Apellis

Apellis Company Presentation

March 2019

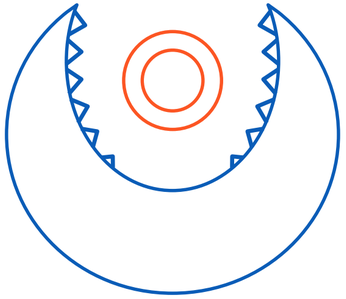
Forward looking statements

Statements in this presentation about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements” within the meaning of The Private Securities Litigation Reform Act of 1995. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether Apellis will be able to enroll patients rapidly enough to meet the projected timelines; whether the manufacturing process used for APL-2 will provide the anticipated improvements and be scalable for global commercialization; whether preliminary or interim results from a clinical trial will be predictive of the final results of the trial; whether results obtained in preclinical studies and clinical trials will be indicative of results that will be generated in future clinical trials; whether APL-2 will successfully advance through the clinical trial process on a timely basis, or at all; whether the results of such clinical trials will warrant regulatory submissions and whether APL-2 will receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies for GA, PNH or any other indication; whether, if Apellis’ products receive approval, they will be successfully distributed and marketed; and other factors discussed in the “Risk Factors” section of Apellis’ Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 26, 2019 and the risks described in other filings that Apellis may make with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Apellis specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

BOLDLY DELIVERING REVOLUTIONARY THERAPIES

for people living with serious diseases by harnessing the foundational part of the immune system, known as complement

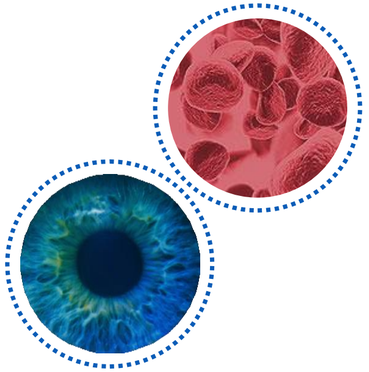
What we do



Pioneers in innate immunity & complement immunology

By regulating its core component C3

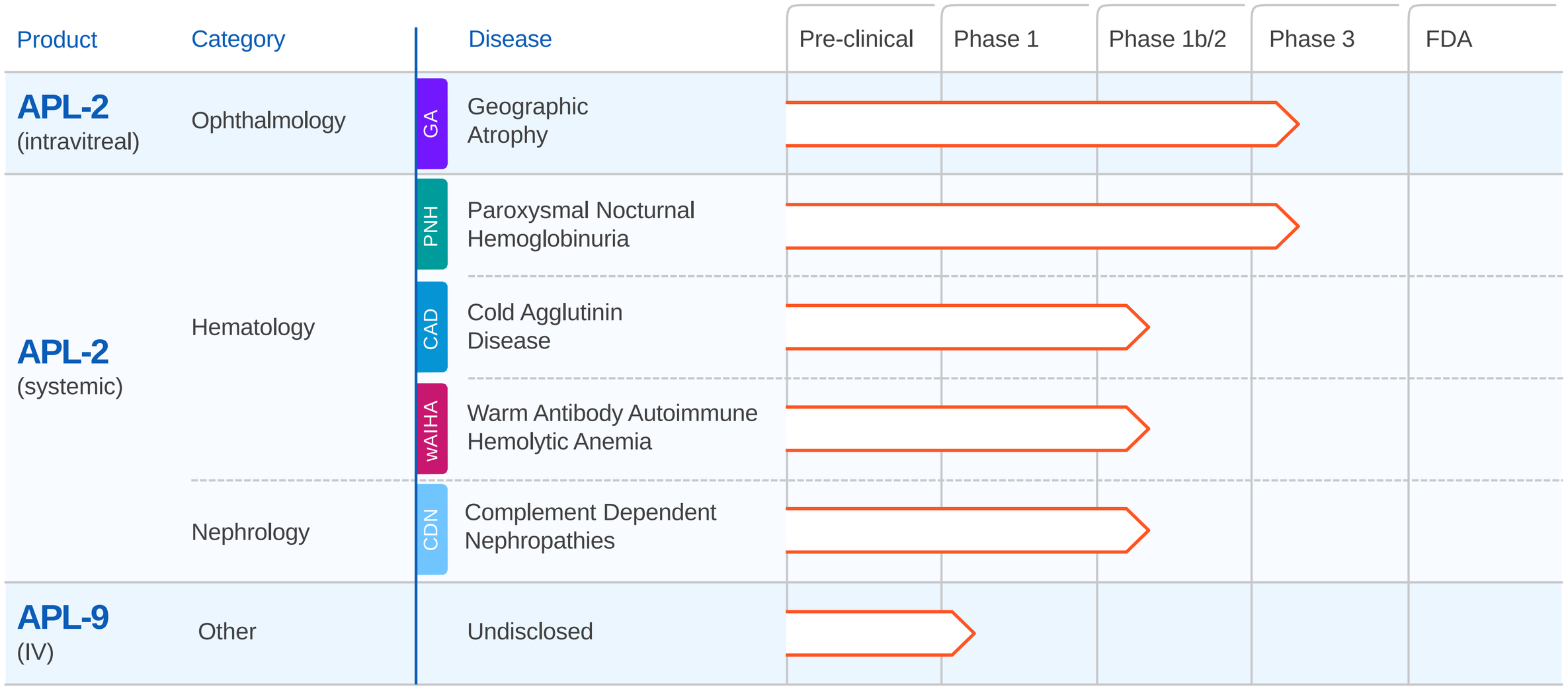
Value & patient outcomes at the center of our programs



Focused on AMD, PNH, CAD and wAIHA

Broad potential in other immune conditions

Pipeline

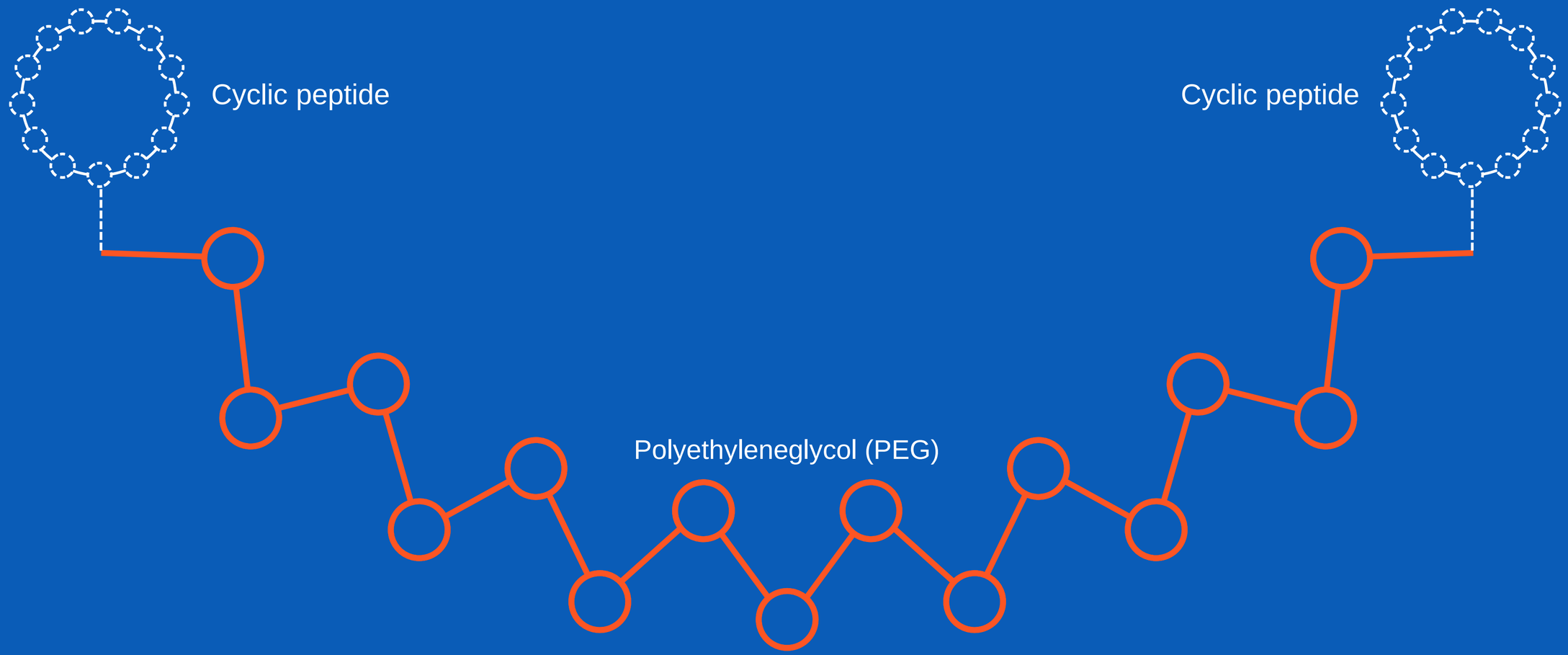

Product
Category
Disease
Pre-clinical
Phase 1
Phase 1b/2
Phase 3
FDA
APL-2
(intravitreal)
Ophthalmology
GA
Geographic Atrophy
APL-2
(systemic)
Hematology
PNH
Paroxysmal Nocturnal Hemoglobinuria
CAD
Cold Agglutinin Disease
wAIHA
Warm Antibody Autoimmune Hemolytic Anemia
Nephrology
CDN
Complement Dependent Nephropathies
APL-9
(IV)
Other
Undisclosed

Apellis

VISION 2020

- Prepare for potential commercial launch of APL-2 in PNH
- Fully enroll GA Phase 3 Program
- Continue clinical development in CAD or wAIHA or both
- PoC in new indications
- 2x global employee footprint

Apellis lead molecule: APL-2



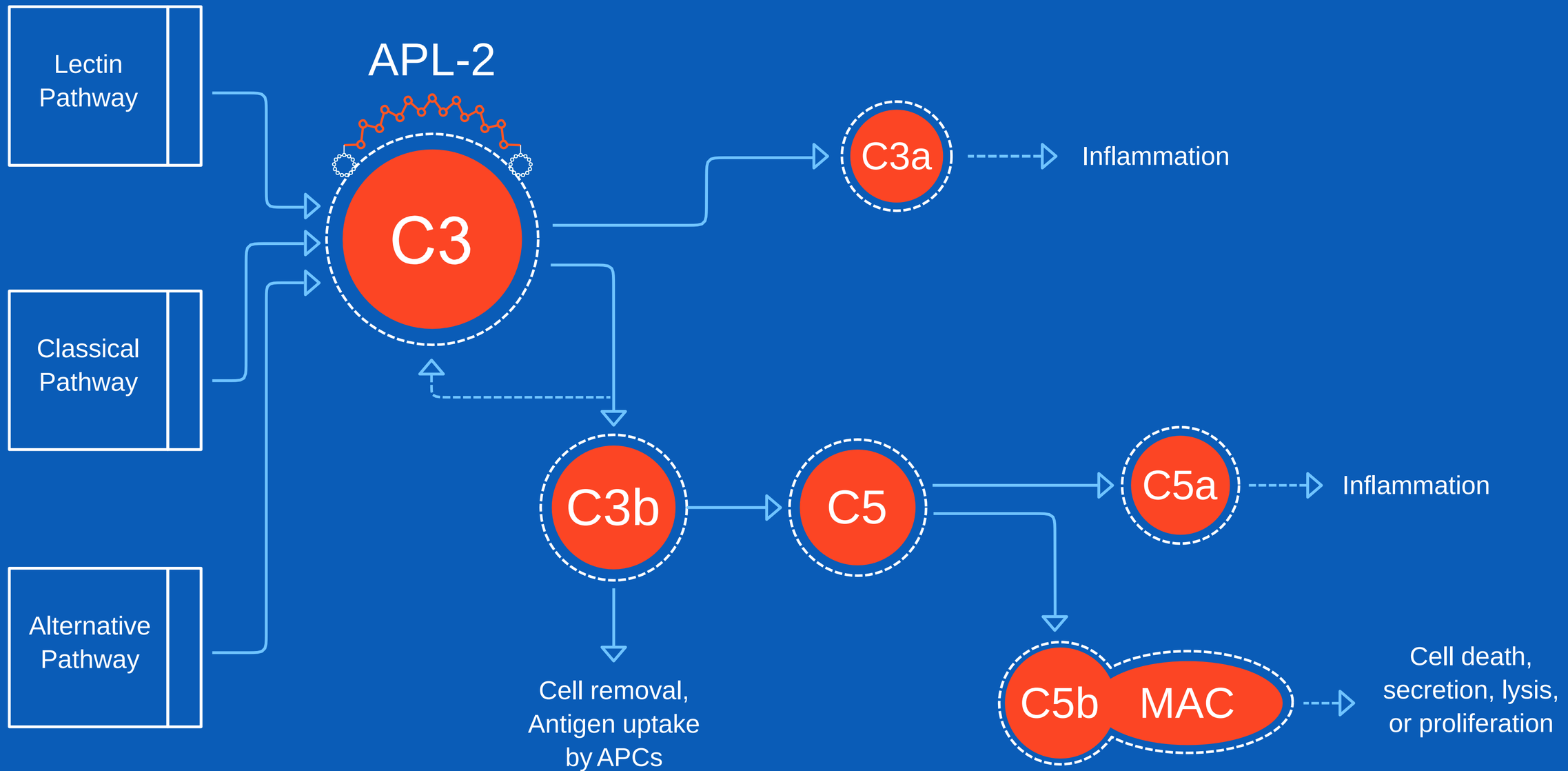
Peptides of the APL-2 family bind to a pocket of C3 and inhibit activation*

