pulsar

Extension

# PULSAR Extension: Fluid Resolution in Patients with nAMD Receiving Aflibercept 8mg or Switching from 2mg to 8mg

**Marion R. Munk,[1,2,3] Praveen J. Patel,[4,5] Paolo Lanzetta,[6,7] Michael W. Stewart,[8] Richard Gale,[9,10] Javier Zarranz-Ventura,[11] Jean-François Korobelnik,[12,13] Sobha Sivaprasad,[4] Sergio Leal,[14] Andrea Schulze,[15] Tobias Machewitz,[15] Xin Zhang,[14]**
**on behalf of the PULSAR study investigators**

*[1]Augenarzt-Praxisgemeinschaft Gutblick AG, Pfäffikon, Switzerland; [2]Department of Ophthalmology, Inselspital, University Hospital Bern, Bern, Switzerland; [3]Department of Ophthalmology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; [4]National Institute for Health Research Biomedical Research Centre, Moorfields Eye Hospital, NHS Foundation Trust, London, UK; [5]UCL Institute of Ophthalmology, London, UK; [6]Department of Medicine – Ophthalmology, University of Udine, Udine, Italy; [7]Istituto Europeo di Microchirurgia Oculare (IEMO), Udine and Milan, Italy; [8]Mayo Clinic College of Medicine and Department of Ophthalmology, Mayo Clinic, Jacksonville, FL, USA; [9]Hull York Medical School, University of York, York, UK; [10]York and Scarborough Teaching Hospital NHS Foundation Trust, York, UK; [11]Hospital Clínic de Barcelona Institut Clinic de Oftalmología (ICOF), Barcelona, Spain; [12]CHU Bordeaux GH Pellegrin, Service d'Ophtalmologie, Place Amelie Raba Leon, 33000 Bordeaux, France; [13]University of Bordeaux, INSERM, Bordeaux Population Health Research Center, UMR1219, F-33000, Bordeaux, France; [14]Bayer Consumer Care AG Pharmaceuticals, Basel, Switzerland; [15]Bayer AG, Berlin, Germany*

*Presented at the American Academy of Ophthalmology (AAO) 2025 Congress, Orlando, FL, USA, October 18–20, 2025*

# Disclosures

pulsar
nAMD
Extension

- **Marion R. Munk** receives consulting fees from to AbbVie, Alcon, Alimera, Allergan, Amgen, Apellis Pharmaceuticals, Astellas, Aviceda Therapeutics, Bayer, Boehringer Ingelheim, Dandelione, Eyegnos Consulting, EyePoint Pharmaceuticals, Evolve Medical Education, GenSight Biologics, Isarna Therapeutics, Iveric Bio, Kubota, LumiThera, Novartis, Oculis, OD-OS, ONL Therapeutics, OcuTerra Therapeutics, RetinAI, Roche, UBS Analytics, and Zeiss
    - **PJP**: Honoraria/attendance at advisory boards for Bayer, Boehringer Ingelheim, and Roche; and speaker fees and educational travel grants from Bayer and Roche. **PL**: Consulting fees from Aerie, Allergan, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, Genentech, I-Care, Novartis, Outlook Therapeutics, and Roche. **MWS**: Consultant for Alkahest and Bayer, and funding from Allergan, Kanghong, and Regeneron. **RG**: Consultant for AbbVie, Allergan, Apellis, Bayer, Biogen, Boehringer Ingelheim, Notal, Novartis, Roche, and Santen, and funding from Bayer, Novartis, and Roche. **JZ-V**: Speaker frees from Alcon, Alimera Sciences, Allergan, AbbVie, Bausch & Lomb, Bayer, Brill Pharma, DORC, Esteve, Novartis, Roche, Topcon Healthcare, and Zeiss; research fees from AbbVie, Allergan Inc., Bayer, Novartis, and Roche; and scientific advisor fees from AbbVie, Allergan Inc., Bayer, Novartis, and Roche. **J-FK**: Consulting fees from AbbVie, Apellis, Bayer, Eyepoint Pharma, Ocuphire, Ocular Therapeutix, Opthea, Roche, Thea, and Carl Zeiss Meditec, and data safety monitoring board member for Alexion, Novo Nordisk, and Opthea. **SS**: Consulting fees from AbbVie, Alimera Science, Amgen, Astellas, Bayer, Biogen, Boehringer Ingelheim, Clearside Biomedical, Eyebiotech, Eyepoint Phamaceuticals, Iveric Bio/Astellas Pharma, Janssen Pharmaceuticals, Kriya Therapeutics, Nova Nordisk, Ocular Therapeutix, OcuTerra, Optos, Ripple Therapeutics, Roche, Stealth Biotherapeutics, and Sanofi. **SL** and **XZ**: Employees of Bayer Consumer Care AG, Basel, Switzerland. **AS** and **TM**: Employees of Bayer AG.
- The PULSAR study was sponsored by Bayer AG (Leverkusen, Germany) and co-funded by Regeneron Pharmaceuticals, Inc. (Tarrytown, NY, USA). The sponsor 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
- The data in this presentation were originally presented at the 25th European Society of Retina Specialists (EURETINA) Congress, Paris, France, September 4–7, 2025
- Medical writing support, under the direction of the authors, was provided by ApotheCom and funded by Bayer Consumer Care AG (Basel, Switzerland), in accordance with Good Publication Practice (GPP) standards (*Ann Intern Med.* 2022;175:1298–1304)

