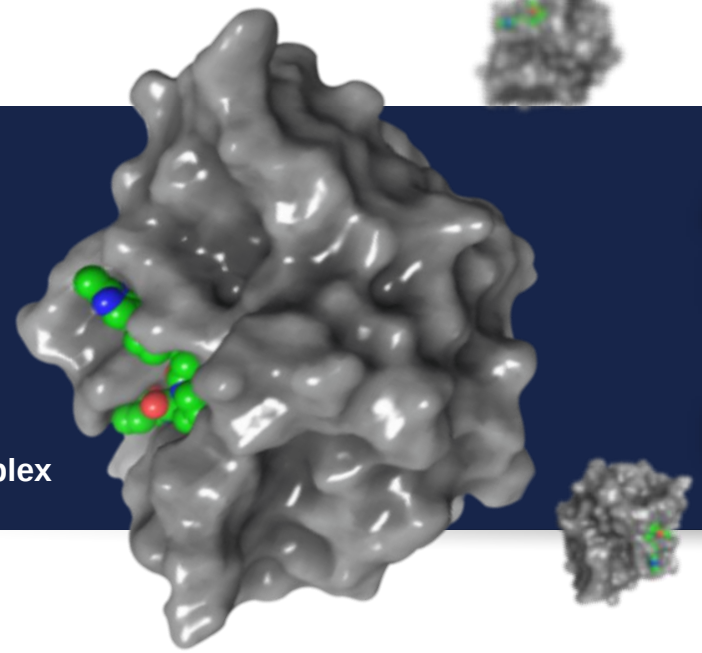

ACH-4471:
Factor D Complex

ACH-4471 in Combination with Eculizumab in Patients with PNH

Interim Data from Phase 2 Clinical Trial

May 17, 2019

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Cautionary Note Regarding Forward-Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other important factors that could cause actual results to differ materially from those indicated by such forward-looking statements. Achillion may use words such as “expect,” “anticipate,” “project,” “target,” “intend,” “plan,” “aim,” “believe,” “seek,” “estimate,” “can,” “could” “focus,” “will,” “look forward,” “continue,” “goal,” “strategy,” “objective,” “may,” “potential,” and similar expressions to identify such forward-looking statements.

These forward-looking statements also include statements about: the potential benefits of factor D inhibition as a treatment for complement-mediated diseases, including ACH-4471 for PNH in combination with eculizumab; the potential benefits of, and indications for, Achillion’s compounds that inhibit factor D, including ACH-4471, ACH-5228 and ACH-5548; Achillion’s belief that its portfolio of compounds could expand factor D portfolio opportunities, provide strategic optionality or create significant value; the status of enrollment in Achillion’s ongoing clinical trials; Achillion’s expectations regarding the advancement of, and timeline for reporting results from, clinical trials of its product candidates as well as its ability to advance additional compounds; Achillion’s expectations regarding the timing of regulatory interactions and filings; Achillion’s anticipated cash expenditures for 2019 and the sufficiency of its existing cash resources; and other statements concerning Achillion’s strategic goals, efforts, plans, and prospects. Among the important factors that could cause actual results to differ materially from those indicated by such forward-looking statements are risks relating to, among other things, Achillion’s ability to: demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its product candidates; advance the preclinical and clinical development of its complement factor D inhibitors under the timelines it projects in current and future preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of that trial or whether results of early clinical trials or preclinical studies will be indicative of the results of later clinical trials; enroll patients in its clinical trials on its projected timelines; obtain and maintain patent protection for its product candidates and the freedom to operate under third party intellectual property; obtain and maintain necessary regulatory approvals, and the granting of orphan designation does not alter the standard regulatory requirements and process for obtaining such approval; establish commercial manufacturing arrangements; identify, enter into and maintain collaboration and other commercial agreements with third-parties; compete successfully in the markets in which it seeks to develop and commercialize its product candidates and future products; manage expenses; manage litigation; raise the substantial additional capital needed to achieve its business objectives; and successfully execute on its business strategies. These and other risks are described in the reports filed by Achillion with the U.S. Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2019, and any other SEC filings that Achillion makes from time to time

In addition, any forward-looking statement in this presentation represents Achillion's views only as of the date of this presentation and should not be relied upon as representing its views as of any subsequent date. Achillion disclaims any duty to update any forward-looking statement, except as required by applicable law.

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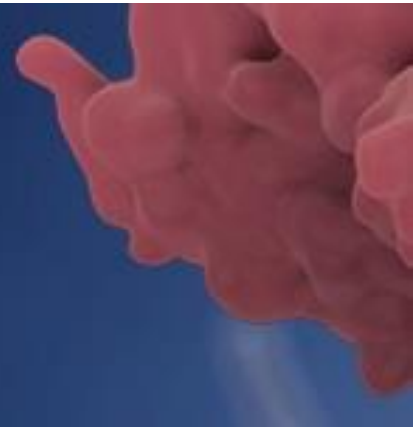
About ACH-4471 in PNH



Paroxysmal Nocturnal Hemoglobinuria (PNH)

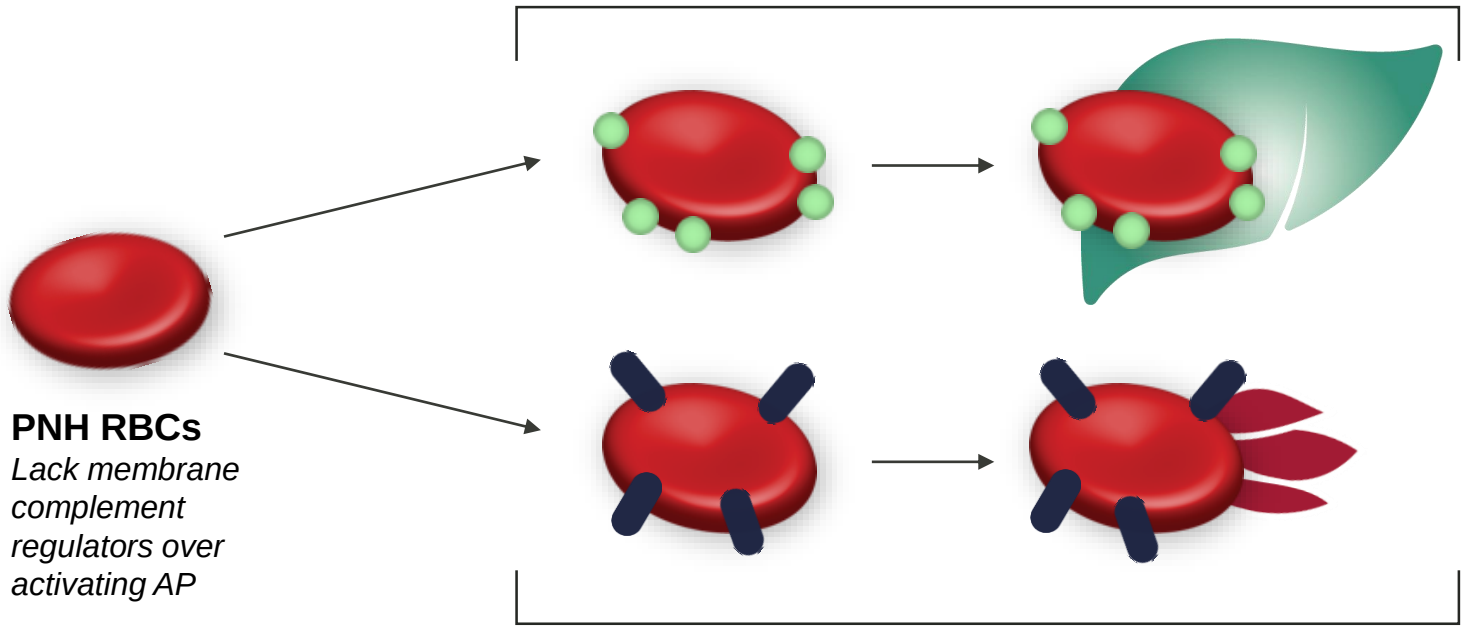
Driven by Deficient Red Blood Cells

Rare, acquired, blood disorder with remaining unmet medical need

Two paths to PNH red blood cell (RBC) destruction driven by the alternative pathway (AP)

