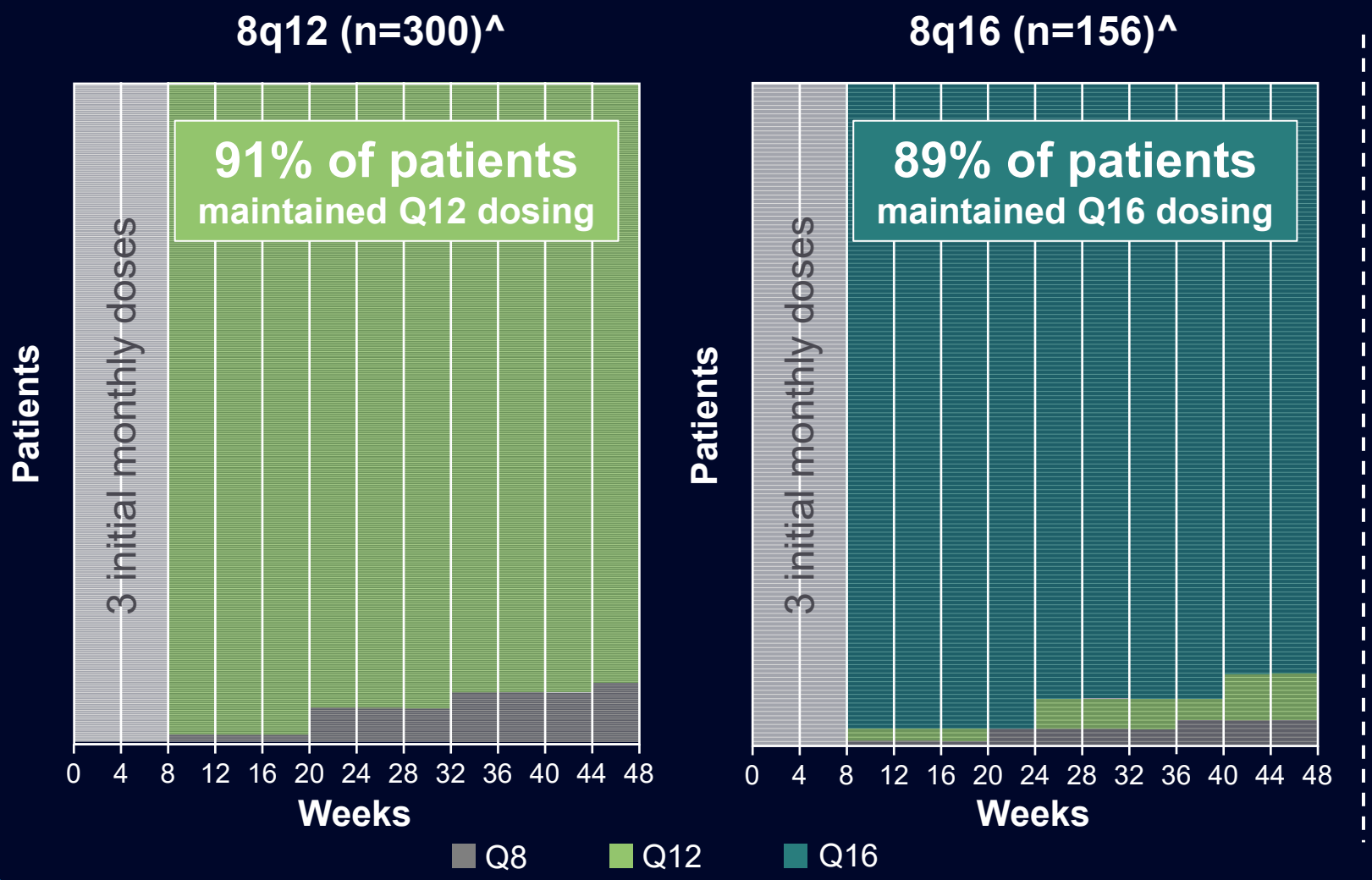
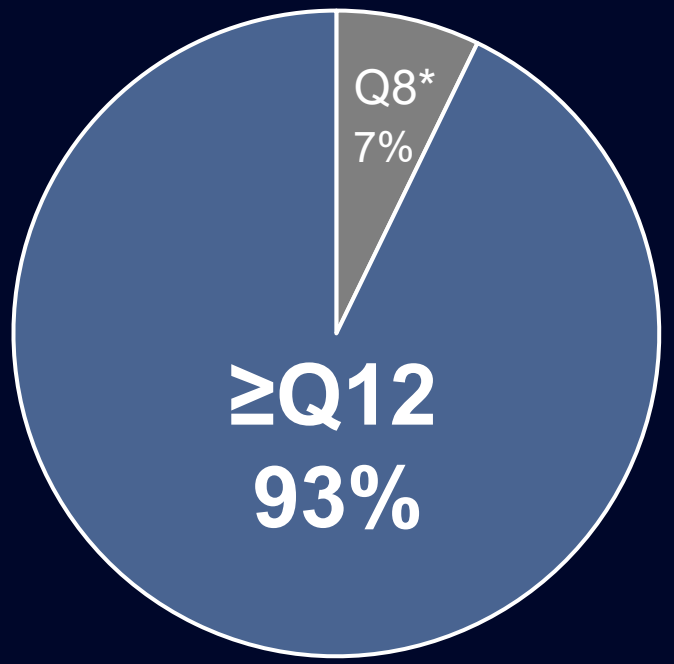
DME