# PULSAR Extension Design

pulsar nAMD Extension

## PULSAR *(Masked)*

**Patients with treatment-naïve nAMD**

**2q8 arm**
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections
**n=336**

**8q12 arm**
Aflibercept 8 mg every 12 weeks after 3 initial monthly injections
**n=335**

**8q16 arm**
Aflibercept 8 mg every 16 weeks after 3 initial monthly injections
**n=338**

## PULSAR Extension *(Open-label and optional)*[a]

**2q8→8mg arm**
**Patients originally assigned to 2q8 switched to aflibercept 8 mg every 12 weeks**
**n=208**

**8mg arm**
**Patients originally assigned to 8q12 or 8q16 continued aflibercept 8 mg on last assigned dosing interval**
**n=417**

**Week**

0 — 48 — 96 — 156

**Primary endpoint**
Change from baseline in BCVA (non-inferiority)

**Start of PULSAR Extension**
Optional phase added while PULSAR was ongoing; therefore, not all patients were able to enroll due to time constraints

**End of PULSAR Extension**

[a]To be eligible for PULSAR Extension, patients had to have ≥1 BCVA and CRT assessments between Week 84 and Week 92. The masked transition period (Week 96–108) was followed by the open-label part (Week 108–156). **BCVA**, best-corrected visual acuity; **CRT**, central retinal subfield thickness; **nAMD**, neovascular age-related macular degeneration.

# PULSAR Extension Design

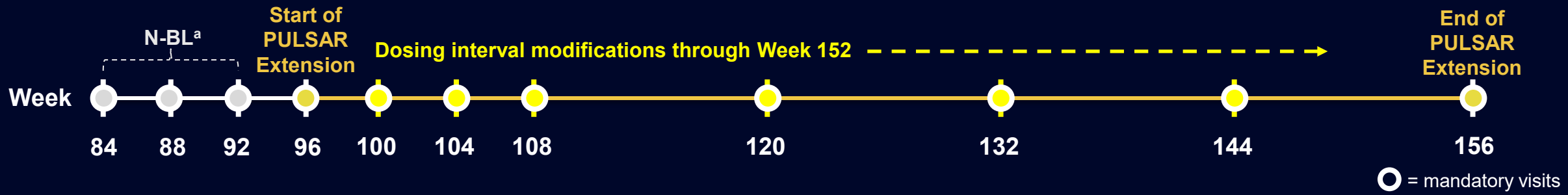
pulsar
nAMD
Extension

**2q8→8mg**
**n=208**

Patients initially treated with aflibercept 2q8 were switched to aflibercept 8 mg at Week 96 and immediately assigned to a 12-week dosing interval

**8mg**
**n=417**

Patients initially treated with aflibercept 8q12 or 8q16 continued with aflibercept 8 mg at their last assigned dosing interval




## E-DRM: Interval Shortening During Year 3

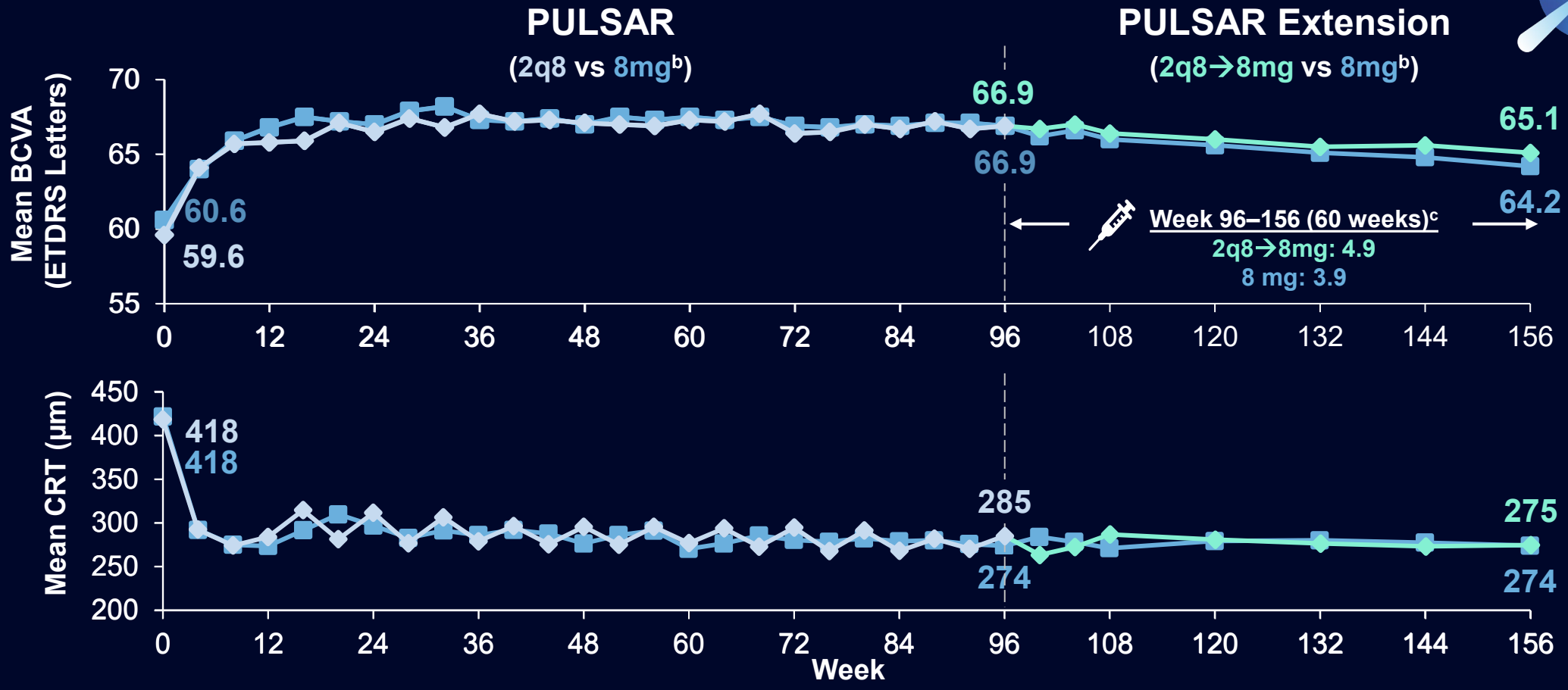
- Patients were assessed at ***any visit*** beginning at Week 100
- **Criteria for interval shortening:**
  - >5-letter loss in BCVA from N-BL due to persistent or worsening nAMD **AND either:**
    - >25 µm increase in CRT from N-BL **OR**
    - New onset of foveal neovascularization **OR**
    - New foveal hemorrhage
  - **OR** >10-letter loss in BCVA from N-BL due to worsening nAMD
- Dosing intervals shortened by **2-week** increments to a **minimum of Q8**