1. Extravascular Hemolysis (EVH)

C3b targets RBCs for destruction by liver and spleen



PNH RBCs
Lack membrane complement regulators over activating AP

2. Intravascular Hemolysis (IVH)

Membrane Attack Complex (MAC) targets RBCs for destruction in circulation

Factor D Inhibition
Targets EVH ( ) and IVH ( )

C5 Inhibition
Targets IVH ( ) only

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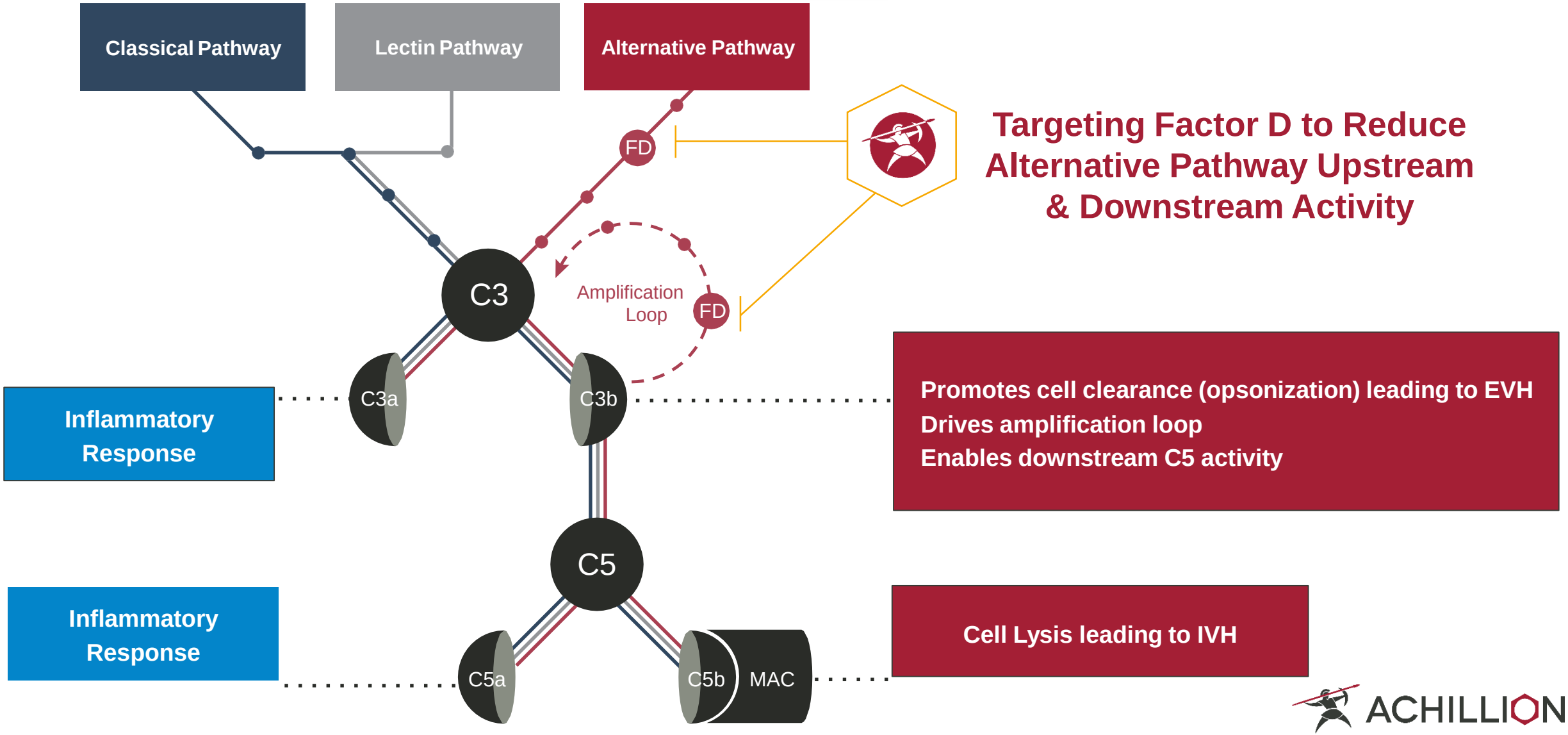
Targeting Factor D (FD)

Critical Control Point for Alternative Pathway Activity



Targeting Factor D to Reduce Alternative Pathway Upstream & Downstream Activity

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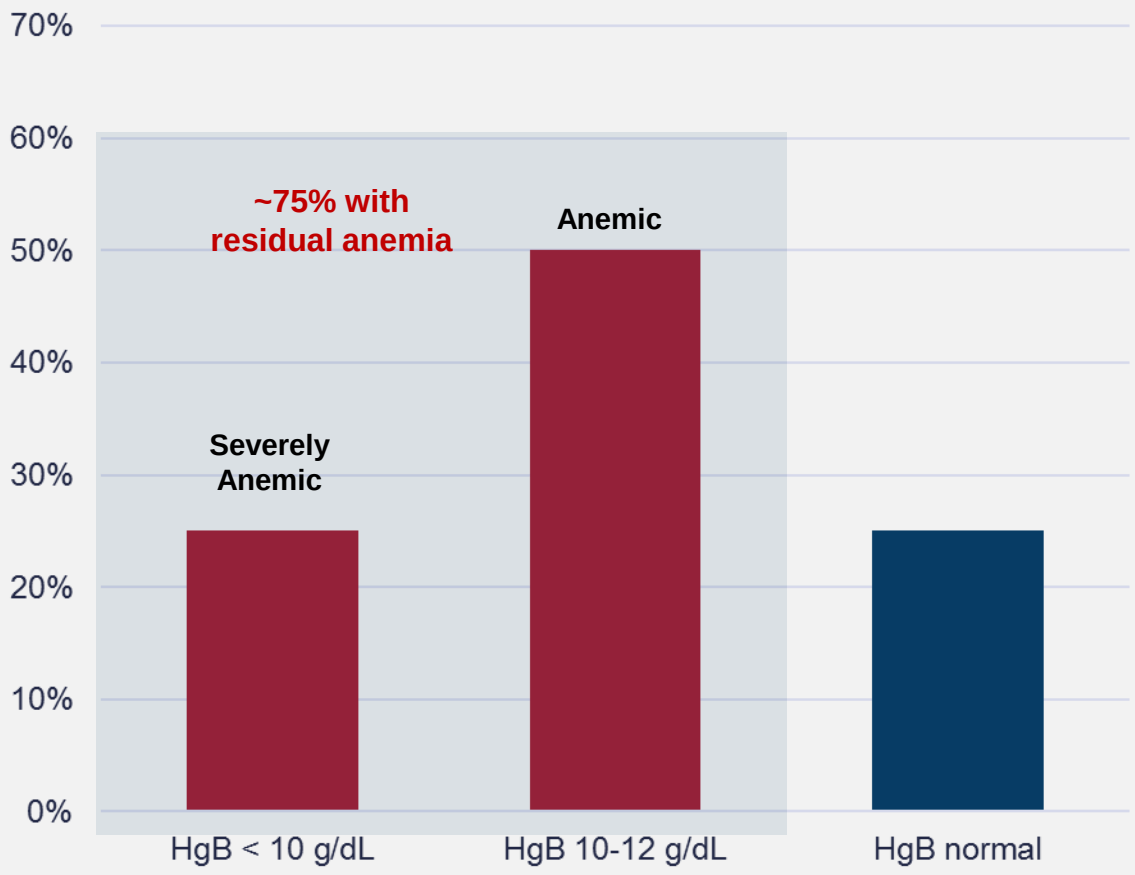
PNH Patients Treated with Eculizumab

Up to 75% Remain Anemic with C5 Inhibition Only

Hgb for Eculizumab-Treated Patients (ACHN Market Research)[1]



Studies of Eculizumab-Treated Patients

- 141 PNH patients treated with eculizumab for >13 months[2]
  - 72% had a mean hemoglobin <12.0 g/dL
    - Mean Hgb was 10.9 g/dL
  - **36% had at least one transfusion** in the last 12 months
  - **Reticulocyte count** correlated with indicators of **extravascular hemolysis**, including **C3 loading** of PNH cells
- 195 PNH patients >66 months on eculizumab[3]
  - Mean Hgb was 10.5 g/dL at 24 and 36 months
- 123 PNH patients treated with eculizumab after a median follow-up of 4.5 years[4]
  - 72% were anemic

1 Achillion Internal Physician Interviews of 14 US/EU KOLs 2018. **2** McKinley et al, ASH Dec 2017. Abst. 3471. **3** Hillmen et al. *Br J Haematol.* 2013. **4** Loschi et al. *Am J Hematol*. 2016.