Subcutaneous or intravitreal injections

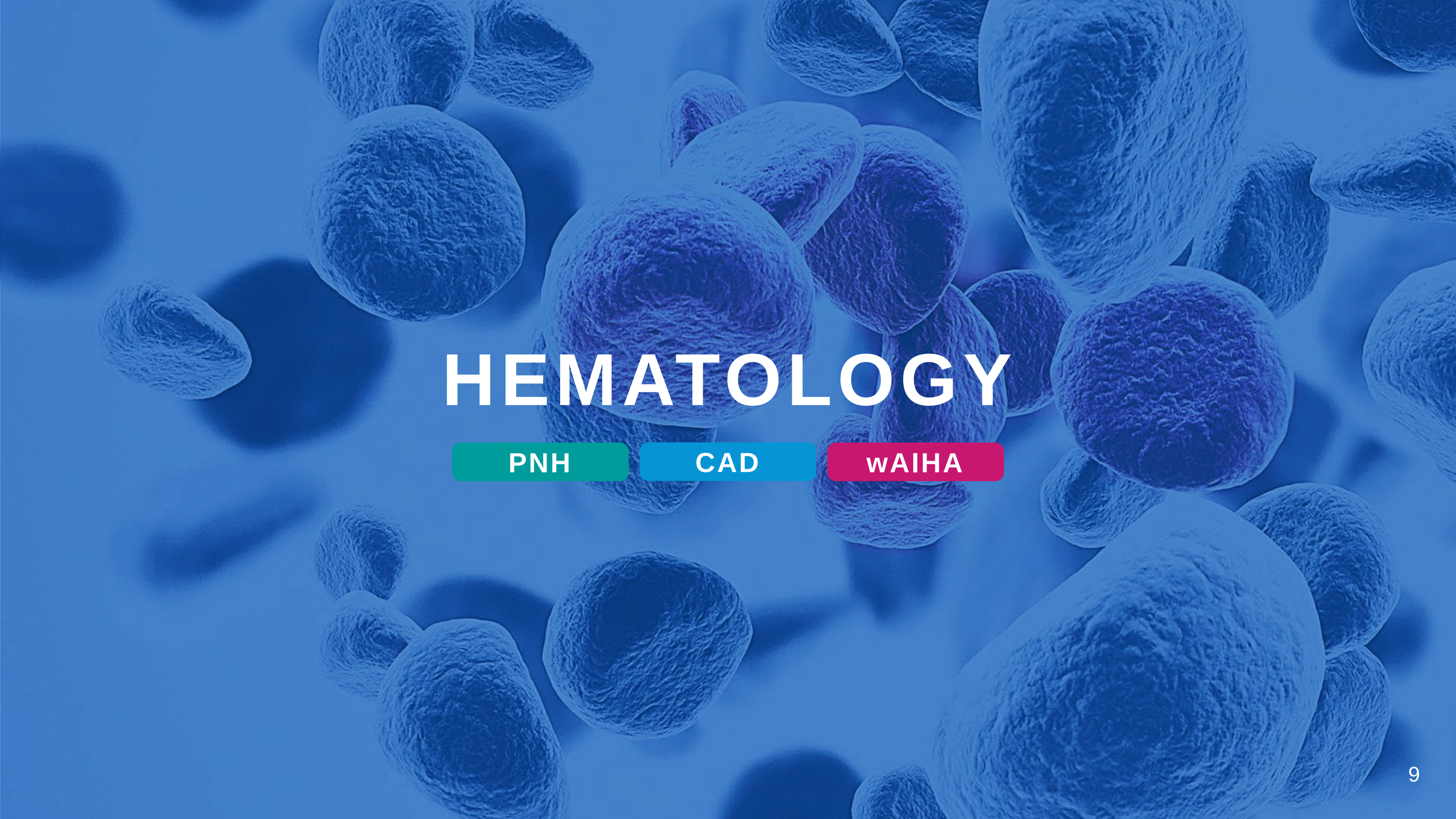
* Janssen, J. Biol. Chem., 282(40), 29241-29247, 2007

Apellis

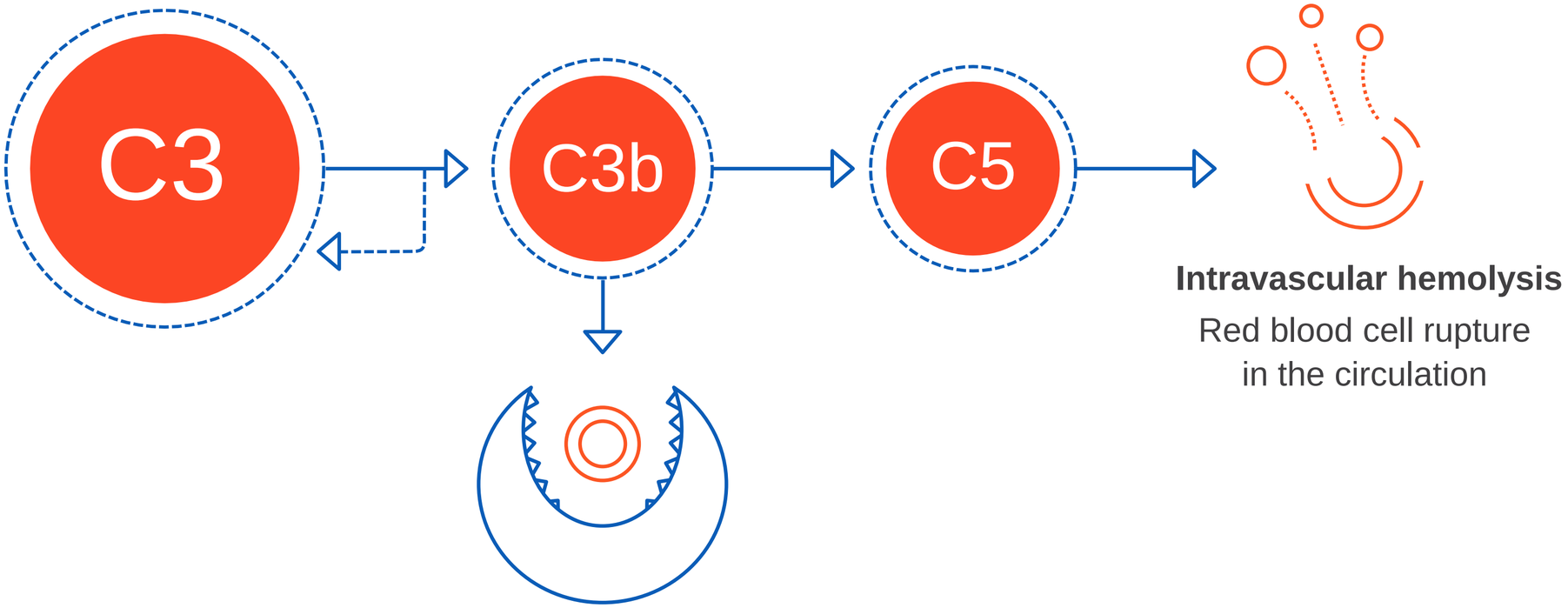
Central inhibition of complement



Apellis


HEMATOLOGY
PNH
CAD
wAIHA

Paroxysmal Nocturnal Hemoglobinuria (PNH) is characterized by intravascular & extravascular hemolysis



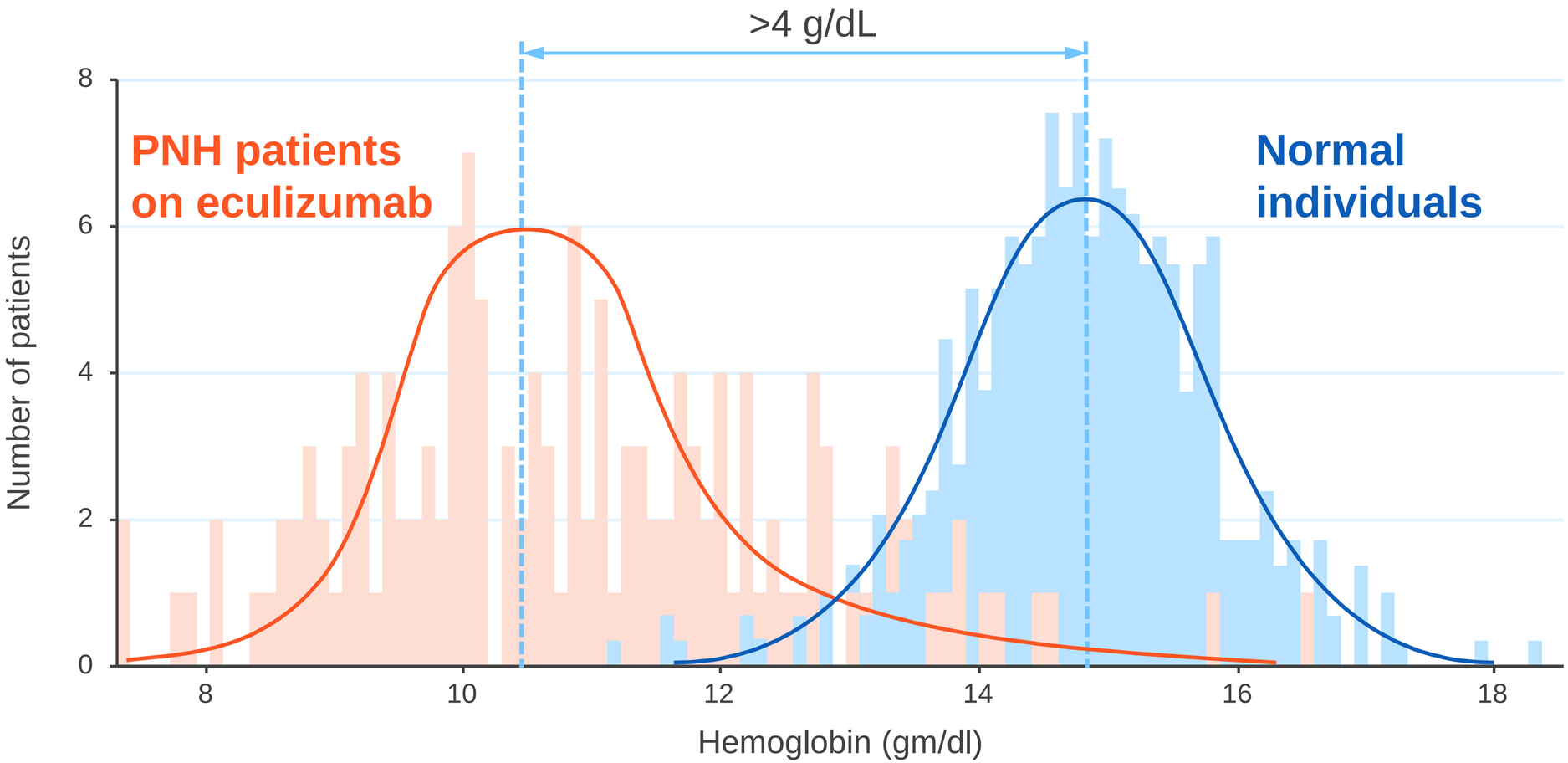
Intravascular hemolysis

Red blood cell rupture in the circulation

Extravascular hemolysis

Red blood cell destruction by macrophages in spleen and liver

Hemoglobin levels in patients with PNH receiving eculizumab (n=141; all hemolytic)



PNH

Apellis

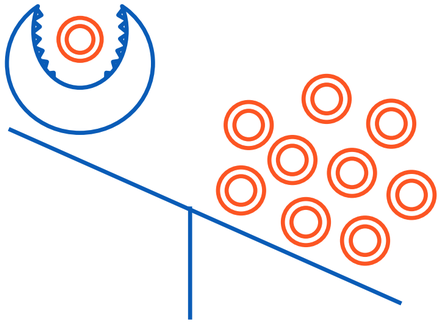
McKinley CE, Richards SJ, Munir T, Griffin M, Mitchell LD, Arnold L, Riley K, Copeland N, Newton DJ, Hill A, Hillmen P. Extravascular hemolysis due to C3-loading in patients with PNH treated with eculizumab: defining the clinical syndrome. Blood. 2017:130:3471.

Only 30% of patients on Soliris® have bone marrow function strong enough to keep patients from experiencing anemia and/or transfusion

PNH

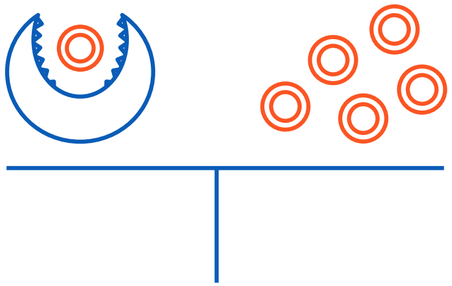
30% Soliris® patients

70% Soliris® patients unmet need



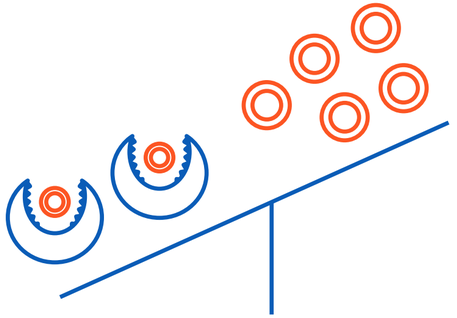
~30% of Patients

- Transfusion -
- Hb >12



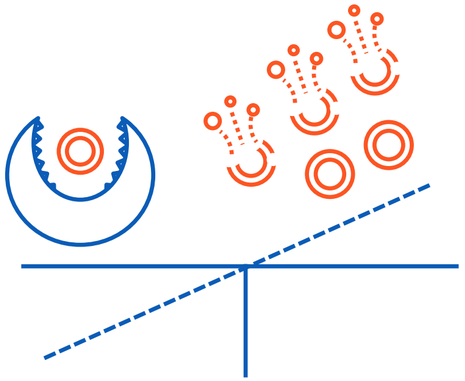
~40% of Patients

- Transfusion -
- Hb <12



~20% of Patients

- Transfusion ++
- Hb <10



~10% of Patients

- Breakthrough ++
- Hb = any

Apellis

McKinley CE, Richards SJ, Munir T, Griffin M, Mitchell LD, Arnold L, Riley K, Copeland N, Newton DJ, Hill A, Hillmen P. Extravascular hemolysis due to C3-loading in patients with PNH treated with eculizumab: defining the clinical syndrome. Blood. 2017:130:3471.;
https://news.alexion.com/press-release/product-news/alexion-announces-positive-top-line-results-showing-successful-phase-3-cl

What is the unmet need on Soliris®?