## E-DRM: Interval Extension During Year 3

- Patients were assessed at ***dosing visits*** beginning at Week 100
- **Criteria for interval extension:**
  - <5-letter loss in BCVA from N-BL **AND**
  - No fluid (IRF or SRF) in the central subfield on OCT **AND**
  - No new onset of foveal neovascularization or foveal hemorrhage
- Dosing intervals extended by **2-week** increments to a **maximum of Q24**

[a]N-BL was an average of BCVA and CRT values from Weeks 84, 88, and 92. **E-DRM**, dosing regimen modification criteria during the PULSAR Extension; **IRF**, intraretinal fluid; **N-BL**, new baseline; **OCT**, optical coherence tomography; **Q8**, every 8 weeks; **Q24**, every 24 weeks; **SRF**, subretinal fluid.

# Mean BCVA and CRT Through Week 156[a]




Mean number of active injections over 48-week periods:[c]

**BL–Week 48**
2 mg: 6.9
8q12: 6.1
8q16: 5.2

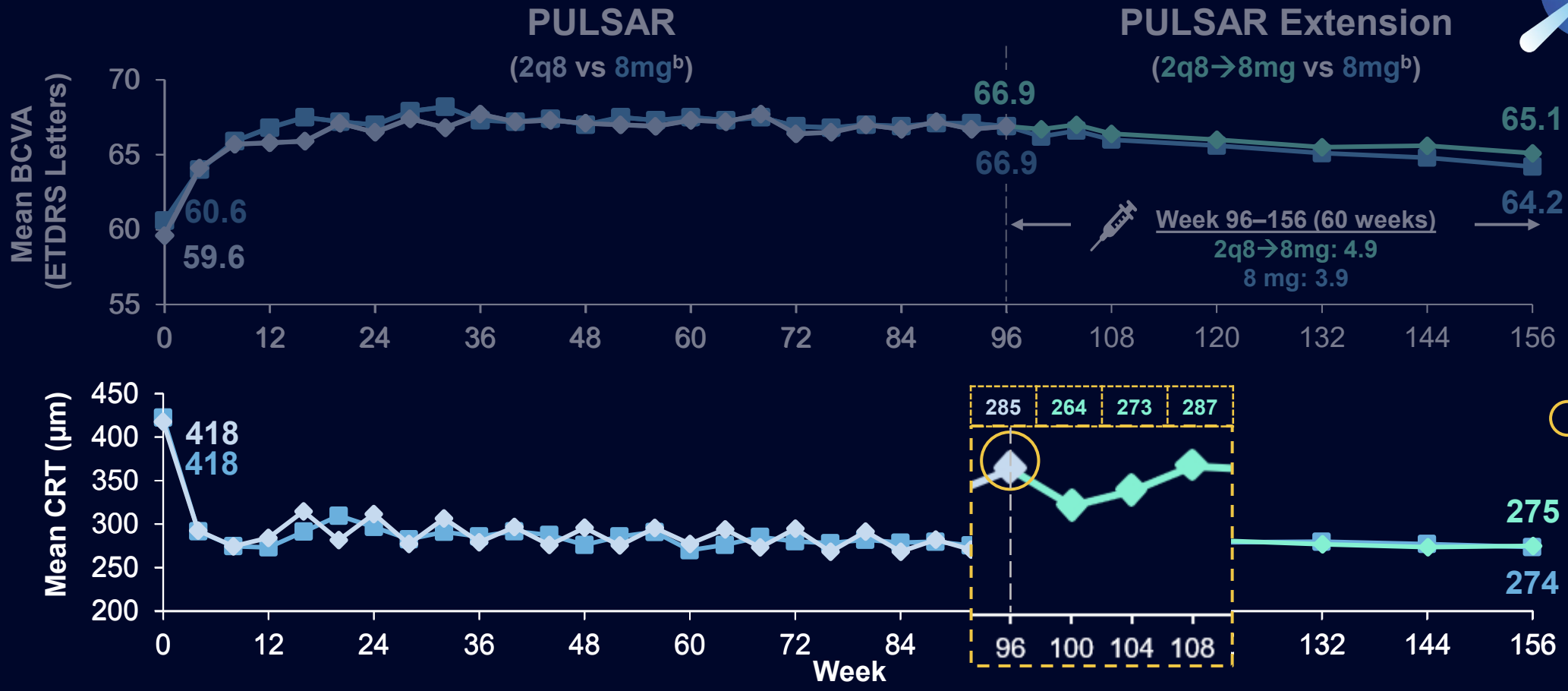
**Week 48–96**
2 mg: 5.9
8q12: 3.6
8q16: 3.1