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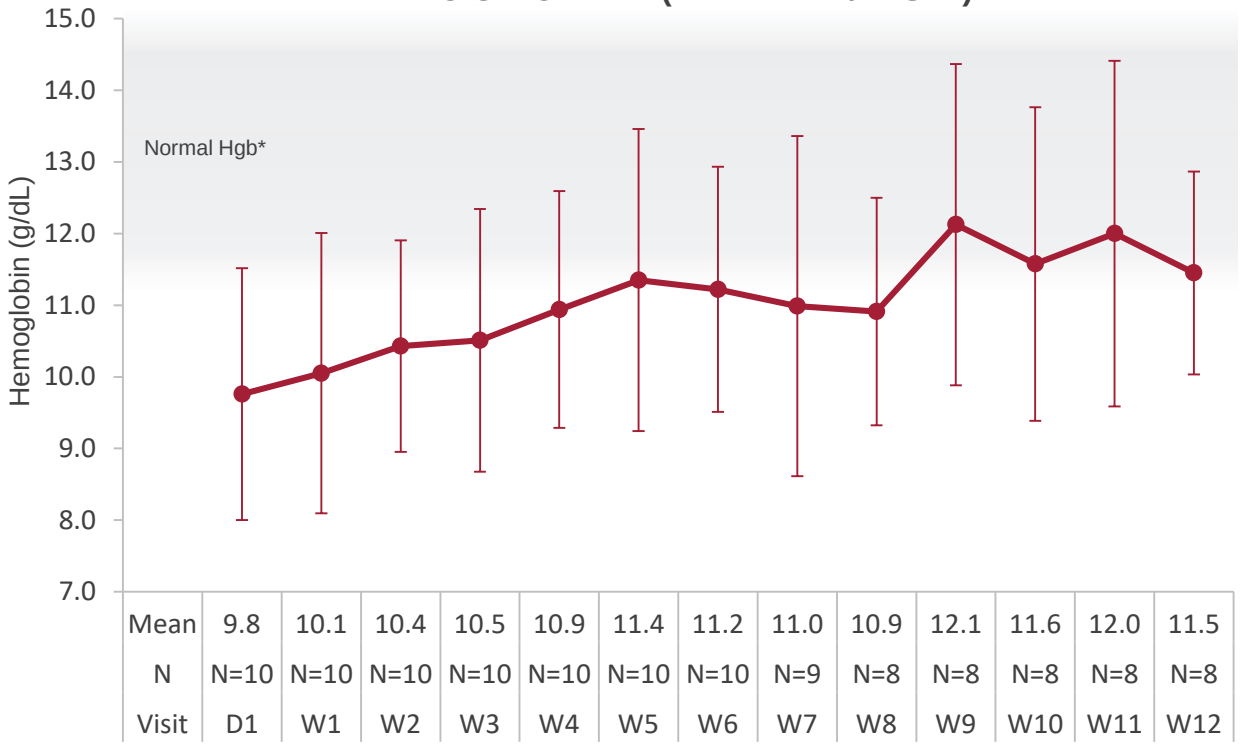
ACH-4471 Experience in Untreated PNH Patients

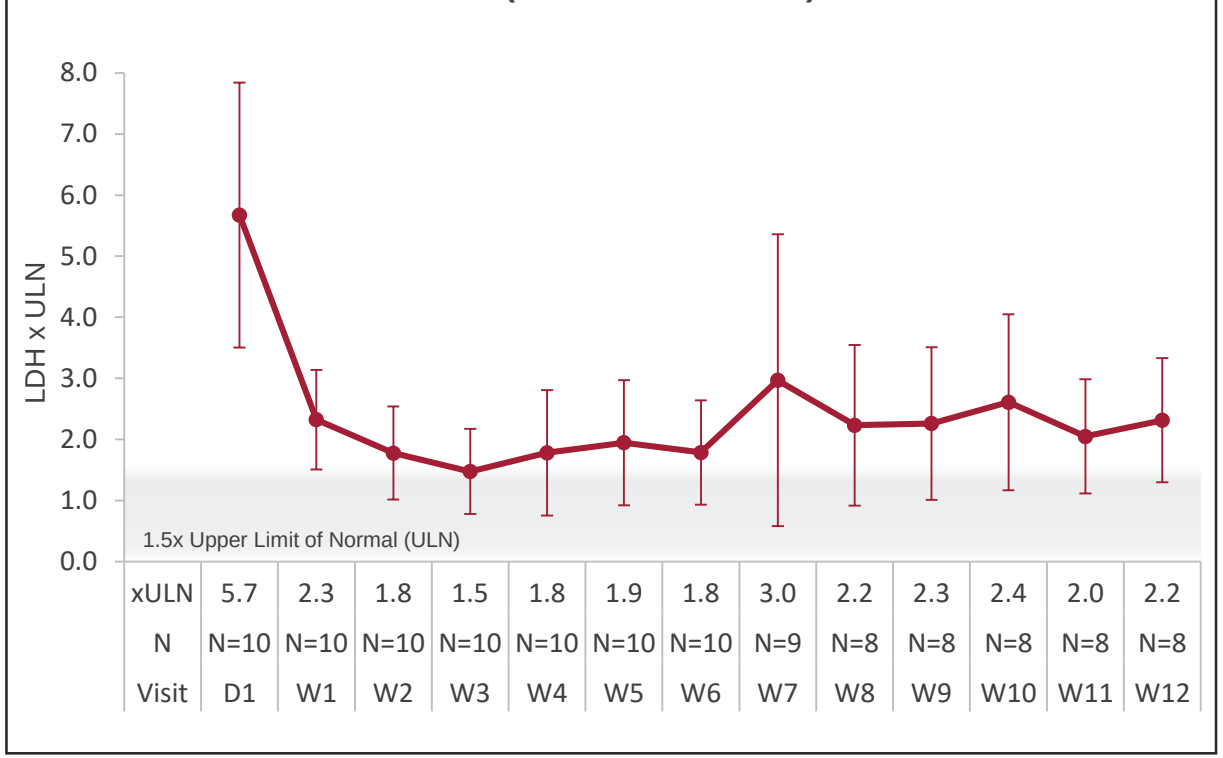
Topline Results – December 2018

Mean Hemoglobin Near Normal Range



Mean	9.8	10.1	10.4	10.5	10.9	11.4	11.2	11.0	10.9	12.1	11.6	12.0	11.5
N	N=10	N=10	N=10	N=10	N=10	N=10	N=10	N=9	N=8	N=8	N=8	N=8	N=8
Visit	D1	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12

Reductions in LDH



xULN	5.7	2.3	1.8	1.5	1.8	1.9	1.8	3.0	2.2	2.3	2.4	2.0	2.2
N	N=10	N=10	N=10	N=10	N=10	N=10	N=10	N=9	N=8	N=8	N=8	N=8	N=8
Visit	D1	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12

*Normal (female): 11.8-15.9 g/dL; Normal (male): 13.1-17.9 g/dL
Individual subject's missing data points were imputed by taking the arithmetic mean of the two adjacent time points.