PNH

RESULTS

72%

of patients remain anemic on Soliris

36%

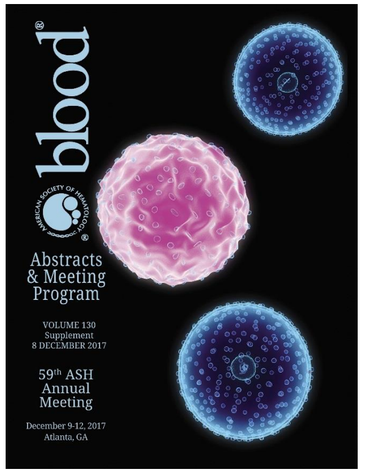
of patients had ≥ 1 transfusion in the prior year

1.9x ULN

Average Reticulocytes

Study of 141 patients by Hillmen et. al

- Excluded patients with aplastic anemia & bone marrow failure
- Included 21% on higher than label eculizumab dose



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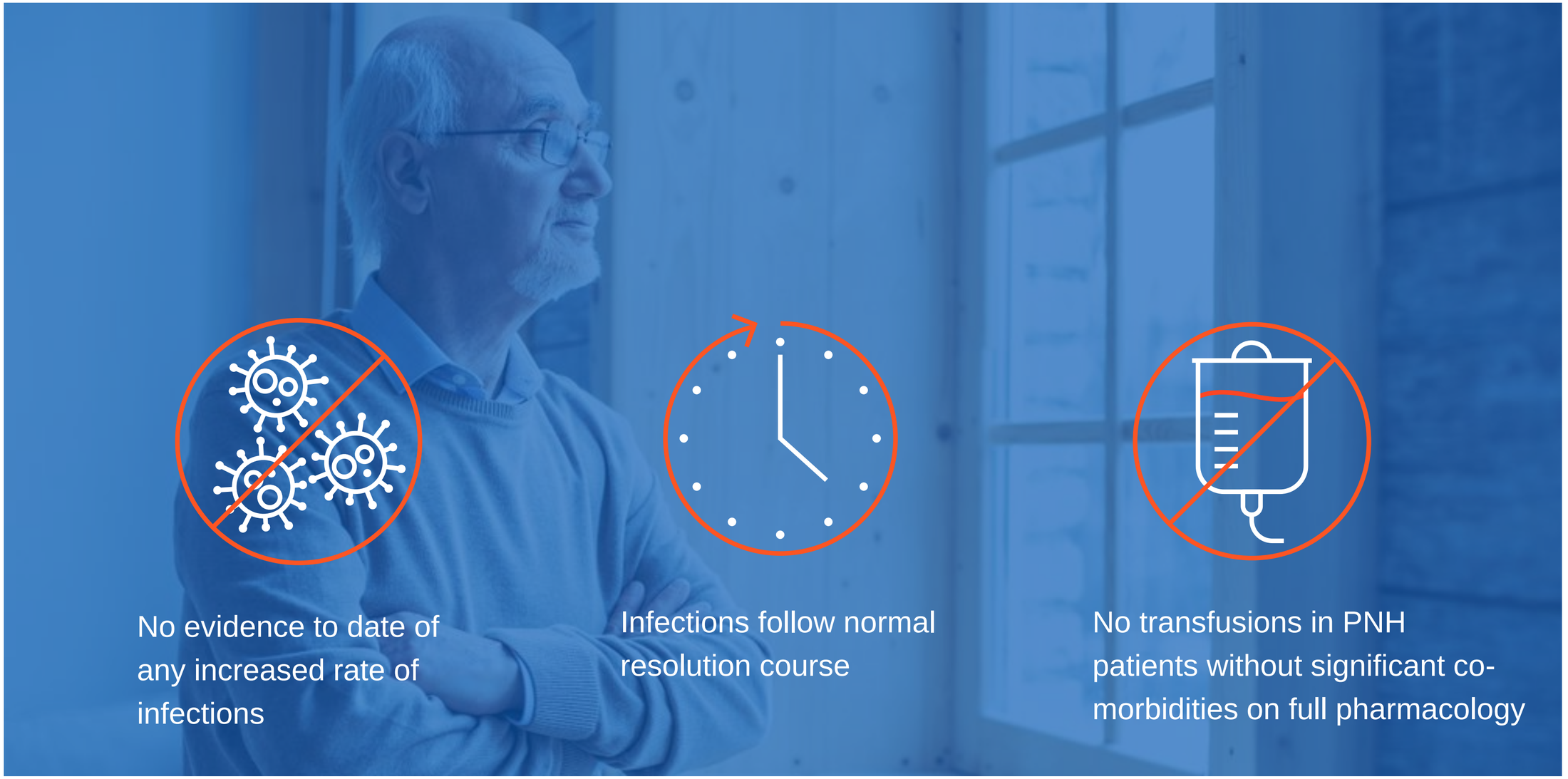
APL-2 safety

PNH



No evidence to date of any increased rate of infections

Infections follow normal resolution course

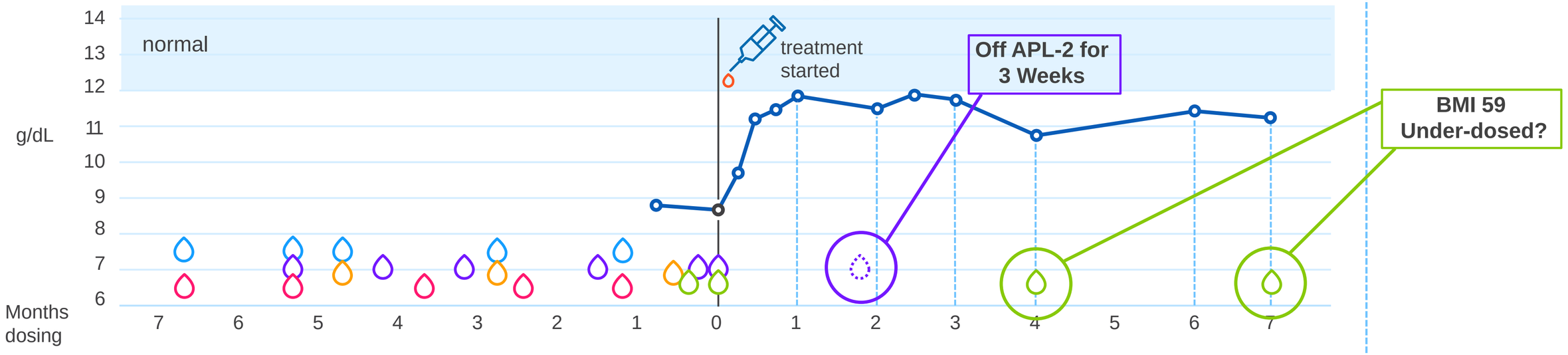
No transfusions in PNH patients without significant co-morbidities on full pharmacology

Excludes one patient with bone marrow failure

PHAROAH: APL-2 shows potential to improve eculizumab outcomes as add-on therapy in PNH – 270 mg/day, N=6

PNH

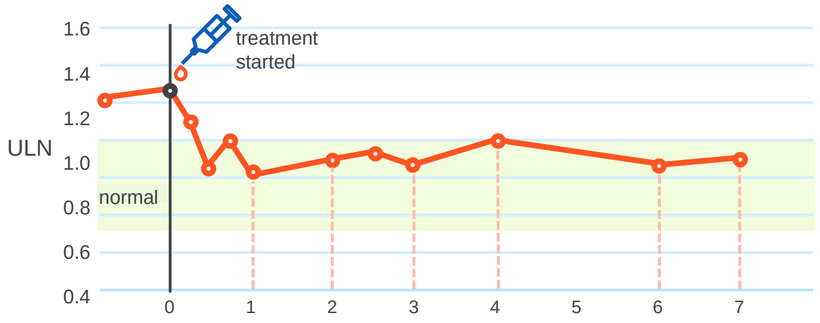
Mean Hemoglobin



Patient transfusions

Patient 1
Patient 2
Patient 3
Patient 4
Patient 5
Patient 6

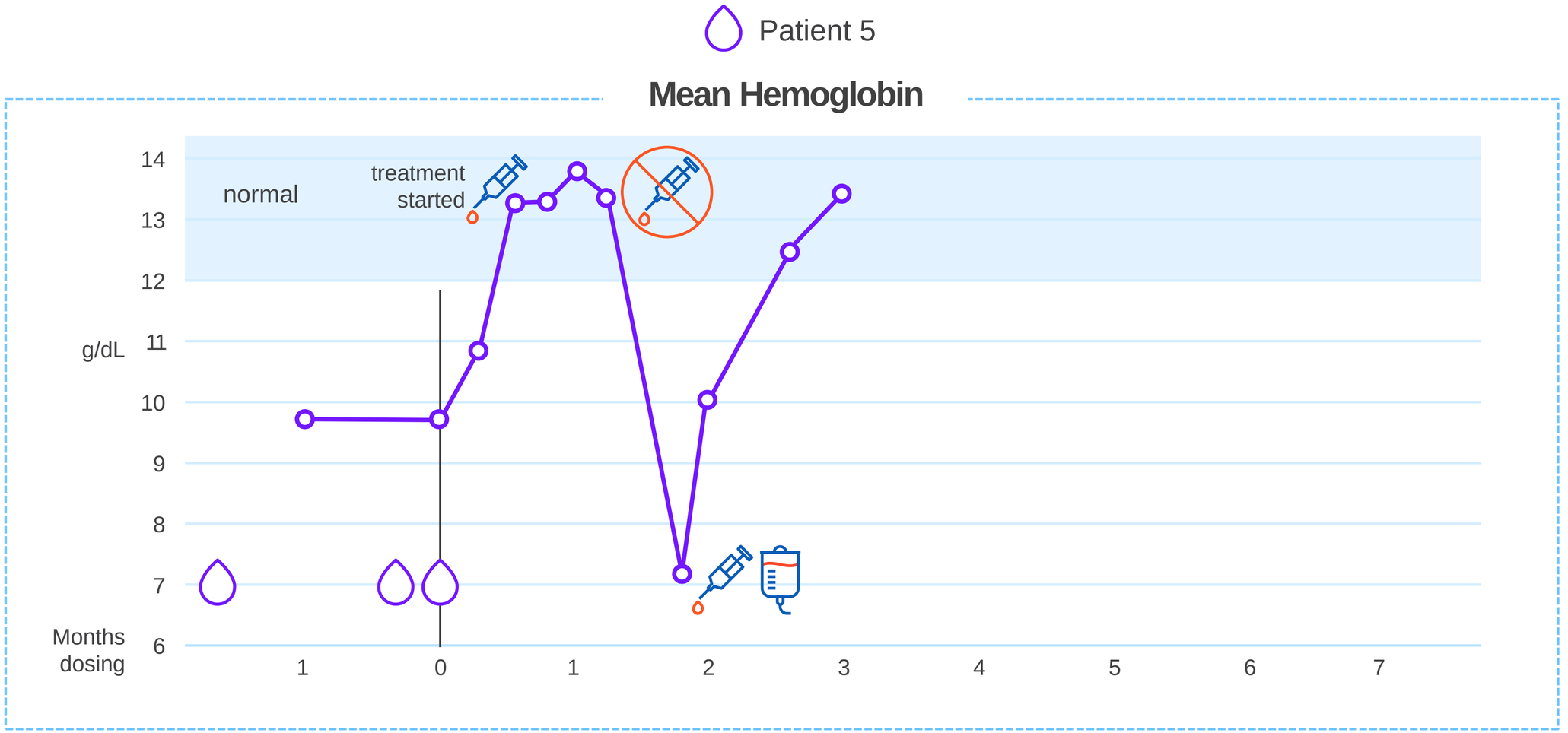
Mean LDH



Interim data as reported Sept 4, 2018

Apellis

PHAROAH: APL-2 shows potential to improve eculizumab outcomes as add-on therapy in PNH – 270 mg/day, N=6