**Week 108–156**
8 mg: 2.9
8 mg: 2.9

Note: At Week 156, the 2q8→8mg group (n=208) and 8mg group (n=417) reported LS mean (95% CI) changes from BL (MMRM) in BCVA of +4.6 (2.6, 6.6) letters and +3.4 (1.9, 4.9) letters, respectively, and in CRT of −145 (−155, −136) µm and −148 (−156, −140) µm, respectively. MMRM was used to generate BCVA/CRT LS means for the eFAS with BL BCVA/CRT as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and BL BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and BL BCVA/CRT and the interaction between visit and treatment. [a]eFAS (observed cases). [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **BL**, baseline; **CI,** confidence interval; **eSAF**, safety analysis set in the PULSAR Extension; **LS**, least squares; **MMRM,** mixed model for repeated measures.

# Mean BCVA and CRT Through Week 156[a]

pulsar nAMD Extension




Mean number of active injections over 48-week periods:[c]

**BL–Week 48**
2 mg: 6.9
8q12: 6.1
8q16: 5.2

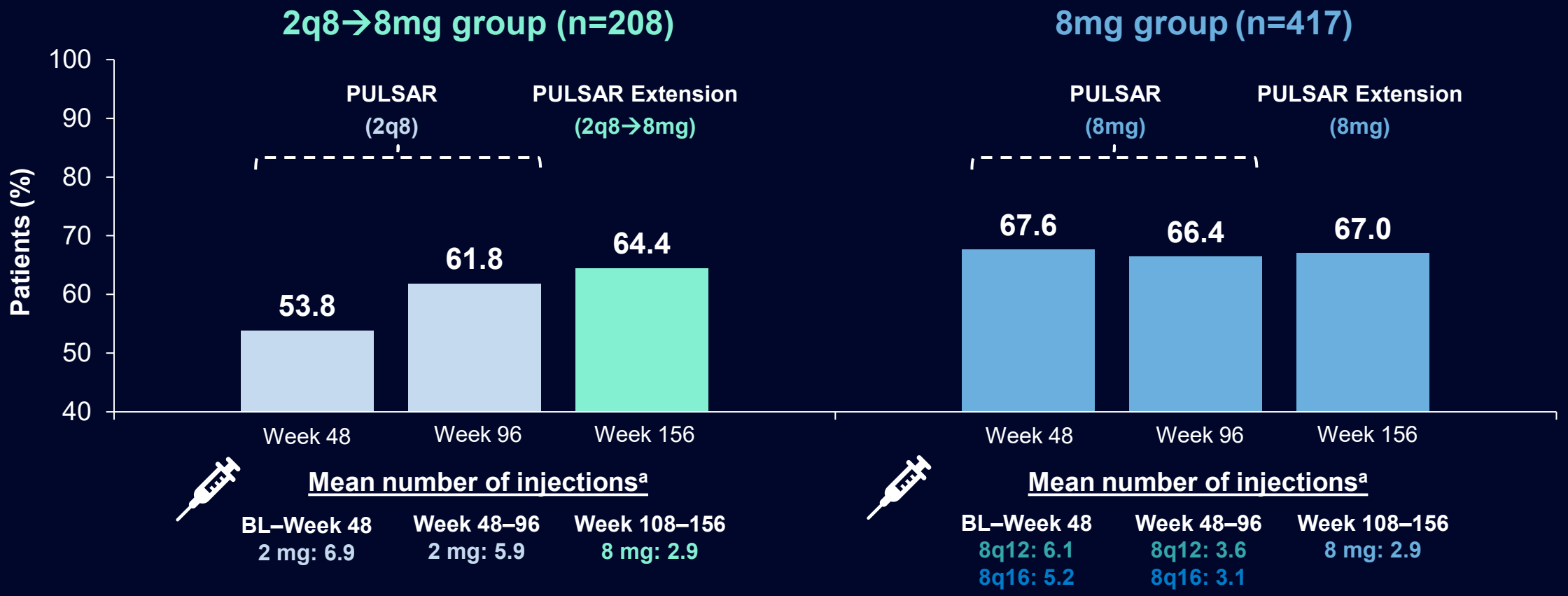
**Week 48–96**
2 mg: 5.9
8q12: 3.6
8q16: 3.1