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ACH-4471 Treatment Experience

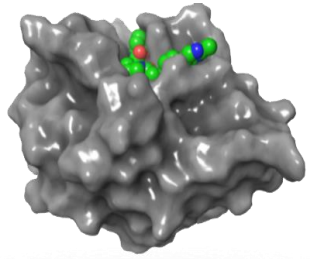
Moving Towards Phase 3 Development

Treatment & Safety Experience Summary

- ✓ Completed 6- and 9-month chronic toxicology studies
- ✓ Completed renal & hepatic impairment study
- ✓ Completed thorough QT study
- ✓ Completed Development & Reproductive Toxicology studies
- ✓ Multiple DDI, ADME, and support studies
- • Carcinogenicity studies - ongoing

Patient Exposure Summary

- >300 healthy volunteers and patients dosed to-date
- >16 patient years of dosing
- 24 unique C3G patients dosed
- 21 PNH patients dosed
- 2 PNH patients dosed >24 months
- Agreement from FDA to include adolescents (≥12 yrs) in ongoing 6- and 12-month trials for C3G



ACH-4471: Factor D Complex
0.8 A X-ray Structure

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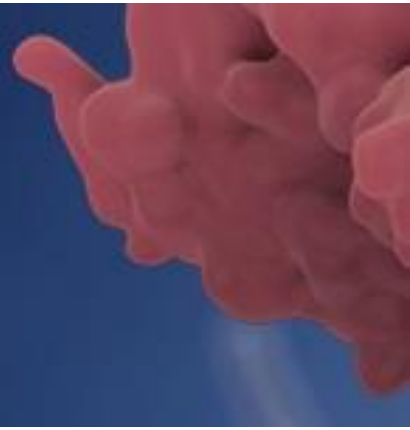
Interim Data from Phase 2 Dose Finding Study in Patients with PNH

Presented at New Era of Aplastic Anemia and PNH Meeting

Napoli, Italy - May 17, 2019



Clinical Trial Investigators

Presenter & Investigator

- **Austin Kulasekararaj**
  - King's College Hospital-NHS Foundation Trust & King's College London, London, United Kingdom

Investigators

- **Robert Brodsky**
  - Johns Hopkins University School of Medicine, Baltimore, Maryland, United States
- **Jaroslaw Maciejewski**
  - Cleveland Clinic, Cleveland, Ohio, United States
- **Rosario Notaro**
  - Azienda Ospedaliera Universitaria Careggi; Instituto per lo Studio, la Prevenzione e la Rete Oncologica, Firenze, Italy
- **Antonio Risitano**
  - Universita Federico II di Napoli, Napoli, Italy

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ACH-4471 in Combination with Eculizumab in PNH Patients

Study Design- Phase 2 Multi-center, Open-label, Multi-Dose

KEY INCLUSION CRITERIA

- RBC transfusion within the last 12 weeks
- Anemia (Hgb <10 g/dL) with adequate reticulocytosis
- On a stable regimen of eculizumab
- Documentation or willingness to receive vaccination for *N. meningitidis*, *H. influenzae*, and *S. pneumoniae*
- Documentation or willingness to receive antibiotic prophylaxis

OBJECTIVES

Primary:

- Increase **Hgb** at 24 weeks

Secondary:

- Reduce **Transfusions**
- Maintenance/Improvements in **LDH**
- Improvements in **FACIT FATIGUE**

Hgb: hemoglobin, LDH: lactose dehydrogenase, RBC : red blood cell, TID: three times daily

Six-month Dose Finding | **Long-term Extension**

Day 1 — **Enrollment: up to 12 pts** — Week 24

OPEN LABEL, MULTI-DOSE STUDY

IV eculizumab: usual dose and schedule

+

ACH-4471 doses: 100 mg TID, 150 mg TID or 200 mg TID

Per protocol, investigator determines clinical response and adjusts dose accordingly to a max of 200 mg TID

EXTENSION STUDY

Continue ACH-4471 plus eculizumab at same doses used at end of study

https://clinicaltrials.gov/ct2/show/NCT03472885?term=NCT03472885&rank=1. Accessed 16 April 2019.

Study Locations: Italy, United Kingdom, United States

Dose Escalation Per Protocol

Six-month Dose Finding

Enrollment: up to 12 pts

Primary Endpoint

Day 1 | Week 4 | Week 8 | Week 12 | Week 24

On a patient-by-patient basis, if dose is well tolerated patient may be escalated to the next highest dose to a maximum dose of 200 mg TID

Week 4: Hgb has not increased by ≥1.5 g/dL from Day 1 OR Transfusion received during the previous 4 weeks

Week 8: Hgb has not increased by ≥3 g/dL from Day 1 OR Transfusion received during the previous 4 weeks

Week 12*: Hgb has not normalized OR Transfusion received during the previous 4 weeks

Extension: Continue ACH-4471 plus eculizumab at same doses used at end of study

*Dose escalations can be made after week 12 based on response

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Baseline Characteristics

Baseline Characteristic	N=11*, †
Sex, n (%)	**N=11**
Female	9 (82)
Male	2 (18)
Race, n (%)	**N=11**
White	6 (55)
Black or African American	3 (27)
African Asian	1 (9)
Asian	1 (9)
Eculizumab Dosing (Q14D), n (%)	**N=11**
900 mg	8 (73)
1200 mg	2 (18)
1500 mg	1 (9)

Baseline Characteristic	N=11[1]
Age, years	**N=11**
Mean (SD)	42.5 (14.98)
Range	19-67
BMI	**N=11**
Mean (SD)	25.4 (2.44)
Range	21.8-29.7

SD- standard deviation; BMI- body mass index; RBC- red blood cell

*Does not include one patient who discontinued ACH-4471 on Day 1 after 2 doses due to SAE of worsening underlying medical condition (pulmonary hypertension/edema), G4 (Life Threatening), considered unlikely related to study drug. This patient's data have otherwise been excluded from this analysis.

† Excludes patient A who also has hereditary elliptocytosis hence another hemolytic anemia that cannot be expected to be impacted by ACH-4471

Baseline Characteristics

Parameter	Mean (SD)	Median	Range
Hemoglobin* (g/dL)[1]	7.9 (1.5)	7.7	5.0-10.4
LDH (xULN)[2]	1.1 (0.32)	0.97	0.59-1.65
Reticulocytes (10^9/µl)[3]	219 (78)	200	120-405
Total Bilirubin (mg/dL)[4]	2.17 (1.12)	2.2	0.56-3.93
Direct Bilirubin (mg/dL)[5]	0.52 (0.22)	0.44	0.23-0.82

n=11; SD- standard deviation; LDH- lactate dehydrogenase
*Excludes Day 1 for patient K. Patient had Hgb 8.4 g/dL at screening. Patient received 1 unit PRBC Day -14 between screening and Day 1 resulting in Day 1 Hgb 14.7 g/dL. This was thought to be not clinically possible for a Hgb at this level in conjunction with markedly elevated retic and low RBC counts.
[1] normal range: 12.8-17.4 (M)/10.8-15.0 (F). One lab had a normal range (F) of 11.6-15.7 g/dL
[2] normal range: 82-216. One lab had a normal range of 0-249 IU/L.
[3] normal range: 10-20. One lab had a normal range of 20-81 10^9/uL
[4] normal range:0.19-1.69 (M)/0.19-1.27 (F). One lab had a normal range (F) of 0-1.19 mg/dL
[5] normal range:0-0.35. One lab had a normal range of 0-0.29 for females

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Transfusions Prior to ACH-4471 Administration

Baseline Transfusion	N=10*	
RBC transfusions in 52 weeks prior to screening	**Number**	**Units**
Total	54	97
Mean (SD)	5.4 (4.20)	9.7 (9.30)
Range	1 -12	1 -27
RBC transfusions in 24 weeks prior to Screening	**Number**	**Units**
Total	34	58
Mean (SD)	3.4 (2.59)	5.8 (4.94)
Range	1 -8	1 - 13

SD- standard deviation

*Patient A excluded from table due to religious objection to receiving transfusions.

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ACH-4471 Treatment Durations

Patient	Age/ Sex	Dose (mg/TID)	ACH-4471 Treatment Duration (months)*
A	41/F	200	11
B	51/F	100	11
C	67/M	150	9
D	29/F	150	7
E	22/F	150	5
F	44/F	150	4
G	35/F	100	4
H	52/F	200	4
I	50/F	150	2
J	19/M	100	2
K	F/57	100	1
Cumulative Summary			**~59 months/4.9 years**
Mean			**5.4 months**
Median			**3.6 months**

Current dose regimen, number of patients
100 mg TID, 4 patients
150 mg TID, 5 patients
200 mg TID, 2 patients

* Data as of 10 May 2019. Months have been rounded to nearest integer.