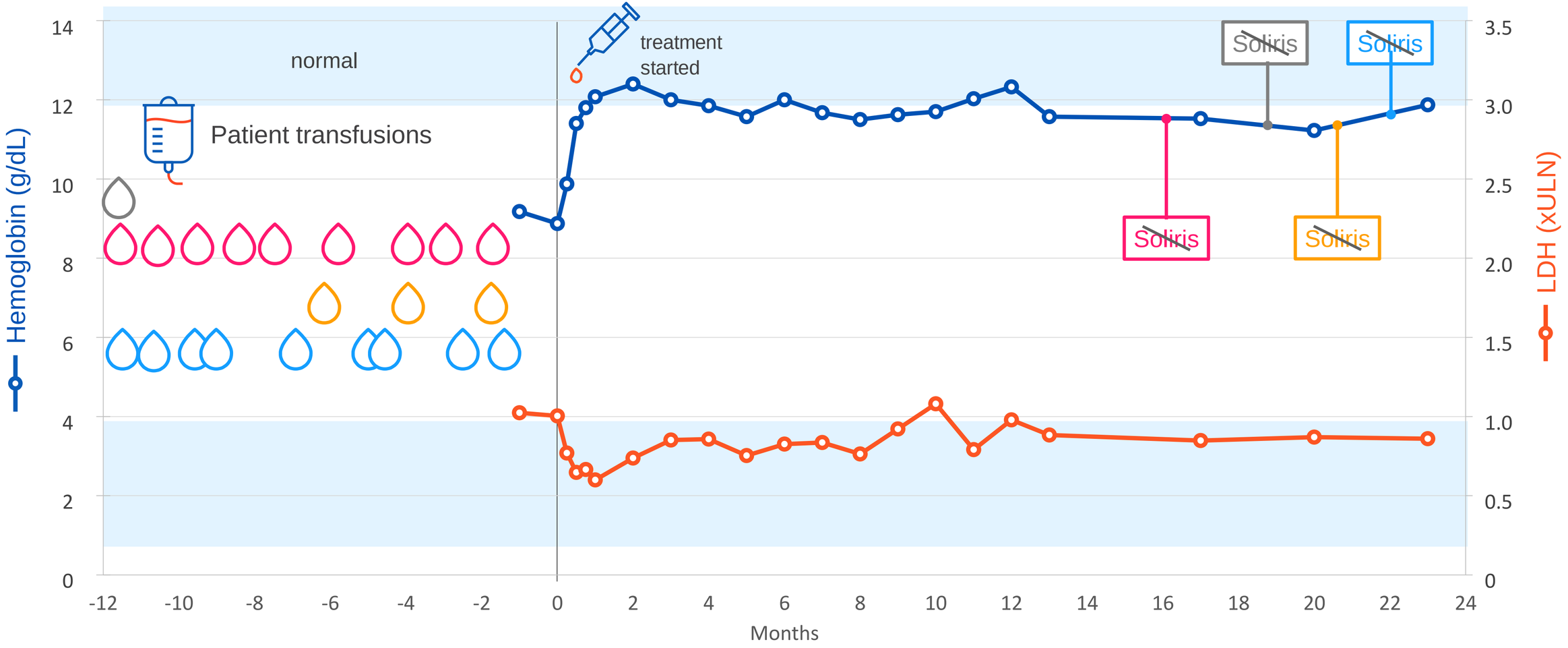


PNH

Interim data as reported Sept 4, 2018

PHAROAH: APL-2 add-on to Soliris® - all four patients successfully transitioned to APL-2 monotherapy

PNH



Interim data as reported Sept 4, 2018

PHAROAH: APL-2 add-on to Soliris® - all four patients successfully transitioned to APL-2 monotherapy

PNH

	Eculizumab Monotherapy[i]	APL-2 + Eculizumab[ii]	APL-2 Monotherapy[iii]
Hemoglobin (g/dL) *	8.9	11.9	11.4
Annual Transfusions (avg.)	6.0	0	0
LDH (ULN) *	1.0x	0.8x	0.9x
Reticulocytes (ULN)*	2.7x	1.2x	0.8x
Patient Years (Total)	NA	5.9 Years	1.9 Years
Multiple of Eculizumab Label Dose (900mg x 2wk.)	1.6x	1.0x	-

*Average last available reading for all four patients on each dosing regimen

(i) last reading during eculizumab monotherapy prior to co-treatment with APL-2

(ii) last reading during co-treatment and prior to APL-2 monotherapy

(iii) last reading while on APL-2 monotherapy

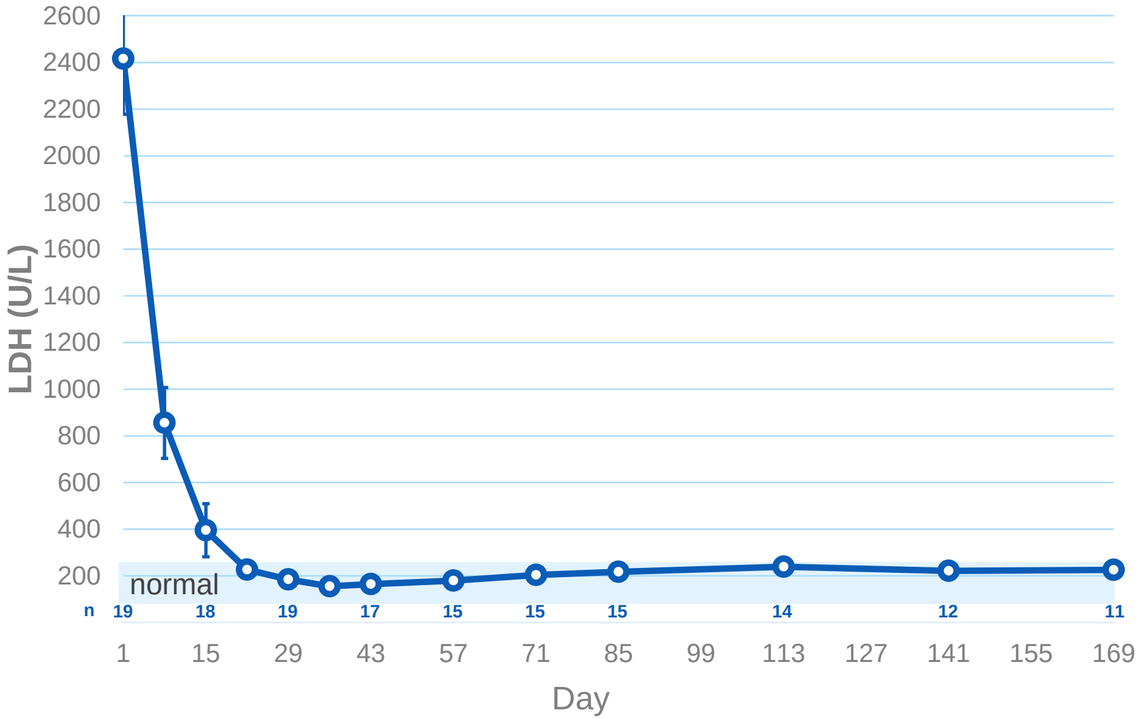
Apellis

Interim data as reported Sept 4, 2018

PADDOCK (interim): APL-2 shows potential to reach normal LDH levels as monotherapy in treatment in naïve PNH patients – 270 mg/day

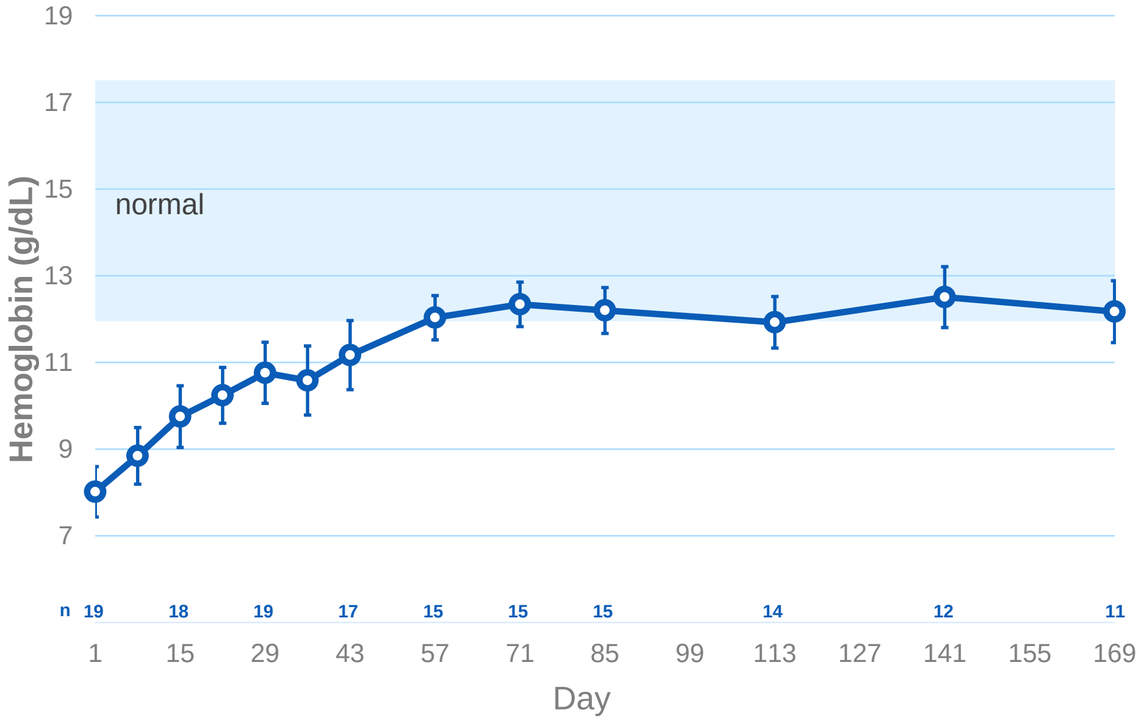
PNH

Decrease in LDH



- Reductions in LDH were rapid following initiation of APL-2 therapy, with 95% of subjects achieving an LDH in the normal range by day 29
- Reductions in LDH have been sustained and durable, with mean LDH maintained within the normal range at all timepoints beyond day 29

Increase in Hemoglobin



- All 19 subjects responded rapidly after initiating APL-2 therapy, and by day 29 mean baseline Hb increased from 8.0 g/dL to 10.8 g/dL
- Increases in Hb were sustained and durable as represented by a mean Hb of 12.2 g/dL at day 85

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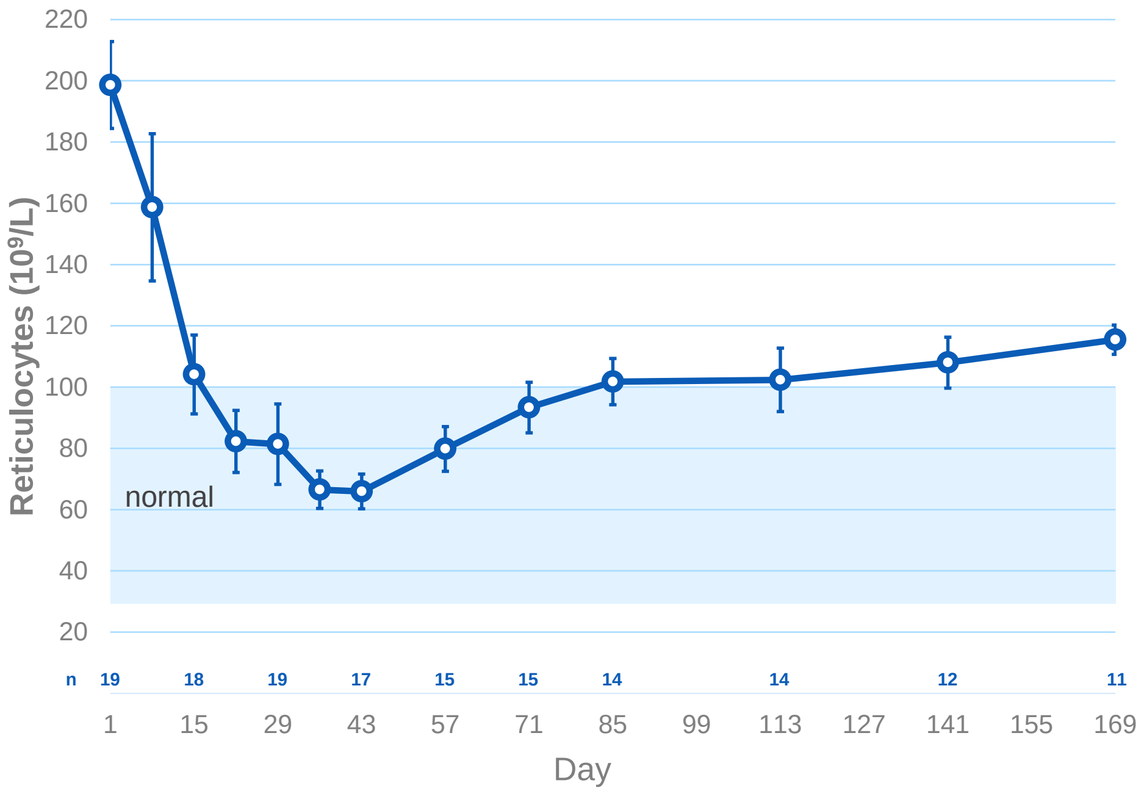
Interim data as reported Dec 2, 2018

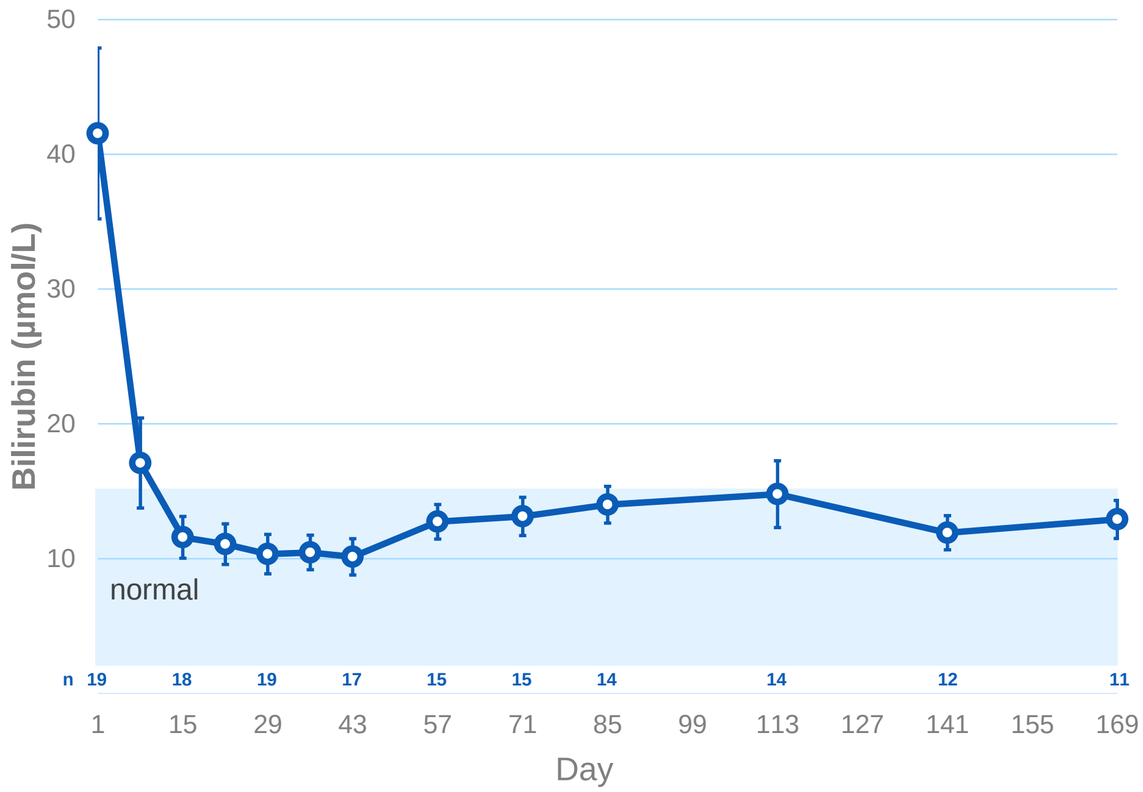
PADDOCK (interim): other measures of anemia meaningfully improved with APL-2 including reticulocytes and bilirubin