93% of 8mg patients maintained dosing intervals ≥12 weeks



All 8mg
(n=456)^

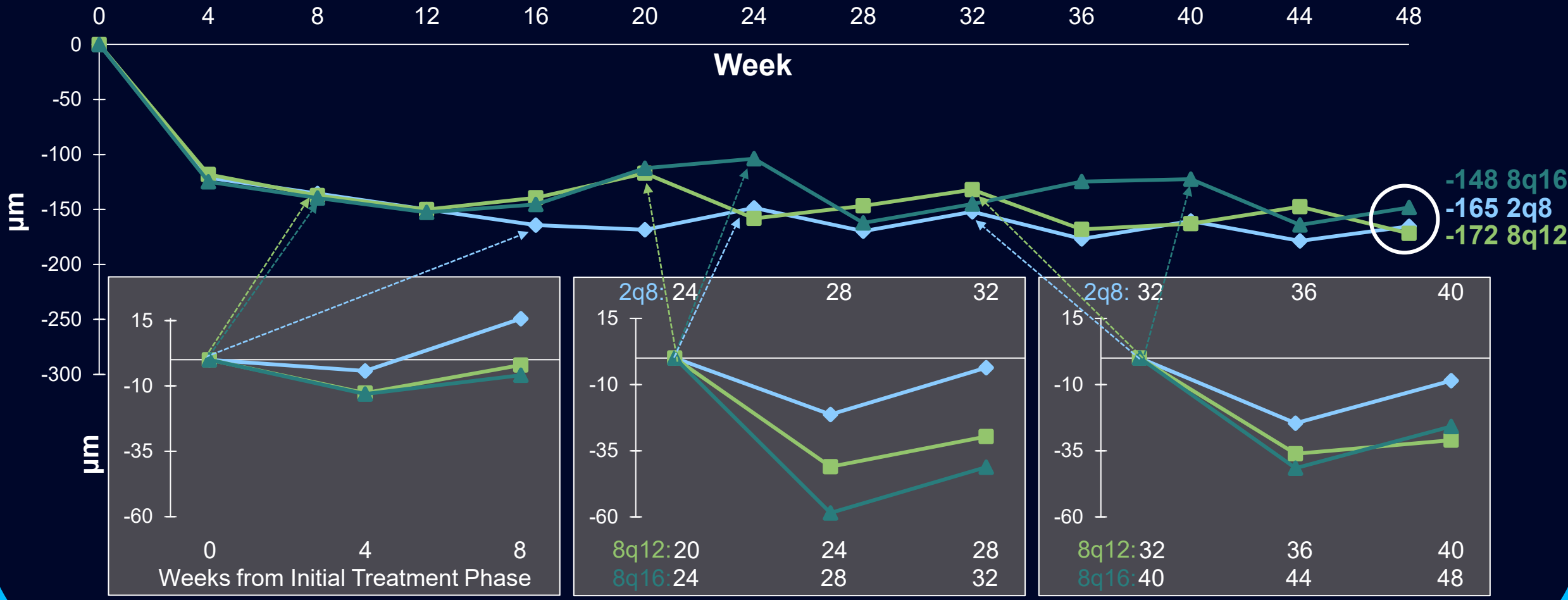
*Patients shortened based on DRM assessments at some point through Week 48
^Patients completing Week 48

Mean Change in Central Retinal Thickness

DME

Note: 2mg arm received 5 initial monthly injections versus 8mg arms, which received only 3 initial monthly injections

Despite fewer initial monthly doses, 8mg exhibited longer duration at each matched interval, thus achieving similar retinal thickness to 2mg by Week 48



First matched interval | Second matched interval | Third matched interval

Observed values (censoring data post ICE); FAS: 2q8 n=167; 8q12 n=328; 8q16 n=163 (at baseline)