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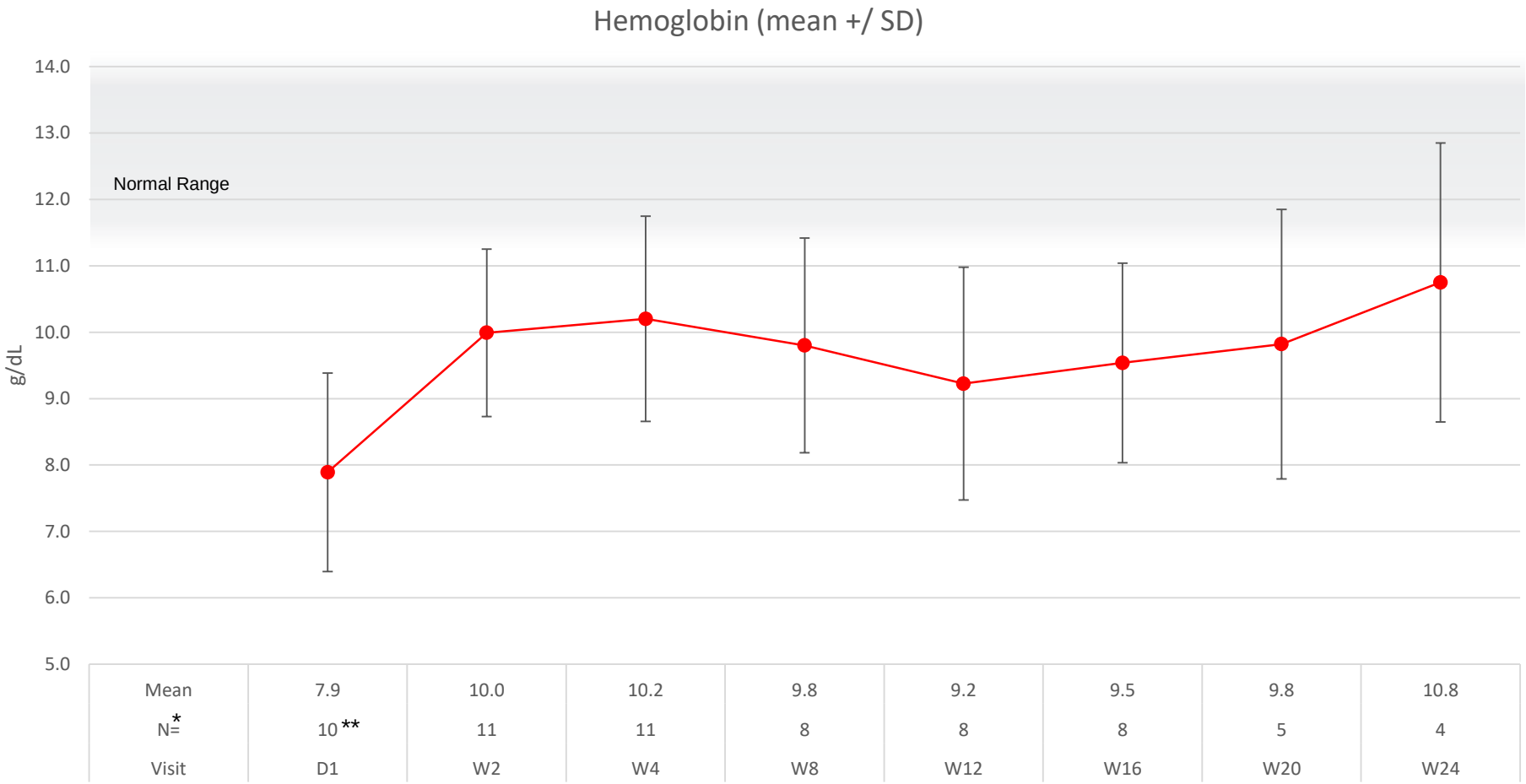
Combination Therapy Results in Fewer Transfusions

Subject*, Sex, Age	-52 to -25 Weeks	-24 to -13 Weeks	-12 Weeks to Screening	Screening to Day 1 (≤60 Days)	Day 1 to 12 Weeks	12-24 Weeks
					On ACH-4471 Treatment	
B, F 51	1 1		1			
C, M 67		1	1			2
D, F 29	2 2 2 1	2 2	1 1 2			
E, F 22			2			
F, F 44	1 2	2	2			
G, F 35	3 3 2 3 3	3 2 2	3 1 2	2		
H, F 52	2 2 2 1 2 2	2 2 2	2 2 2			
I, F 50			1			
J, M 19		2 1 1	2 1 1 2 2	1		
K, F 57	2	1	2	1		

*Patient A excluded from table due to religious objection to receiving transfusions

RBC symbol indicates a transfusion, with number of units of blood given inside

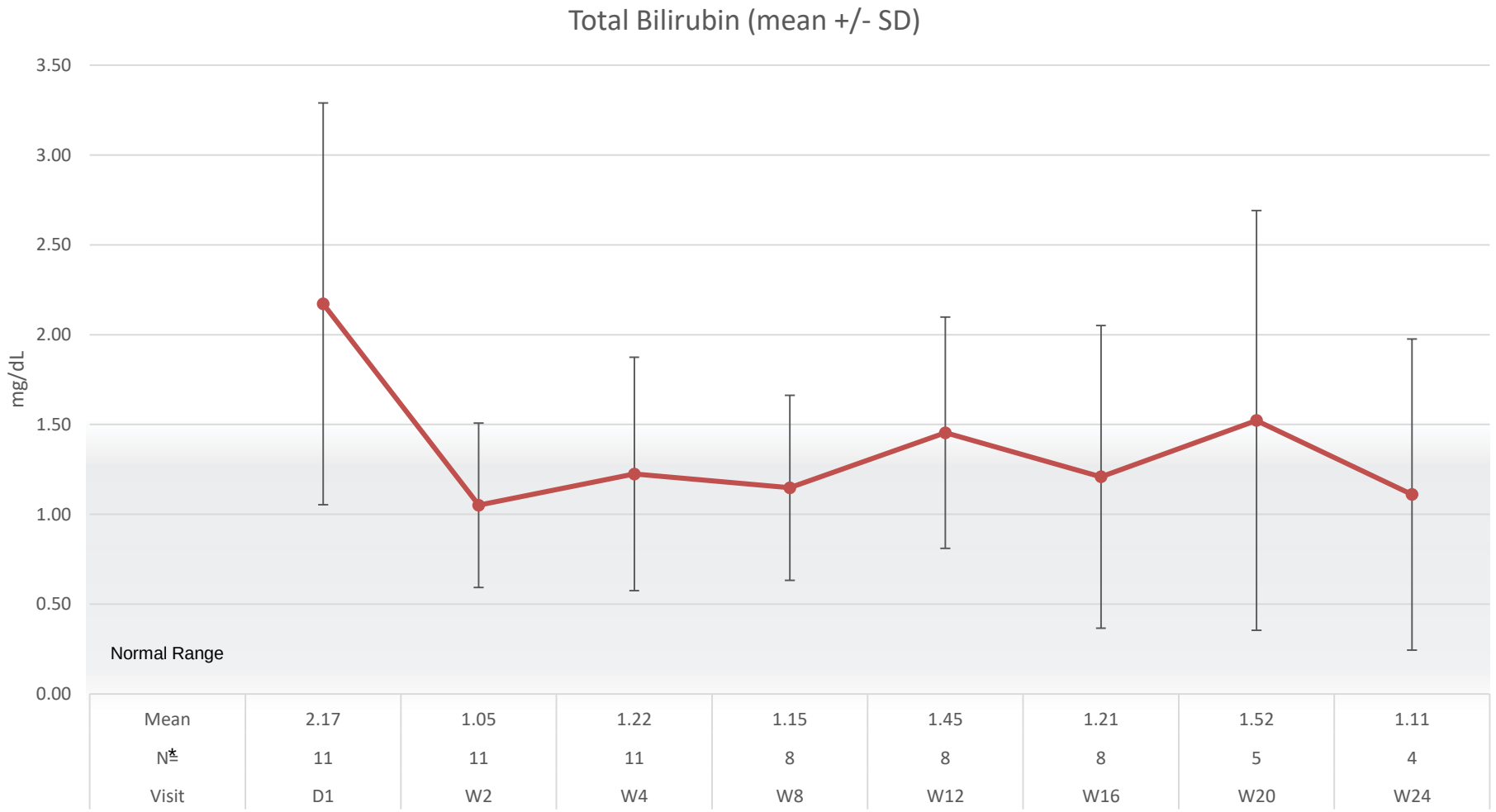
Meaningful Improvement in Hemoglobin Compared to Baseline



Mean increase of 2.6 grams versus baseline for those already at week 24 (n=4)

*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019.
**Excludes Day 1 for patient K. Patient had Hgb 8.4 g/dL at screening. Patient received 1 unit PRBC Day -14 between screening and Day 1 resulting in Day 1 Hgb 14.7 g/dL. This was thought to be not clinically possible for a Hgb at this level in conjunction with markedly elevated retic and low RBC counts.