PNH

Decrease in Absolute Reticulocyte Count (ARC)



Decrease in Serum Total Bilirubin



Apellis

Interim data as reported Dec 2, 2018

PEGASUS – Phase 3 head to head vs. Soliris®

PNH

Eculizumab (n=70)
HgB <10.5g/dL
Transfusions +/-
Any Soliris Dose

1 Month
Run-in

4 Months
Randomized controlled period

Active group
n=70
APL-2
+
Eculizumab

Group 1
n=35
APL-2

Patient transfusions

Group 2
n=35
Eculizumab

Primary endpoint:
- 4 mo. Δ in HgB

Secondary endpoints:
- Transfusion avoidance
- Reticulocytes
- LDH
- FACIT

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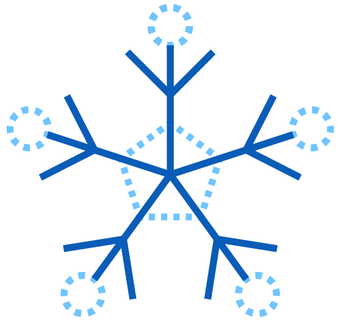
Autoimmune hemolytic anemia (AIHA) is a group of rare autoimmune disorders characterized by the premature hemolysis of red blood cells (RBCs) by autoantibodies

wAIHA

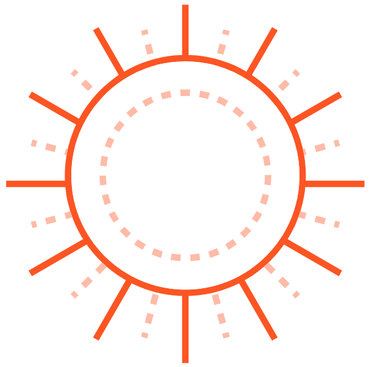
CAD

AIHA presents in two common forms



Cold Agglutinin Disease

Typically associated with IgM autoantibodies – 13-15% of cases



Warm Antibody AIHA

Typically associated with IgG autoantibodies - 60-70% of cases

Est. 40,000 AIHA patients worldwide

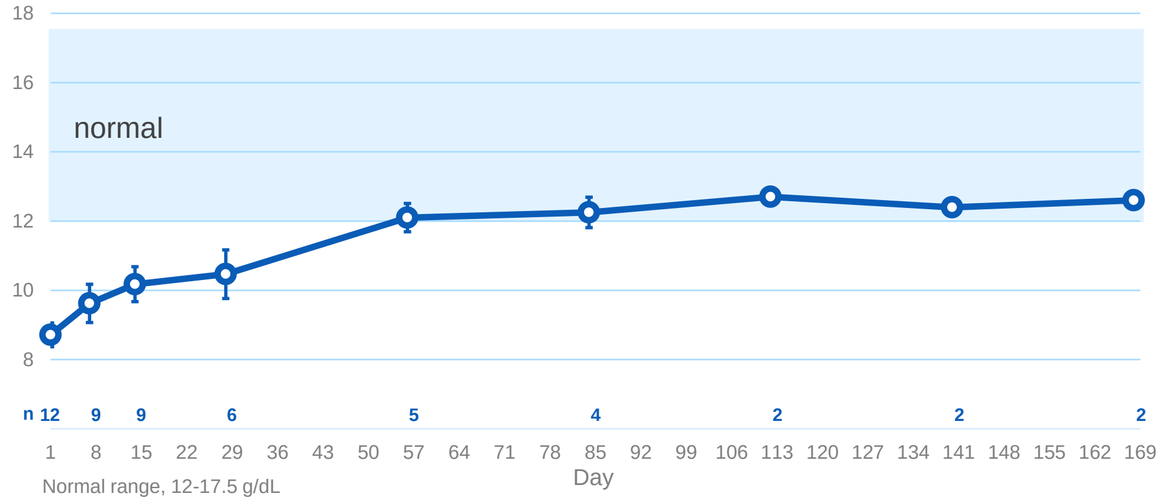
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=98375&lng=EN

Apellis

APL-2 in Cold Agglutinin Disease – preliminary data

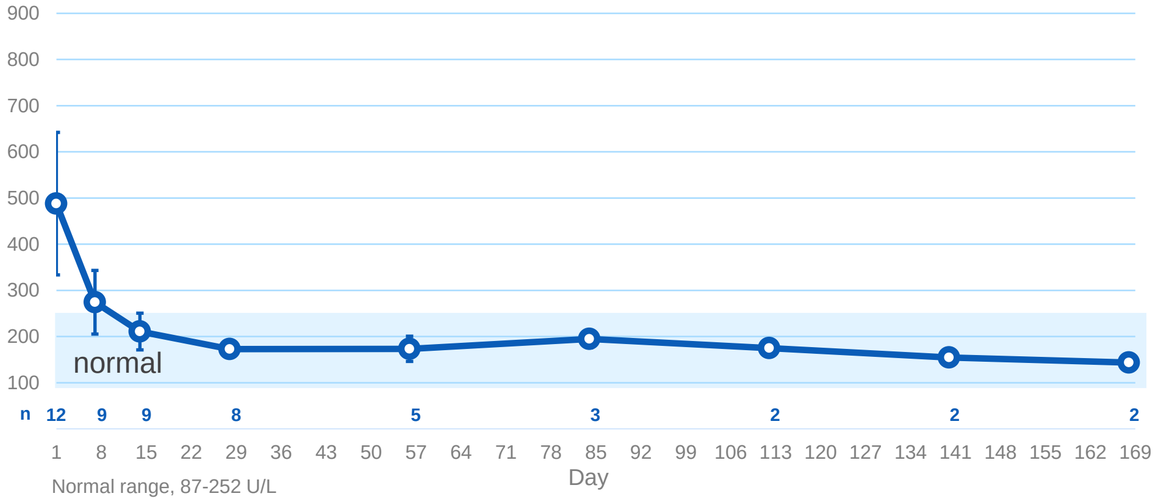
CAD

Hemoglobin (g/dL)



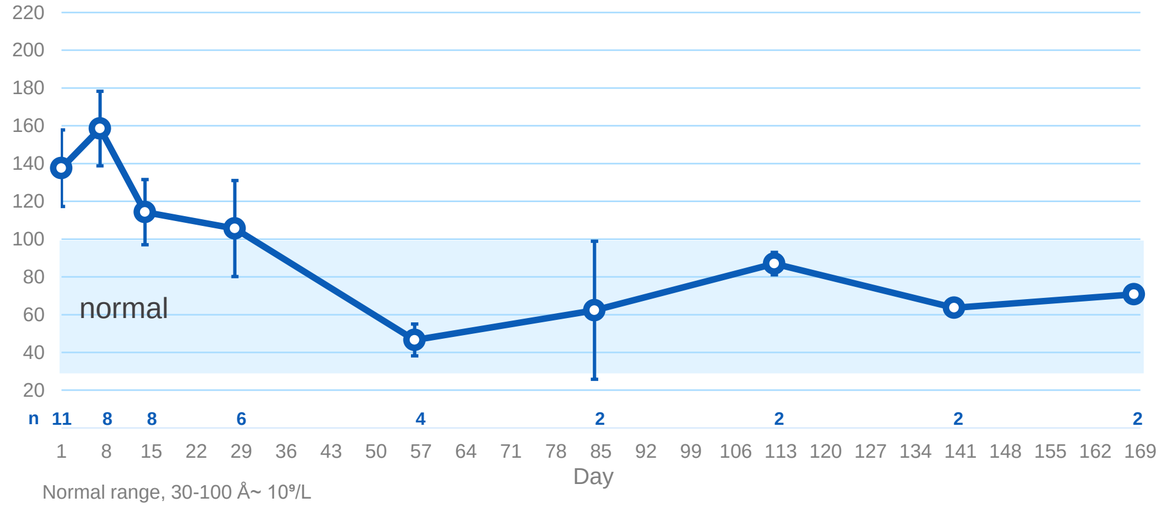
Normal range, 12-17.5 g/dL

LDH (U/L)



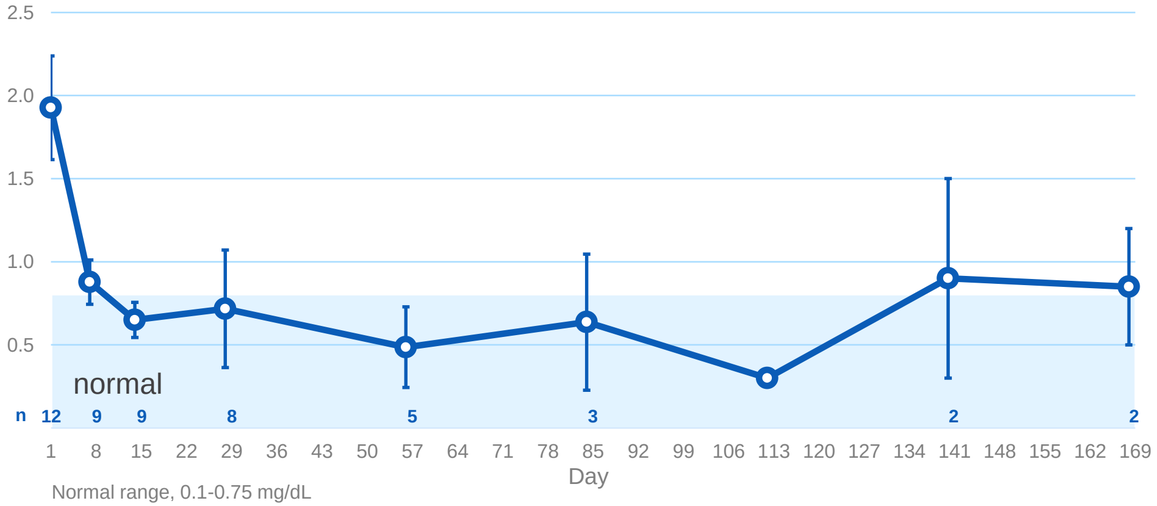
Normal range, 87-252 U/L

Reticulocytes (10^9/L)



Normal range, 30-100 Å~ 10^9/L

Indirect Bilirubin (mg/dL)



Normal range, 0.1-0.75 mg/dL

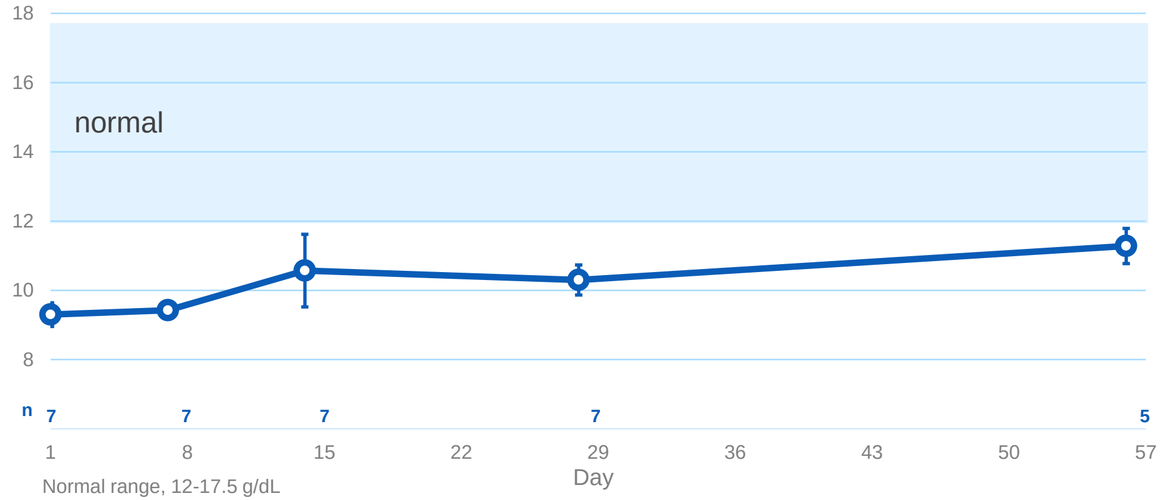
Apellis

Interim data as reported December 3, 2018

APL-2 in DAT C3+ Warm Antibody AIHA – preliminary data

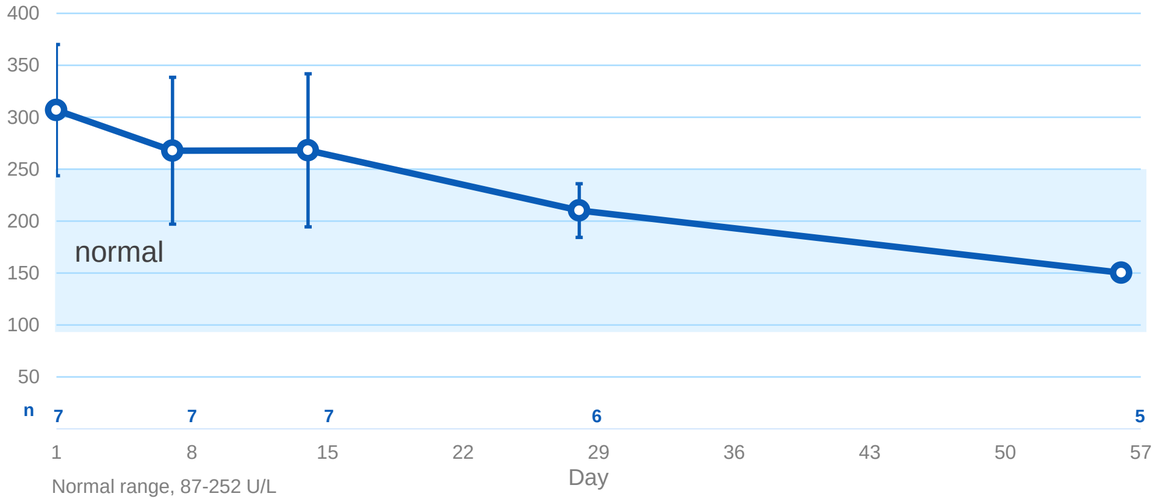
wAIHA

Hemoglobin (g/dL)