Most Frequent Ocular AEs Through Week 48

photon

DME

	2q8	8q12	8q16	All 8mg
N (SAF)	167	328	163	491
Patients with ≥ 1 AE (%)*	27.5%	31.7%	29.4%	31.0%
Cataract	1.2%	1.5%	4.9%	2.6%
Conjunctival hemorrhage	3.6%	4.3%	3.7%	4.1%
Intraocular pressure increased	3.6%	2.1%	0.6%	1.6%
Punctate keratitis	0.6%	1.5%	3.7%	2.2%
Retinal hemorrhage	0.6%	0	3.7%	1.2%
Vitreous floaters	2.4%	4.9%	1.8%	3.9%

*Any ocular treatment-emergent AE in the study eye
AE, adverse event

Intraocular Inflammation Through Week 48

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DME

	2q8	8q12	8q16	All 8mg
N (SAF)	167	328	163	491
Patients with ≥ 1 IOI AE (%)*	0.6%	1.2%	0	0.8%

- No cases of endophthalmitis or occlusive retinal vasculitis

Reported IOI terms: iridocyclitis, iritis, uveitis, vitreal cells, vitritis
*Treatment-emergent events

Non-Ocular Safety Through Week 48

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DME

	2q8	8q12	8q16	All 8mg
N (SAF)	167	328	163	491
Patients (%):				
APTC events*	3.6%	2.4%	4.3%	3.1%
Hypertension events*	12.0%	11.0%	14.1%	12.0%
Non-ocular SAEs*	15.6%	15.9%	13.5%	15.1%
Deaths^	2.4%	2.7%	1.8%	2.4%

*Treatment-emergent events; ^All events
APTC, Anti-Platelet Trialists' Collaboration; SAE, serious adverse events

PHOTON: 48-Week Results
Primary Endpoint Met in Both 8mg Groups

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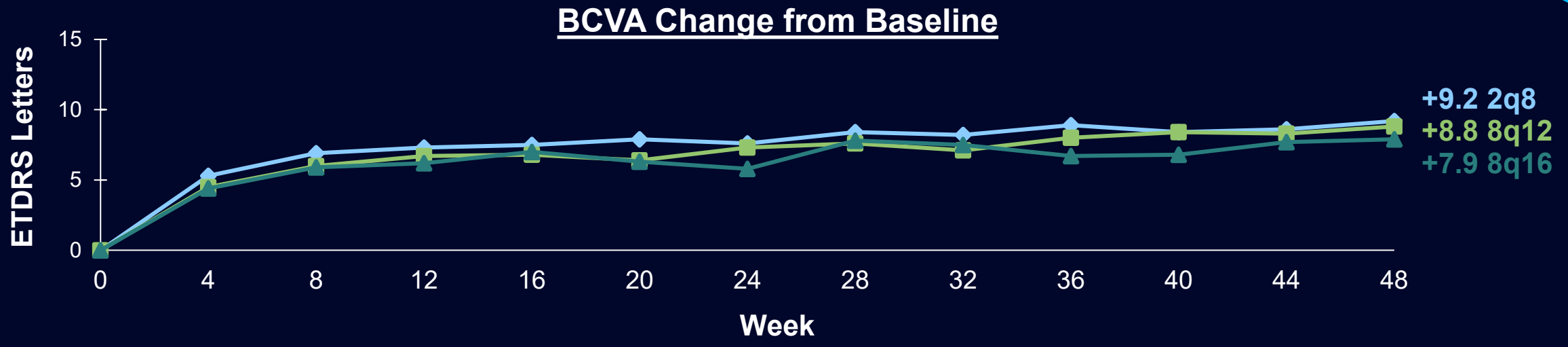
DME

- 8q12 and 8q16 groups had non-inferior BCVA compared to 2q8 at Week 48
- Ocular and non-ocular safety comparable to 2mg



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PHOTON: 48-Week Results
Large Majority of 8mg Patients Maintained Randomized Intervals