Driving Total Bilirubin into Normal Range

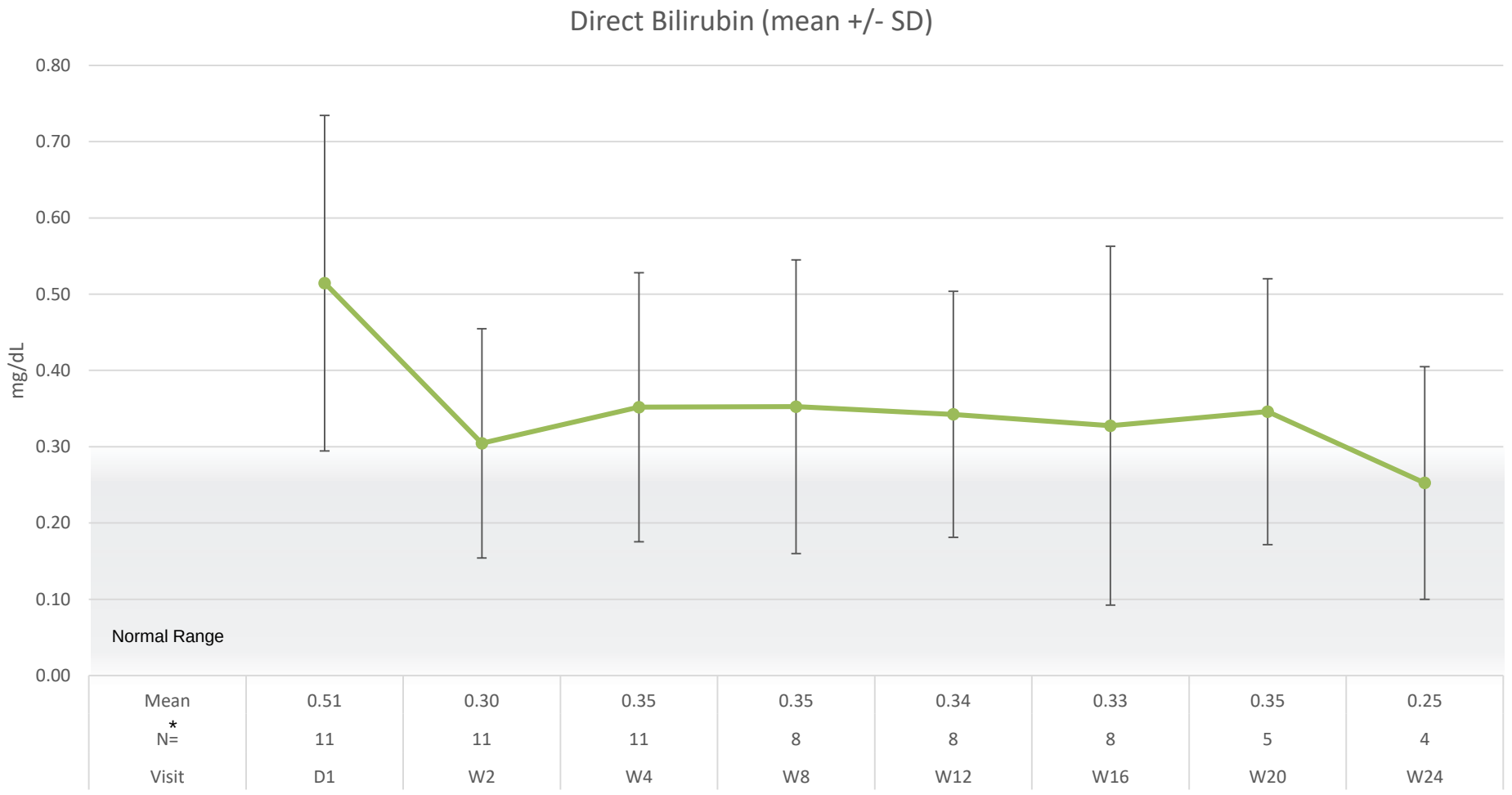


Mean	2.17	1.05	1.22	1.15	1.45	1.21	1.52	1.11
N*	11	11	11	8	8	8	5	4
Visit	D1	W2	W4	W8	W12	W16	W20	W24

Total bilirubin was driven into normal range at week 24 (n=4) versus baseline

*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019.

Driving Direct Bilirubin into Normal Range



Mean	0.51	0.30	0.35	0.35	0.34	0.33	0.35	0.25
N=*	11	11	11	8	8	8	5	4
Visit	D1	W2	W4	W8	W12	W16	W20	W24

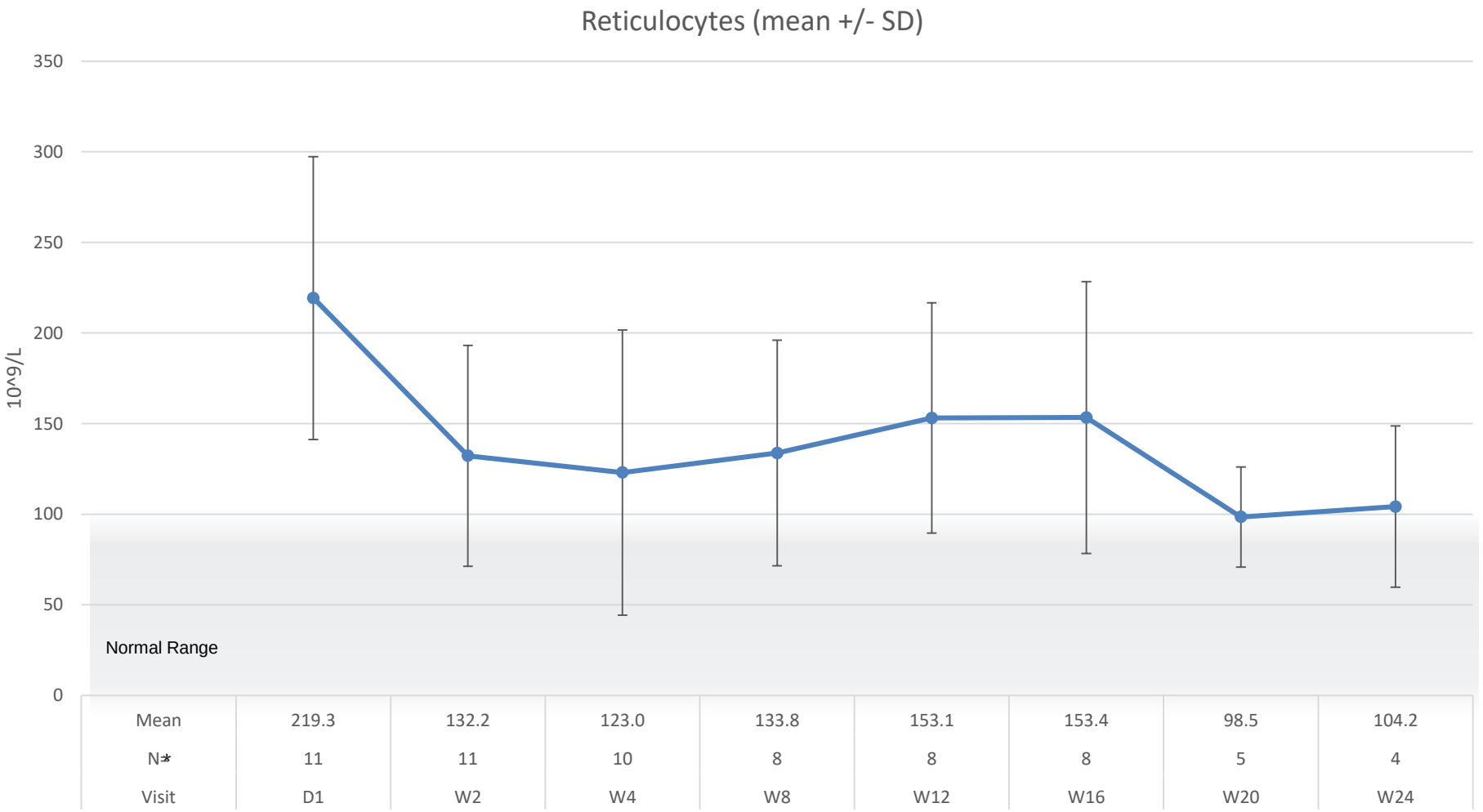
7 of 11 patients had elevated direct bilirubin at screening

5 of 11 patients had direct bilirubin 1.5X ULN at screening

No increase with ACH-4471 treatment with most patients actually showing decline in direct bilirubin

*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019.