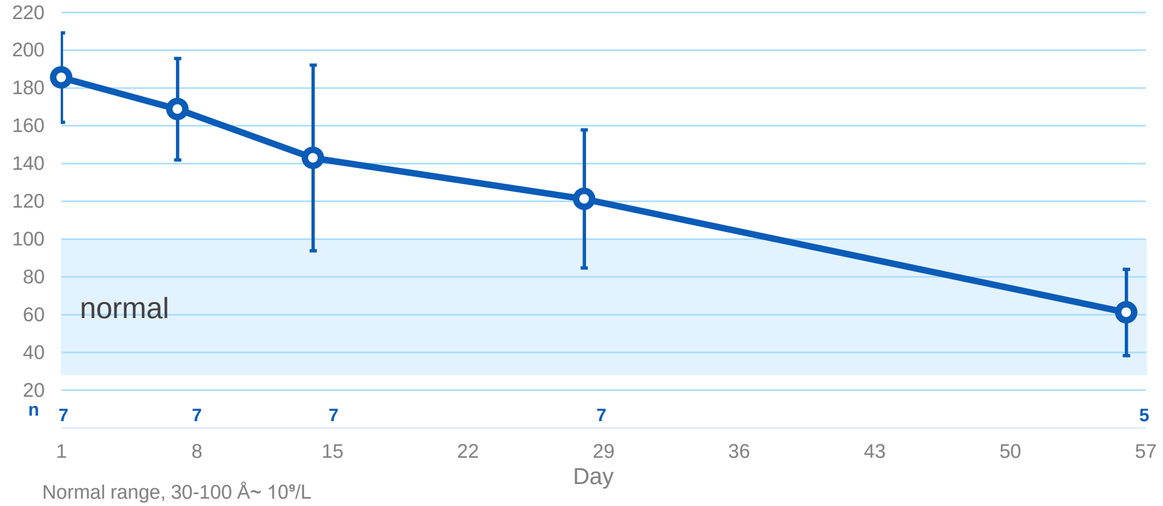
Normal range, 12-17.5 g/dL

LDH (U/L)



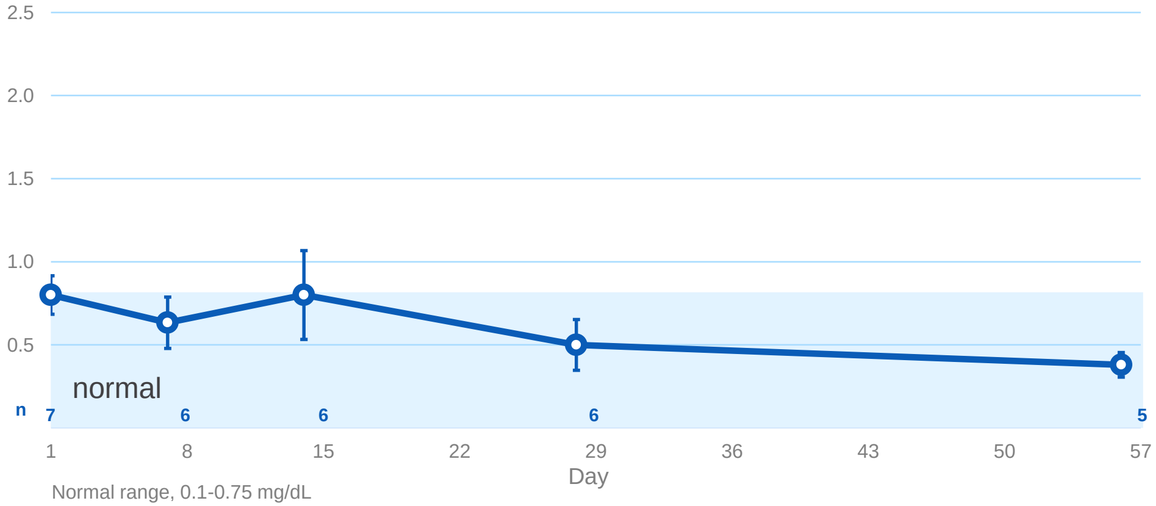
Normal range, 87-252 U/L

Reticulocytes (10^9/L)



Normal range, 30-100 Å~ 10^9/L

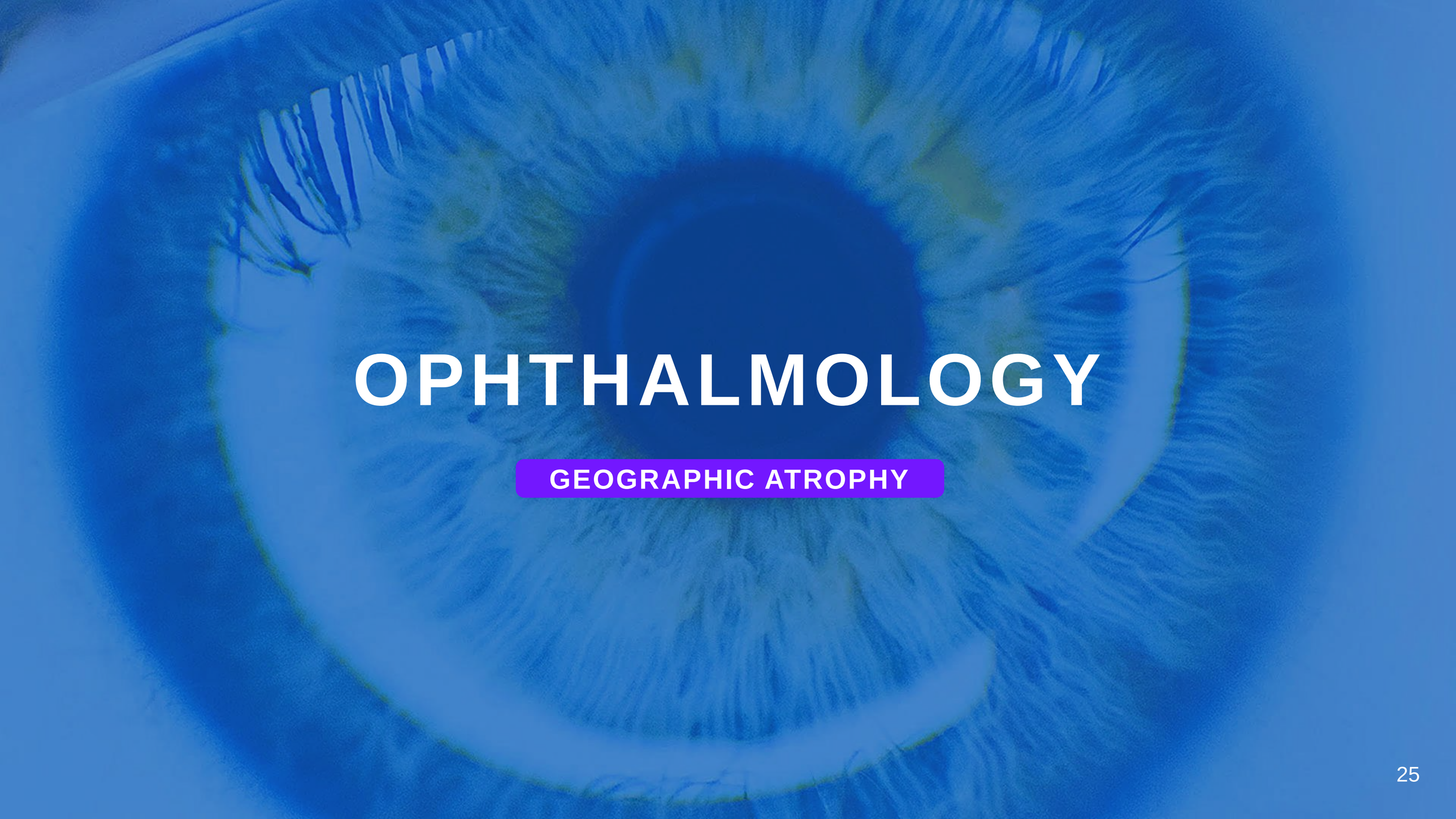
Indirect Bilirubin (mg/dL)



Normal range, 0.1-0.75 mg/dL

Apellis

Interim data as reported December 3, 2018



OPHTHALMOLOGY

GEOGRAPHIC ATROPHY

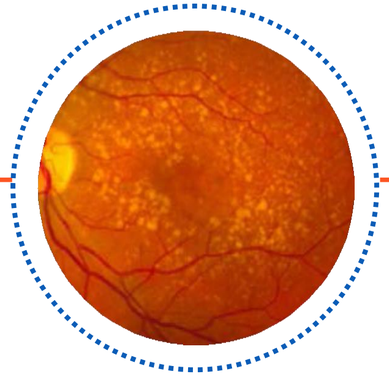
Geographic Atrophy Impacts

One Million People

in the U.S. Alone

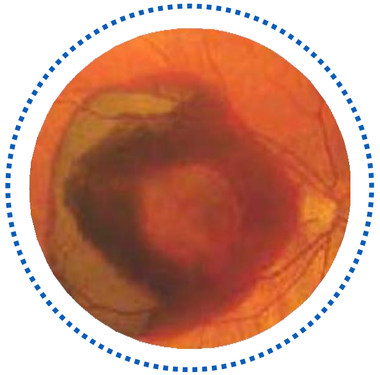
Geographic Atrophy - the leading cause of blindness

GA



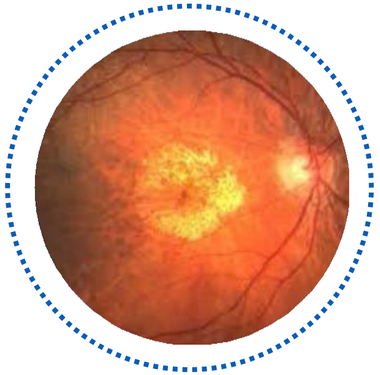
Intermediate AMD

Presence of drusen.
No serious vision loss.



Wet AMD

Rapid, serious vision loss if untreated.
First-line treatment with VEGF inhibitors.
Up to 98% of chronic anti-VEGF patients progress to GA.



Geographic Atrophy

Risk of blindness when central vision is affected. ~1M patients in US alone.
No approved therapies.

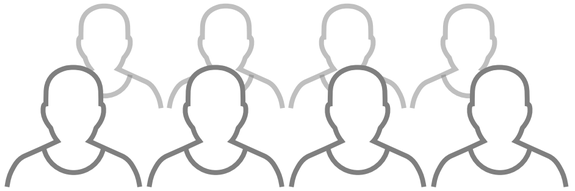
Apellis

Source: American Academy of Ophthalmology; The Lancet; Ophthalmology; L.E.K. interviews and analysis

FILLY - Phase 2 study of APL-2 in Geographic Atrophy

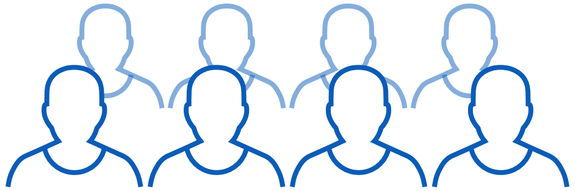
GA

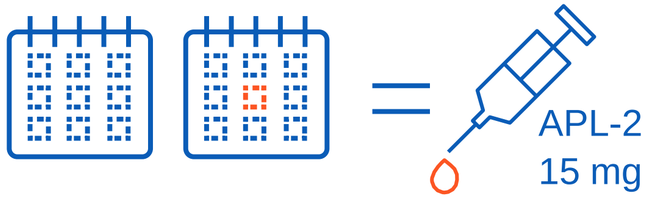
Sham group, n=81 (pooled)