**Week 108–156**
8 mg: 2.9
8 mg: 2.9

Note: At Week 156, the 2q8→8mg group (n=208) and 8mg group (n=417) reported LS mean (95% CI) changes from BL (MMRM) in BCVA of +4.6 (2.6, 6.6) letters and +3.4 (1.9, 4.9) letters, respectively, and in CRT of −145 (−155, −136) µm and −148 (−156, −140) µm, respectively. MMRM was used to generate BCVA/CRT LS means for the eFAS with BL BCVA/CRT as a covariate; treatment group (aflibercept 8q12, 8q16, 2q8), visit, and stratification variables (geographic region [Japan vs rest of the world] and BL BCVA [<60 vs ≥60 letters]) as fixed factors; and terms for the interaction between visit and BL BCVA/CRT and the interaction between visit and treatment. [a]eFAS (observed cases). [b]Patients who were randomly assigned to the 8q12 or 8q16 groups at the beginning of the PULSAR study and continued treatment with aflibercept 8 mg through the PULSAR Extension. [c]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **BL**, baseline; **CI,** confidence interval; **eSAF**, safety analysis set in the PULSAR Extension; **LS**, least squares; **MMRM,** mixed model for repeated measures.

# Patients with Fluid Resolution in the Aflibercept 2q8→8mg and 8 mg Groups at Week 156

pulsar nAMD Extension



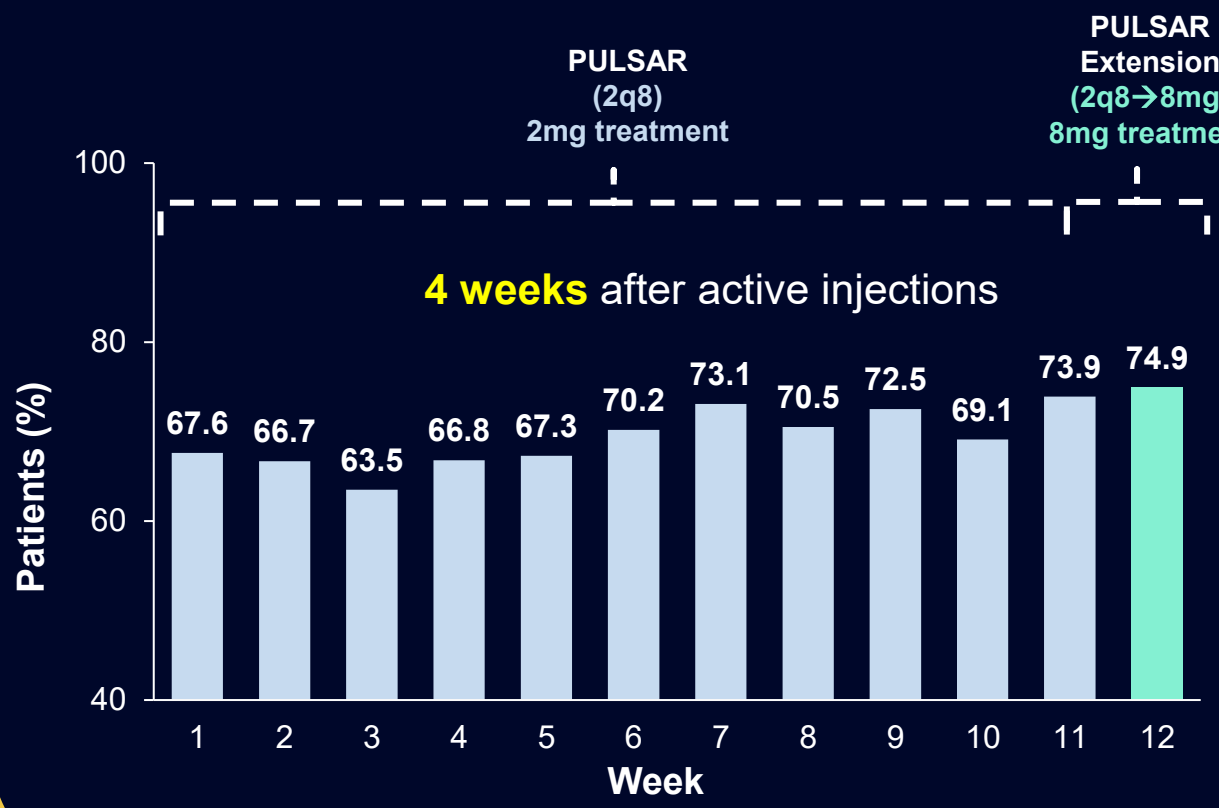

- The proportion of patients with fluid resolution was maintained in the **aflibercept 2q8→8mg** group through 96 weeks, and was **sustained after switching to 8 mg** through Week 156
- **Long-term fluid resolution** was observed in the 8mg group with extended dosing intervals through Week 156
- The proportion of patients with fluid resolution was **similar in the 2q8→8mg and 8 mg groups** at Week 156