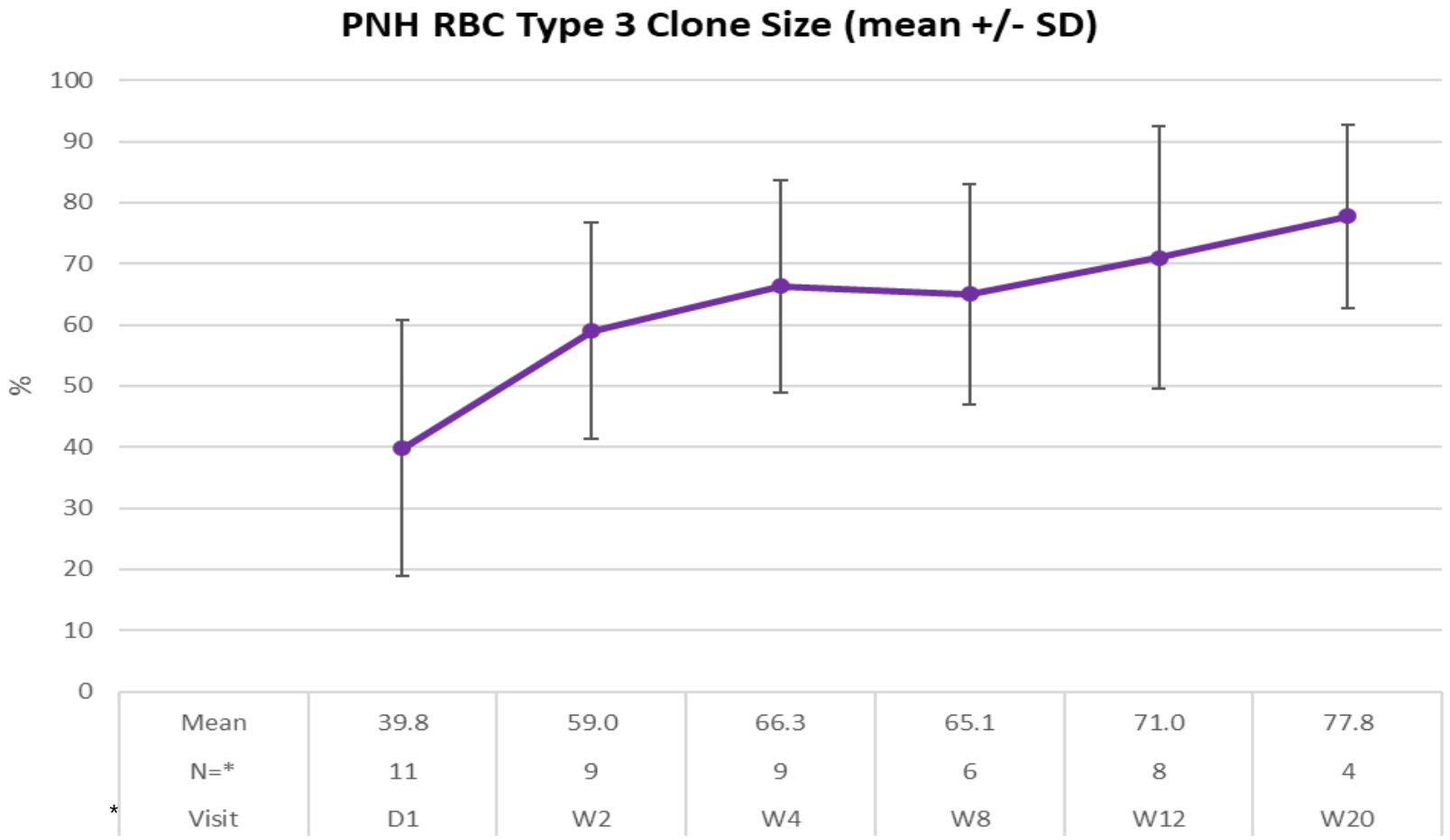
Marked Reduction in Reticulocyte Count



Reticulocyte count was reduced to near normal at week 24 (n=4)

*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019.

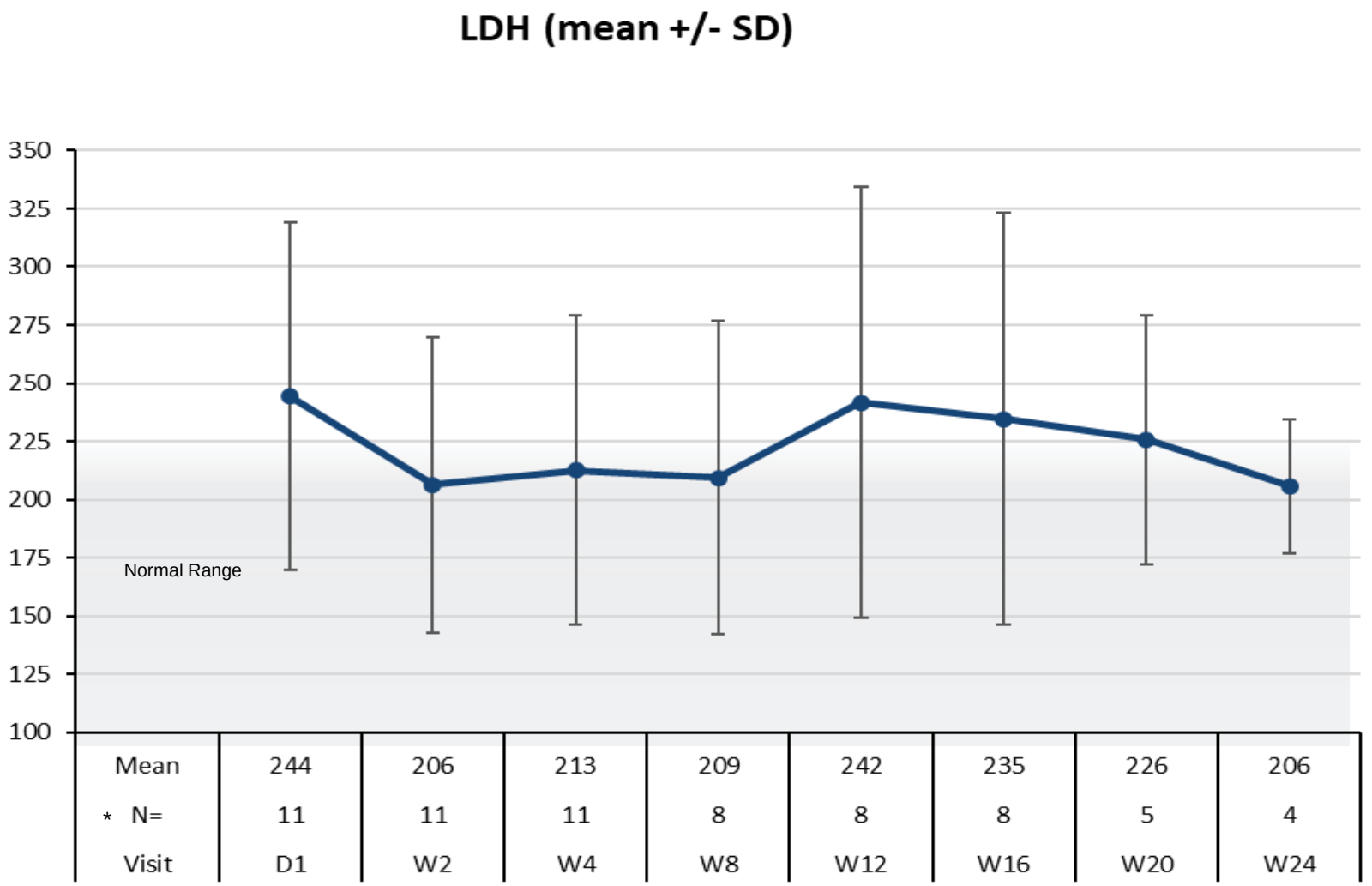
ACH-4471 PNH RBC Type III Clone Size



Steady rise in PNH RBC Type III clone size

*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019. Two samples were cancelled at week 24 due to sample stability issues.