Sham injections

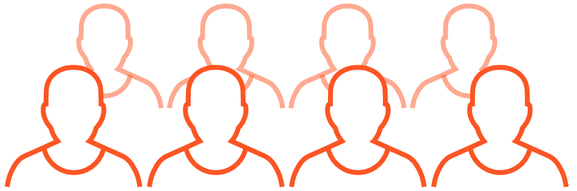
APL-2 EOM, n=79

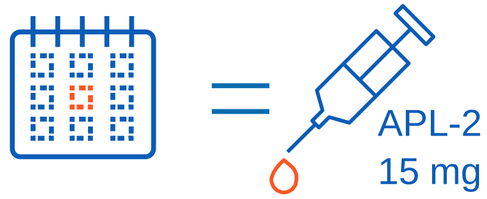




APL-2 injections every other month

APL-2 Monthly, n=86





APL-2 injections every month

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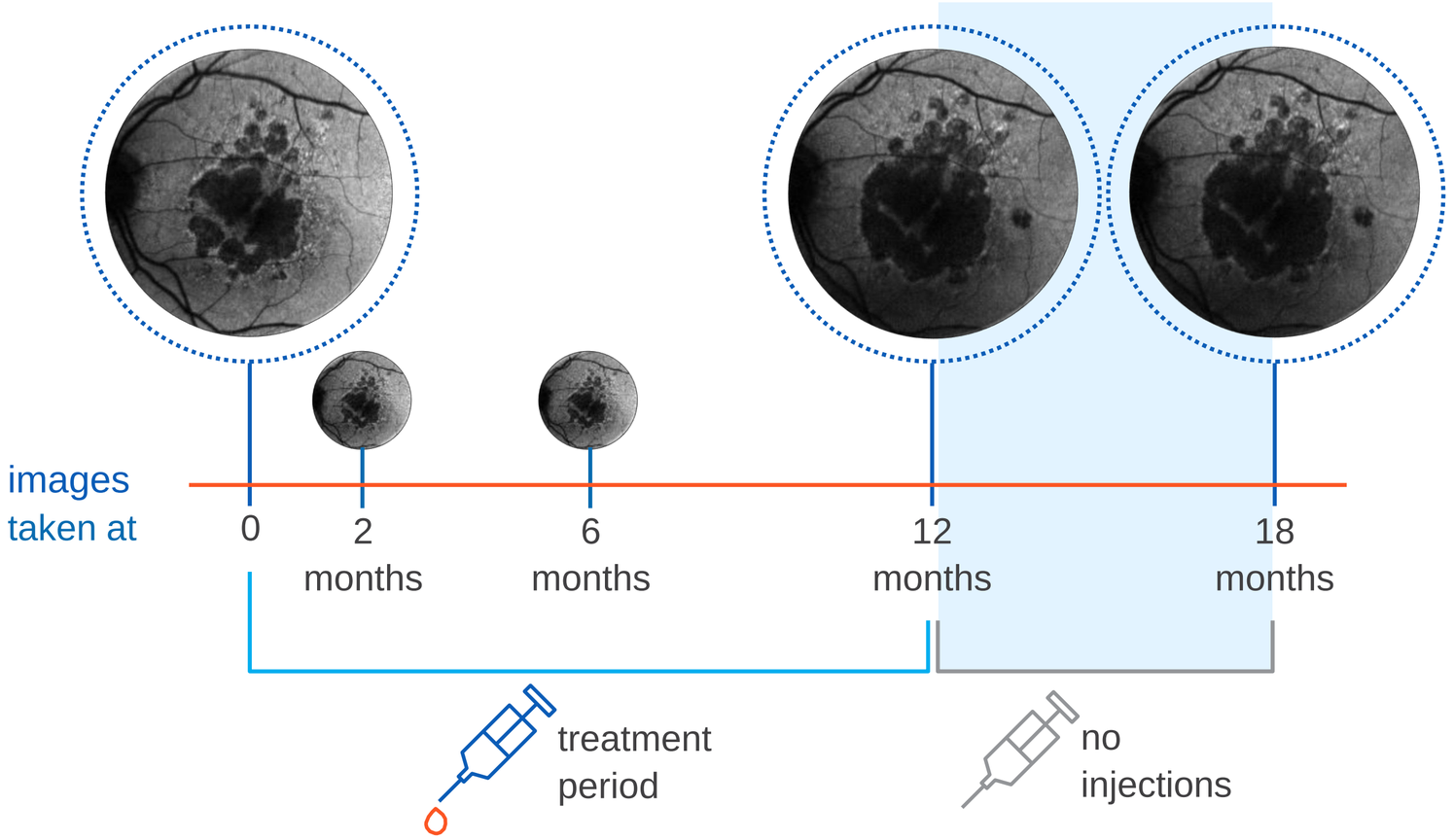
FILLY – timeline and endpoints

GA



Primary efficacy endpoint is the primary registration endpoint

Change in geographic atrophy (GA) lesion size from baseline to month 12.

Primary safety endpoint

Number and severity of local and systemic treatment emergent adverse events (TEAEs).

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FILLY baseline characteristics

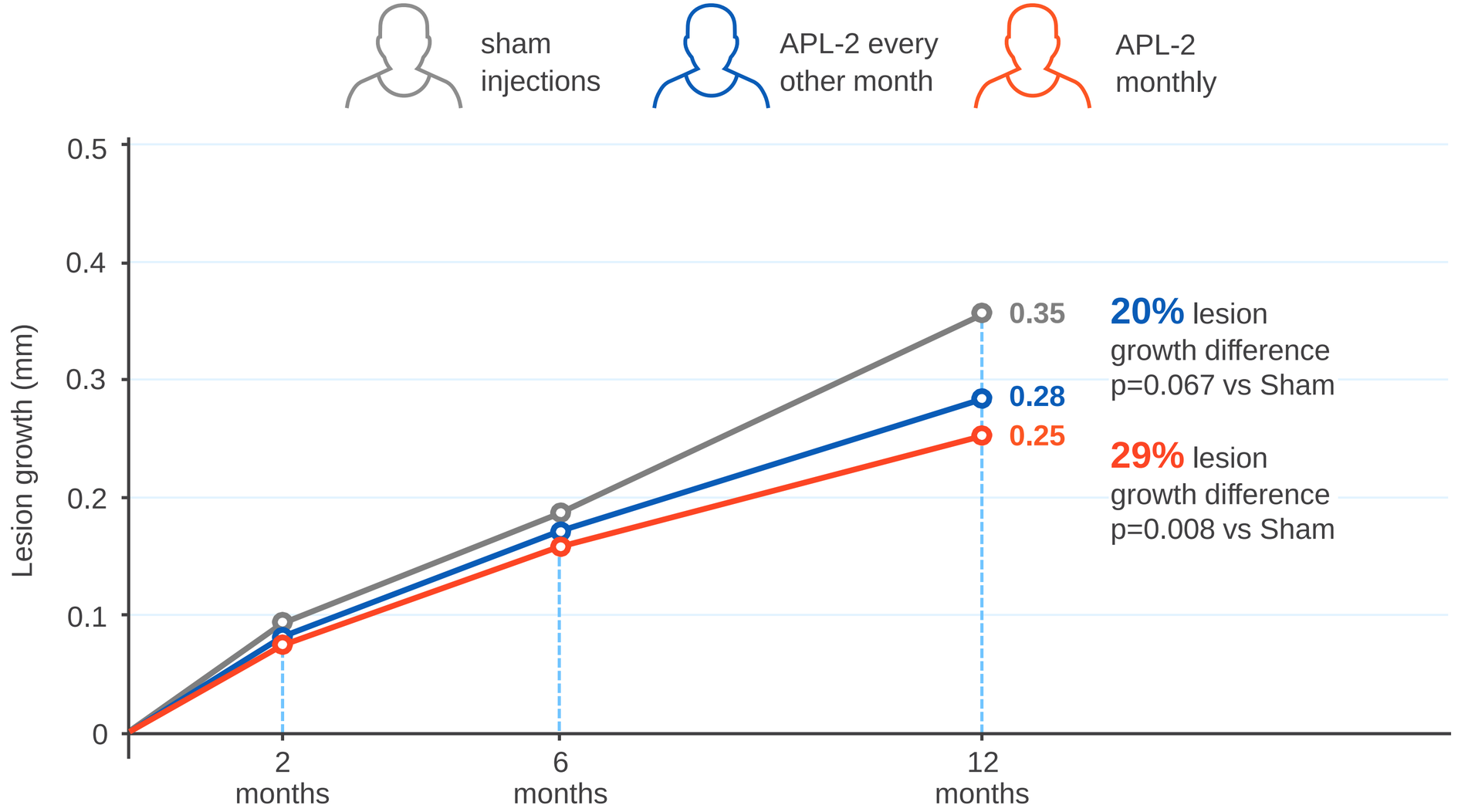
GA

	Sham injections N=81	APL-2 every other month N=79	APL-2 monthly N=86
Bilateral GA, n (%)	72 (90.0%)	64 (82.1%)	71 (85.5%)
History of CNV in Fellow Eye, n (%)	29 (35.8%)	28 (35.4%)	36 (41.9%)
GA lesion size, mean, mm^2 (SD)	8.2 (4.1)	8.9 (4.5)	8.0 (3.8)
BCVA score, mean letters (SD)	59.8 (17.2)	58.4 (16.0)	59.8 (15.7)
BCVA score (Snellen equivalent)	20/63	20/80	20/63
LL-BCVA score, mean letters (SD)	33.6 (17.8)	31.4 (17.1)	36.3 (16.6)

Groups were well balanced as to age, gender and race

APL-2 slowed GA growth at 12 months (*square root) – primary endpoint*

GA



Modified Intent to Treat population (mITT), Observed, Mixed-Effect Model

Apellis

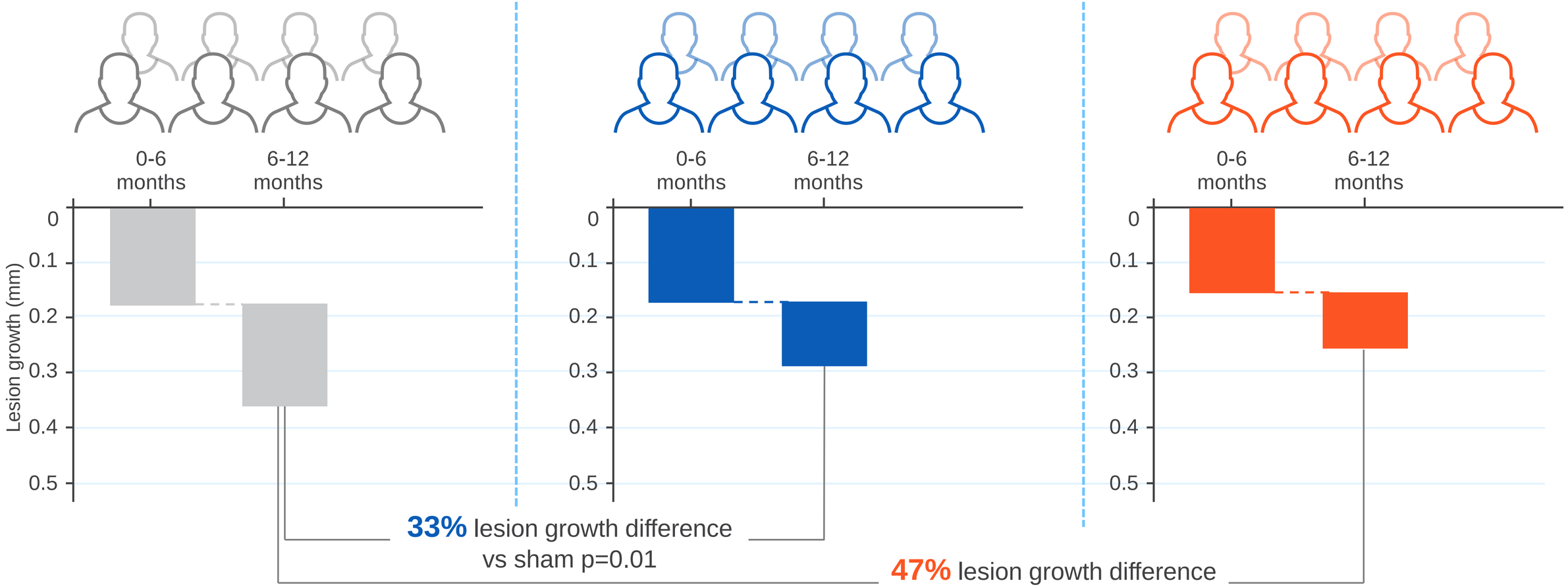
Lesion growth by six-month periods (*square root)*
- post hoc analysis