DME

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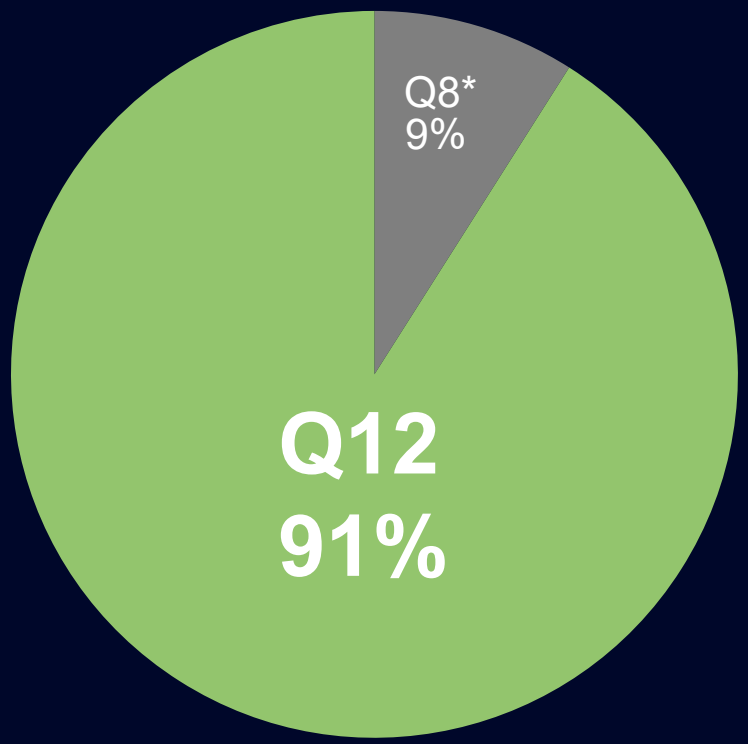
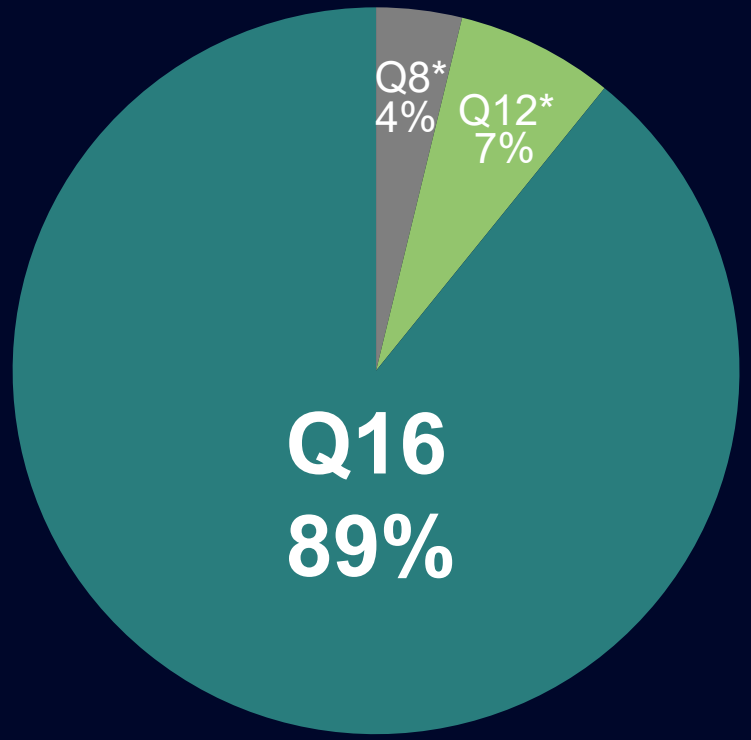
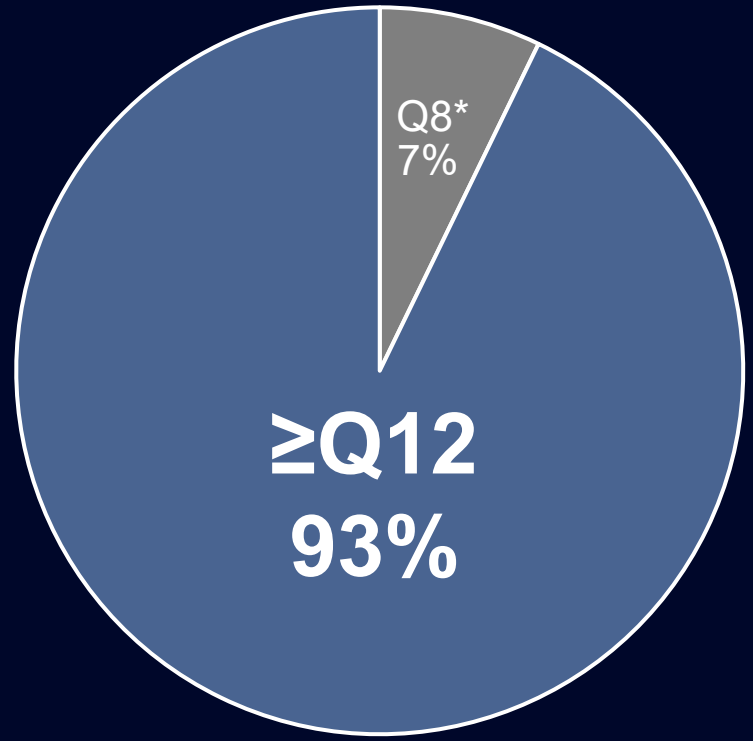


8q12 (n=300)^



8q16 (n=156)^



All 8mg (n=456)^

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