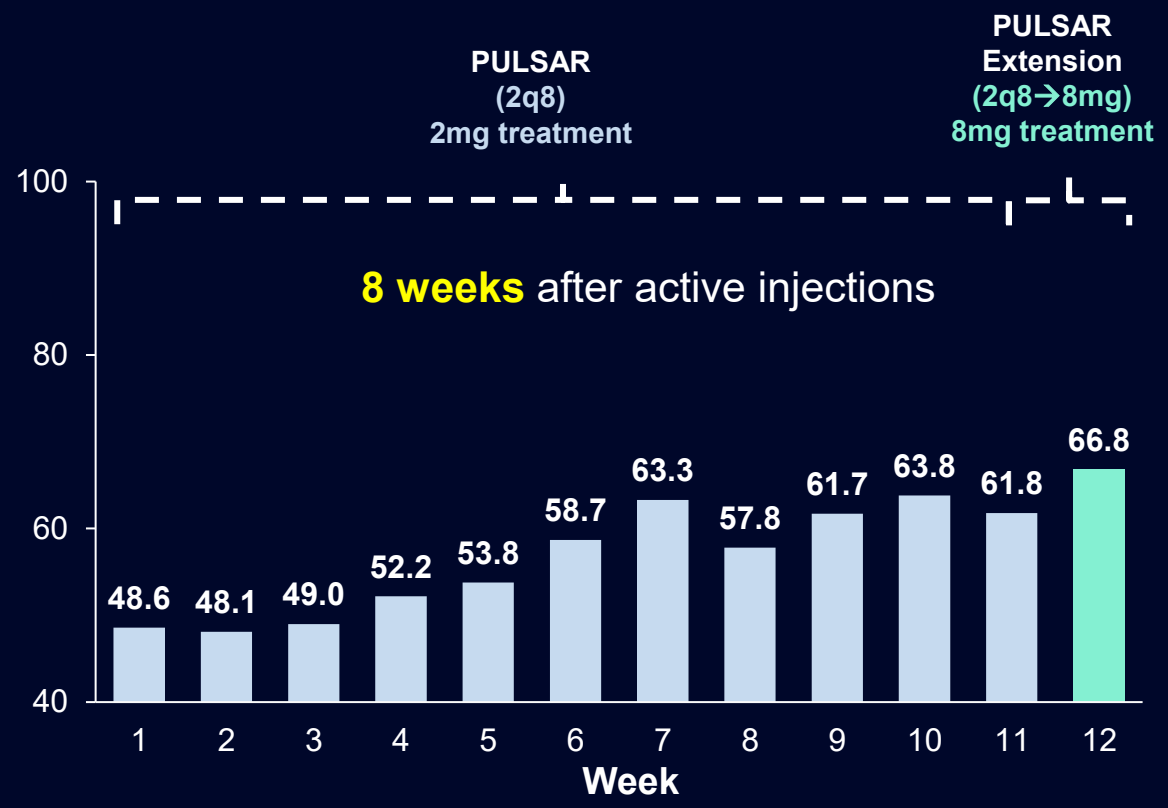
eFAS (LOCF). Fluid resolution defined as no IRF and no SRF in central subfield. Fluid status was evaluated pre-injection. eFAS (LOCF). [a]eSAF (156-week completers; 2q8→8mg, n=186; 8q12, n=185; 8q16, n=190; 8mg, n=375). **LOCF**, last observation carried forward.

# 2q8→8mg Group: Patients with Fluid Resolution 4 and 8 Weeks After Active Injections

pulsar nAMD Extension

| Aflibercept 2q8 dosing regimen through Week 96 of PULSAR | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day 1 | W4 | W8 | W12 | W16 | W20 | W24 | W28 | W32 | W36 | W40 | W44 | W48 | W52 | W56 | W60 | W64 | W68 | W72 | W76 | W80 | W84 | W88 | W92 | W96 |
| X | X | X | | X | o | X | o | X | o | X | o | X | o | X | o | X | o | X | o | X | o | X | o | X |