GA

Sham group
Sham injections

APL-2 EOM
APL-2 injections every other month

APL-2 Monthly
APL-2 injections every month

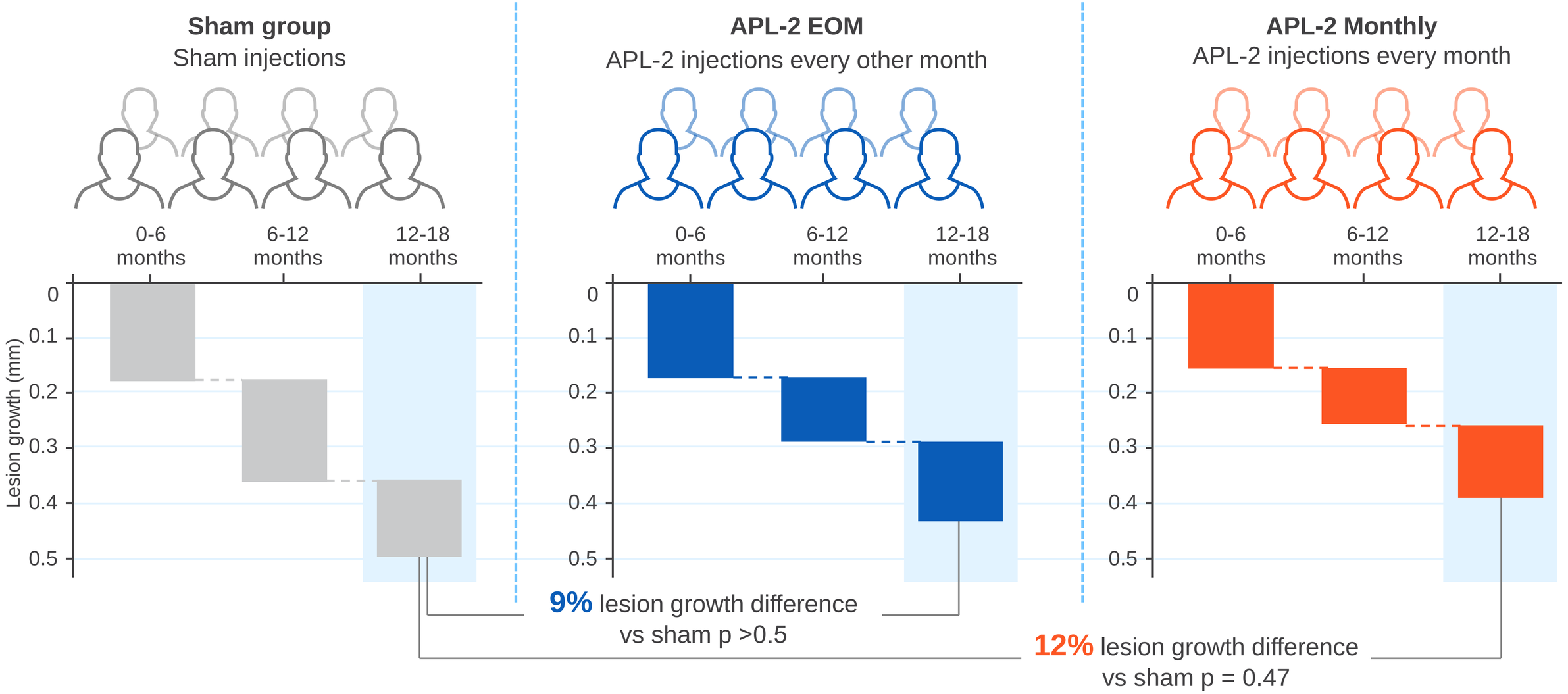


Data from subjects with a measurable GA lesion size at both Months 6 & 12

Apellis

Lesion growth by six-month periods (*square root)*
- post hoc analysis

GA

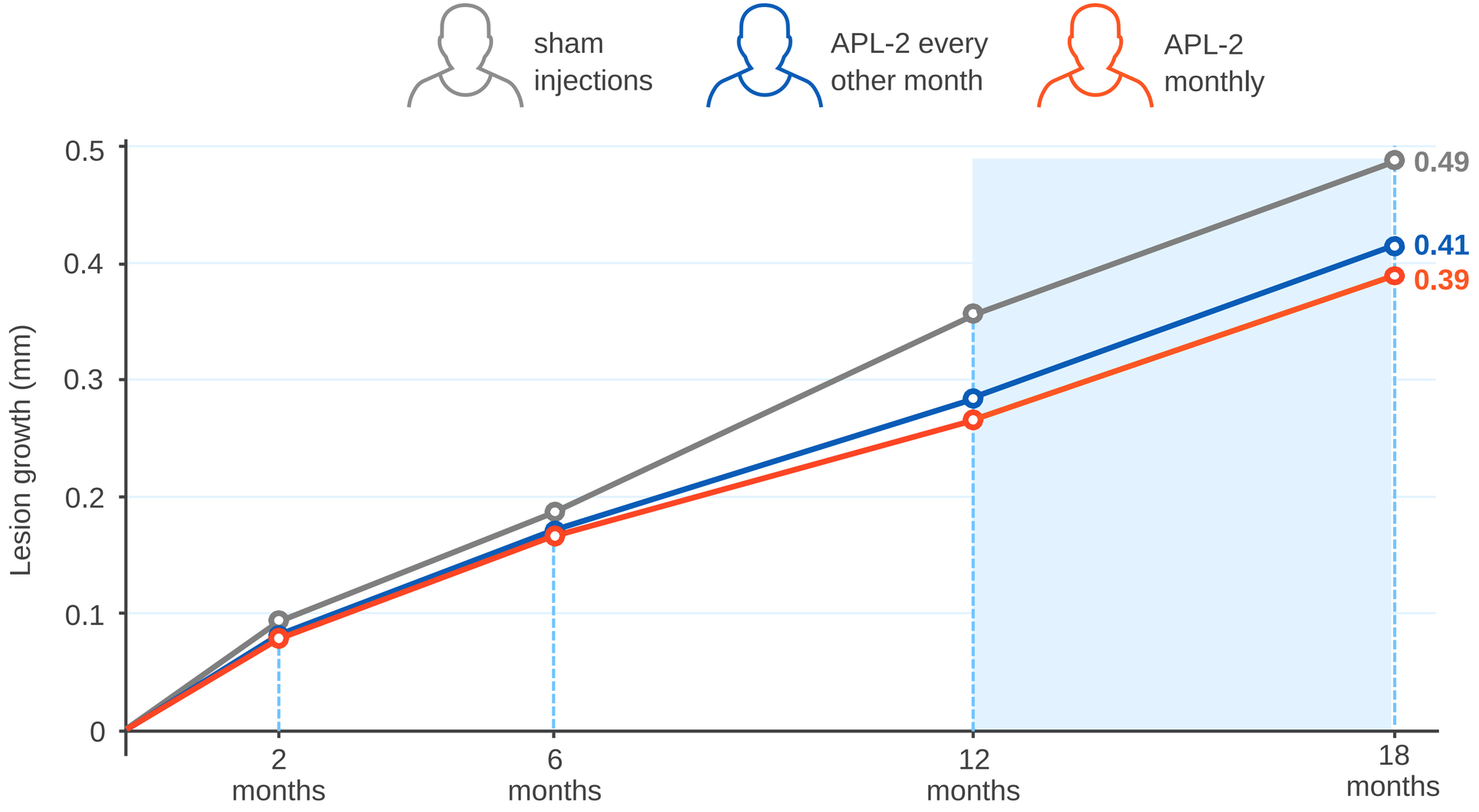


Apellis

Data from subjects with a measurable GA lesion size at both Months 6 & 12 & 18

After cessation of treatment at 12 months, GA growth resumes but treatment effect is maintained through 18 months (square root)

GA



16% lesion growth difference p=0.097 vs Sham

20% lesion growth difference p=0.044 vs Sham

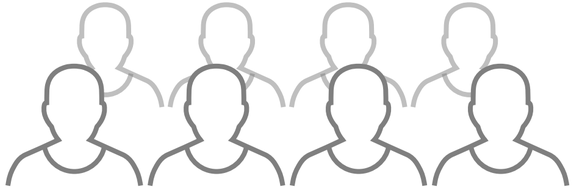
Modified Intent to Treat population (mITT), Observed, Mixed-Effect Model

Apellis

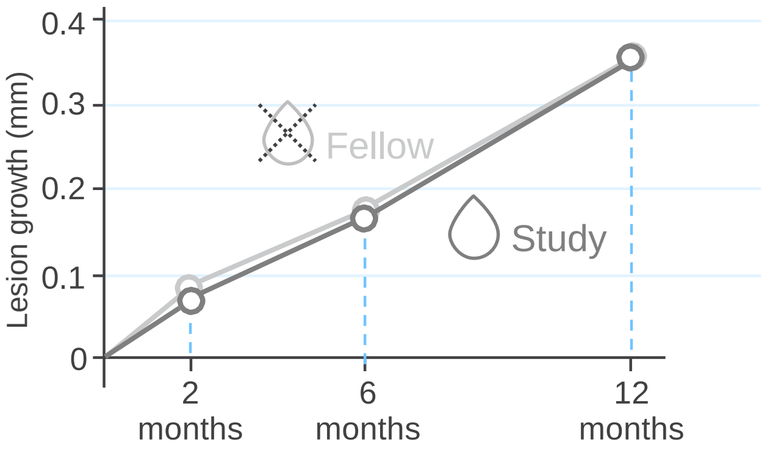
GA growth comparison: fellow eye vs study eye
- post hoc analysis

GA

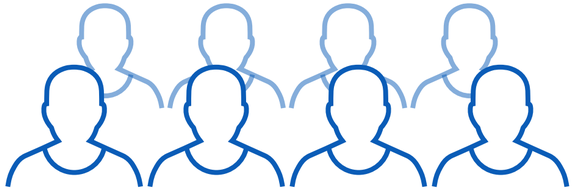
Sham group
Sham injections



N=72

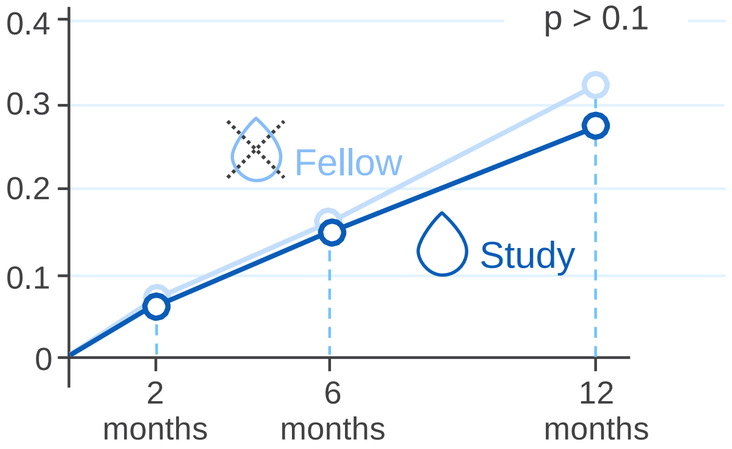


APL-2 EOM
APL-2 injections every other month

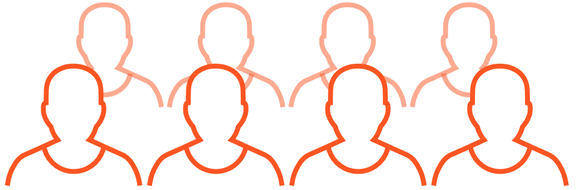


N=63

10%
Difference
p > 0.1

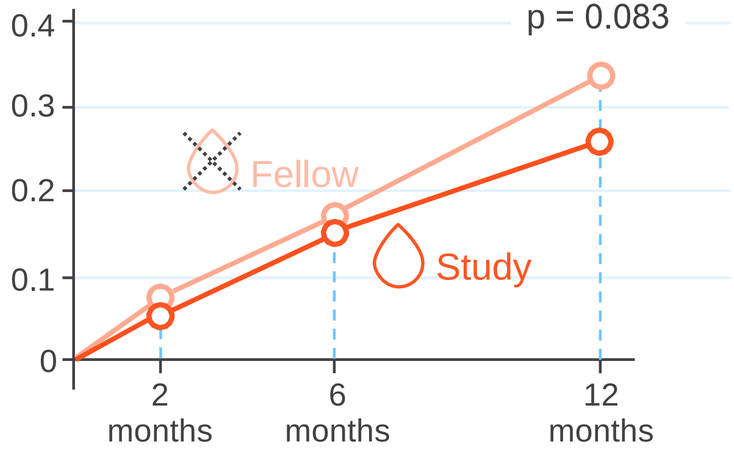


APL-2 Monthly
APL-2 injections every month



N=69

23%
Difference
p = 0.083



Includes patients from the Bilateral GA Population

New onset exudations

FILLY: 38% of enrolled patients had wet AMD in the non-study eye (fellow eye), balanced between the three groups.

GA

Sham group (n=81)

Fellow eye DRY

1%

APL-2 EOM (n=79)

Fellow eye DRY

Fellow eye WET

9%

APL-2 Monthly (n=86)

Fellow eye DRY

Fellow eye WET

21%

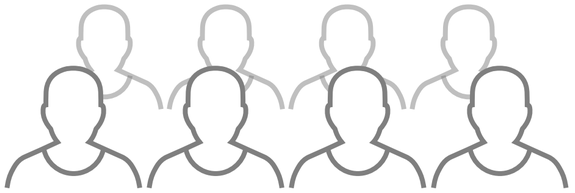
“Expected” based on natural history ~2%/yr for Dry fellow eye patients (Sunness et al 1999) and ~10%/yr for Wet fellow eye patients (Marques et al. 2013)

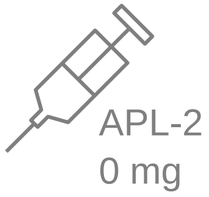
Apellis

DERBY & OAKS - Phase 3 Program Overview

GA

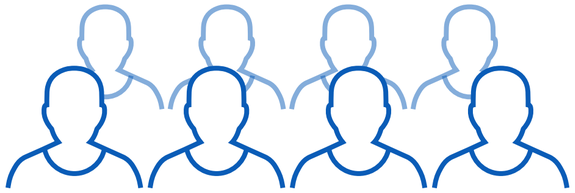
Sham group, n=200 (pooled)

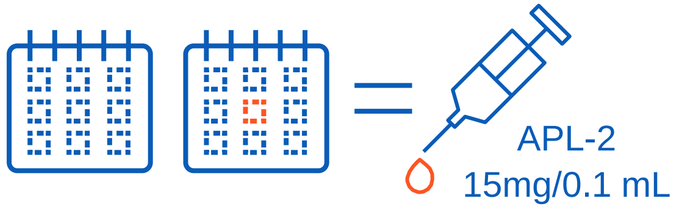




Sham injections

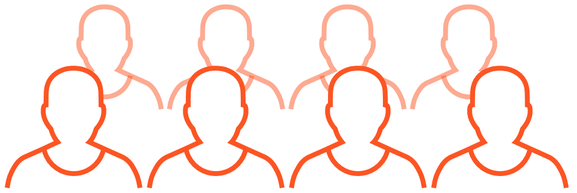
APL-2 EOM, n=200

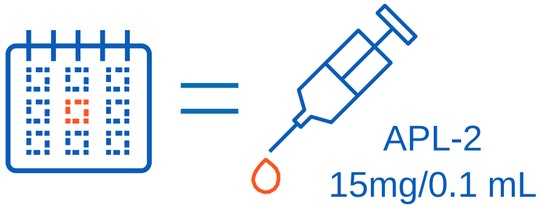




APL-2 injections every other month

APL-2 Monthly, n=200





APL-2 injections every month

Population: Patients with Geographic Atrophy secondary to AMD

1st Endpoint: Change in total area of GA lesion(s) based on FAF at Month 12

Design: Double Masked, Randomized 2:1:2:1

Treatment: 15 mg/0.1 mL Intravitreal Injection vs. Sham Injection

Sample size: 600 Subjects from approx. 100 multinational sites per study

Duration: 2 years

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VISION 2020

- Prepare for potential commercial launch of APL-2 in PNH
- Fully enroll GA Phase 3 Program
- Continue clinical development in CAD or wAIHA or both
- PoC in new indications
- 2x global employee footprint

Thank you

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