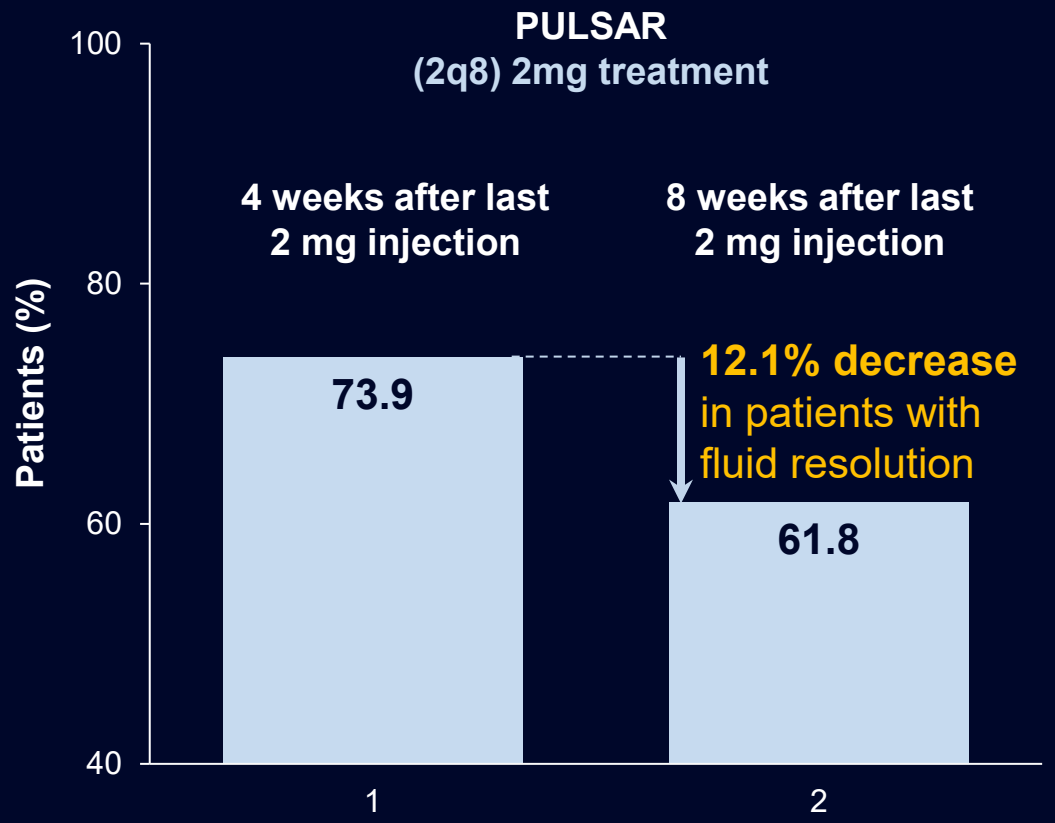




Stippled boxes = initial treatment phase; X = active injection; o = sham injections.
eFAS (LOCF). Patients entering the PULSAR extension: 2q8→8mg group (n=208). Presence of fluid was evaluated prior to active injection administration. Aflibercept 2 mg injections were given at Week 0, 4 and 8, and then 8-weekly from Week 16 to Week 88. The first aflibercept 8 mg injection was administered at Week 96.

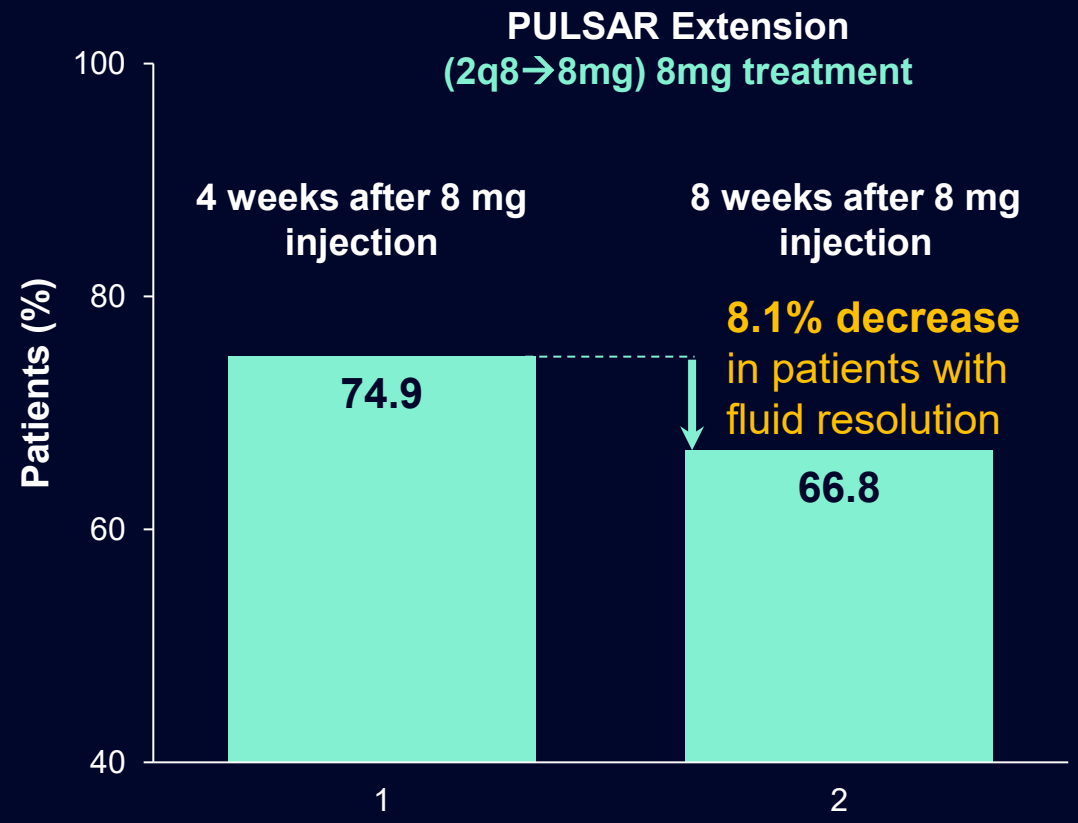
# 2q8→8mg Group: Proportion of Patients with Fluid Resolution 4 and 8 Weeks After Aflibercept 2 mg and 8 mg Injections

pulsar nAMD Extension

**Difference in proportion of patients with fluid resolution 4 and 8 weeks after the last 2 mg injection**




**Difference in proportion of patients with fluid resolution 4 and 8 weeks after the first 8 mg injection**



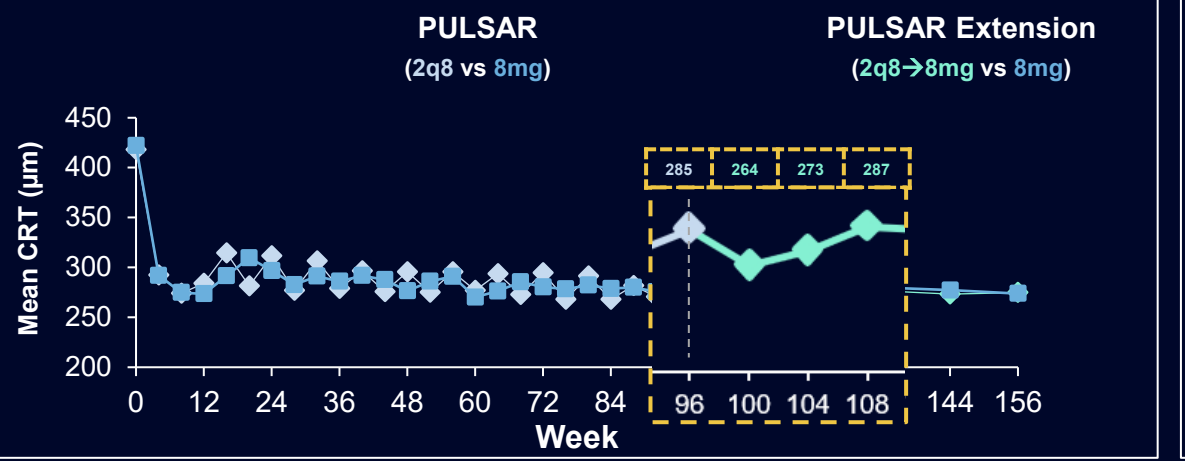

eFAS (LOCF). Patients entering the PULSAR extension: 2q8→8mg group (n=208).

# Conclusions

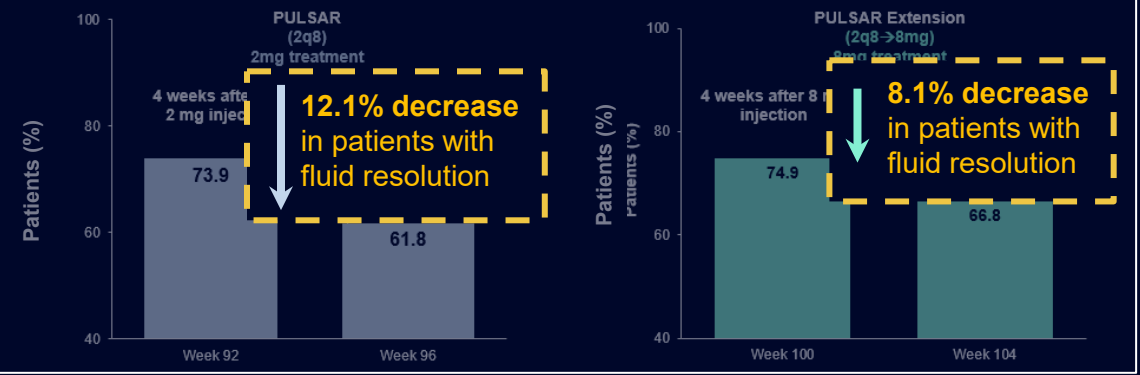
pulsar nAMD Extension

- In the PULSAR Extension, functional and anatomic improvements were sustained through Week 156 in the **2q8→8mg** and **8mg groups**
- At Week 156, the proportion of patients with fluid resolution was **comparable in the 2q8→8mg and 8mg groups**, with extended dosing intervals from Week 96 to Week 156 in the 2q8→8mg group following the switch to aflibercept 8 mg
- Findings from the 8mg group suggest that patients with treatment-naïve nAMD can achieve **durable improvements in fluid resolution with aflibercept 8 mg** administered over extended dosing intervals
- In the **2q8→8mg group**, the proportion of patients with fluid resolution was sustained from Week 96 to Week 156 following the switch to aflibercept 8 mg
  - A **lower proportion** of patients had **fluid re-accumulation** between 4 and 8 weeks **after the first 8 mg injection** in the PULSAR extension than between 4 and 8 weeks after the last 2 mg injection in PULSAR

**Mean CRT Through Week 156[a]**




**2q8→8mg Group: Difference in Proportion of Patients with Fluid Resolution 4 and 8 Weeks After Active Injections[b]**




[a]eFAS (observed cases).[b]eFAS (LOCF).