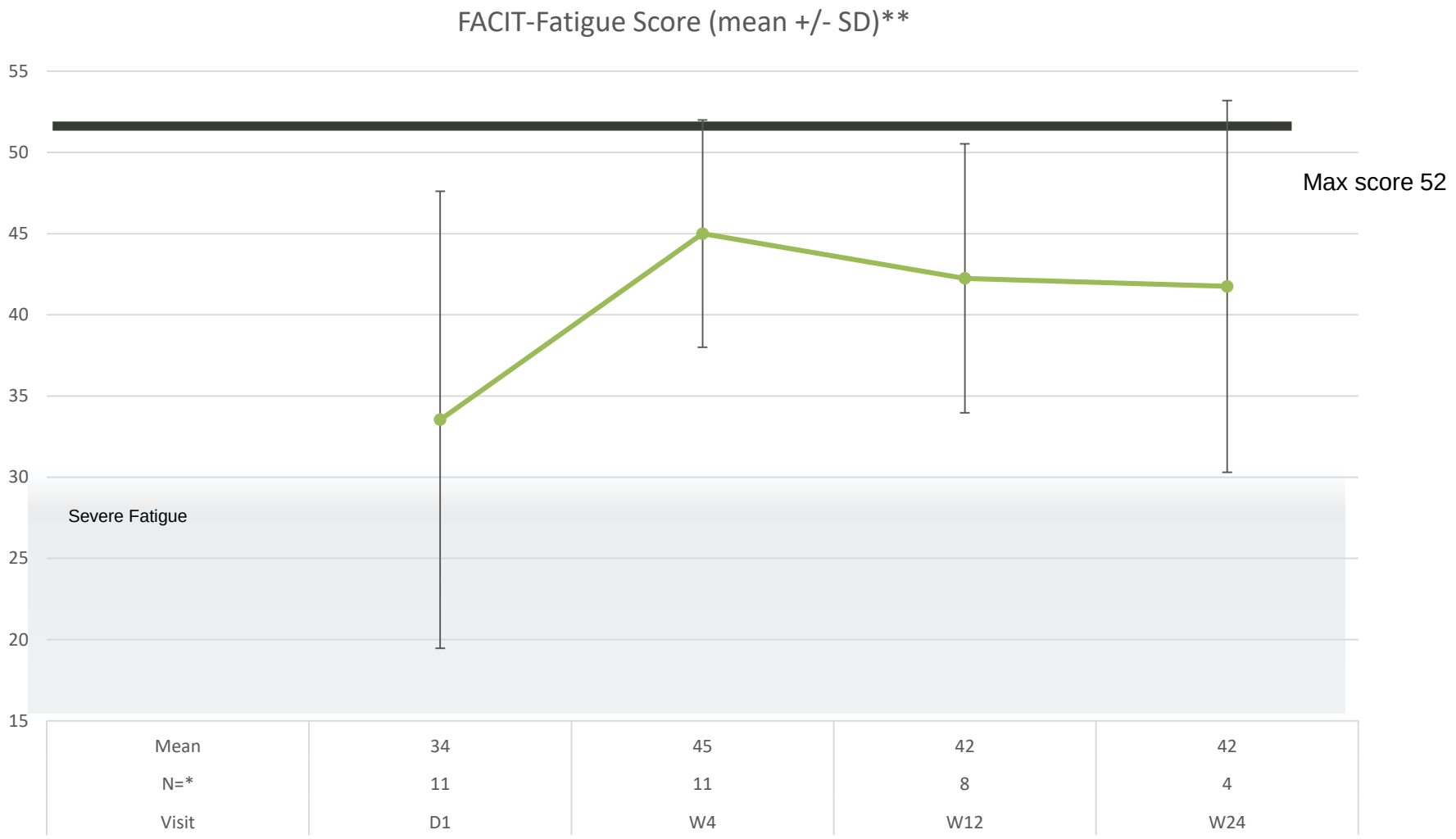
Further Reduction of LDH



Reduction of LDH into normal range versus baseline at week 24 (n=4)

*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019.

Improvement in FACIT- Fatigue Scale



*Subjects with data available at each timepoint. All 11 subjects continue to receive treatment with ACH-4471. Data as of 10 May 2019
**Scores based on the FACIT Fatigue Scale V4. Score range 0-52. A score of less than 30 indicates severe fatigue.

Clinically Meaningful Improvement in Quality of Life: FACIT-Fatigue Scale

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Treatment Emergent Adverse Events

Fifty-three unique TEAEs reported by 11 subjects (data cut-off 24 weeks)

- 51/53 (96%) were mild/moderate in severity
- 46/53 (87%) were determined to be unrelated to study drug

Treatment Emergent Adverse Events*	
Number of TEAEs	53
Number of Patients Reporting a TEAE	11 (100%)
MedDRA Preferred Term	**n (%)**
Headache	3 (27)
Abdominal pain	2 (18)
Contusion	2 (18)
Cough	2 (18)
Fatigue	2 (18)
Nasopharyngitis	2 (18)
Nausea	2 (18)
Oropharyngeal pain	2 (18)
Pain in extremity	2 (18)

* Reported by greater than 10% of patients.

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Treatment Emergent Adverse Events of Interest

Two patients each experienced a Grade 3/Severe TEAE:

- Grade 3 direct bilirubin elevation occurred in concert with a grade 1 ALT elevation at day 70
  - Both adverse events were resolved by Day 77
  - ACH-4471 dose was reduced temporarily from 150 mg TID to 100 mg TID and re-escalated after resolution
  - Investigator considered this to be breakthrough hemolysis as it was associated with an approximate doubling of LDH and decrease in Hgb of 0.8 mg/dL

- SAE of pneumonia occurred at Day 145 requiring hospitalization (recovered Day 152)
  - This pneumonia evolved from a case of viral bronchitis in a patient with a history of neutropenia
  - The patient received a transfusion of 2 units PRBC during the hospitalization
  - ACH-4471 dose was not changed

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Interim Data in Transfusion Dependent Eculizumab Patients Showed a Benefit from Combination Therapy with ACH-4471

- **Benefits observed in multiple laboratory parameters**
  - Mean rise in hemoglobin relative to baseline
  - Both total and direct bilirubin reduced into normal range
  - Marked reductions in reticulocyte count to near normal values
  - Further reduction of LDH into normal range
- **Reductions in transfusion and increase in patient reported outcomes**
  - Only 1 transfusion of 2 units of PRBC in 1 patient noted during combination therapy
    - Versus 34 transfusions totaling 58 units in 10 patients for the 24 weeks preceding screening
    - Meaningful improvement in the health-related quality of life FACIT fatigue scores versus baseline
- **Dose escalation and optimization are ongoing**
  - Majority of dose escalations occurred at or after week 12
- **Risk versus benefit profile favorable to date**
  - 96% of TEAEs were mild/moderate in severity and no patients discontinued treatment due to TEAEs
  - Two patients experiencing Grade 3 TEAEs had resolution of event and continued in trial
  - Other cell lineages not adversely affected (e.g. PLT, ANC)

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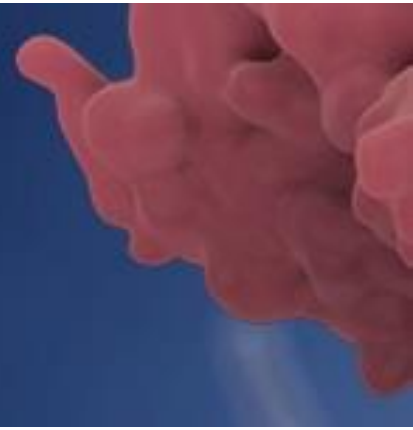
Potential Market Opportunity of ACH-4471 in Combination with C5 Inhibitors



Up to 75% of PNH Patients on Eculizumab Remain Anemic

Source & Periodical	# Patients in Study	% Anemic
McKinley et al, ASH Dec. 2017 ABS 3471	141	72%
Loschi et al: American Journal of Hematology 2016	123	72%
Risitano et al: Blood 2009(1)	41	75.6%(2)

Findings from interviews conducted with 14 US and EU KOLs in 2018 indicate that, on average, ~75% of patients on Eculizumab remain anemic or severely anemic(3)

1. Mean Hemoglobin was 10.5 g/dL across all Eculizumab-treated patients (n=41)
2. Extrapolated from data with Anemia defined as <12 g/dL
3. Achillion Data on File: 2018 PNH KOL Interviews US/EU (n=14)

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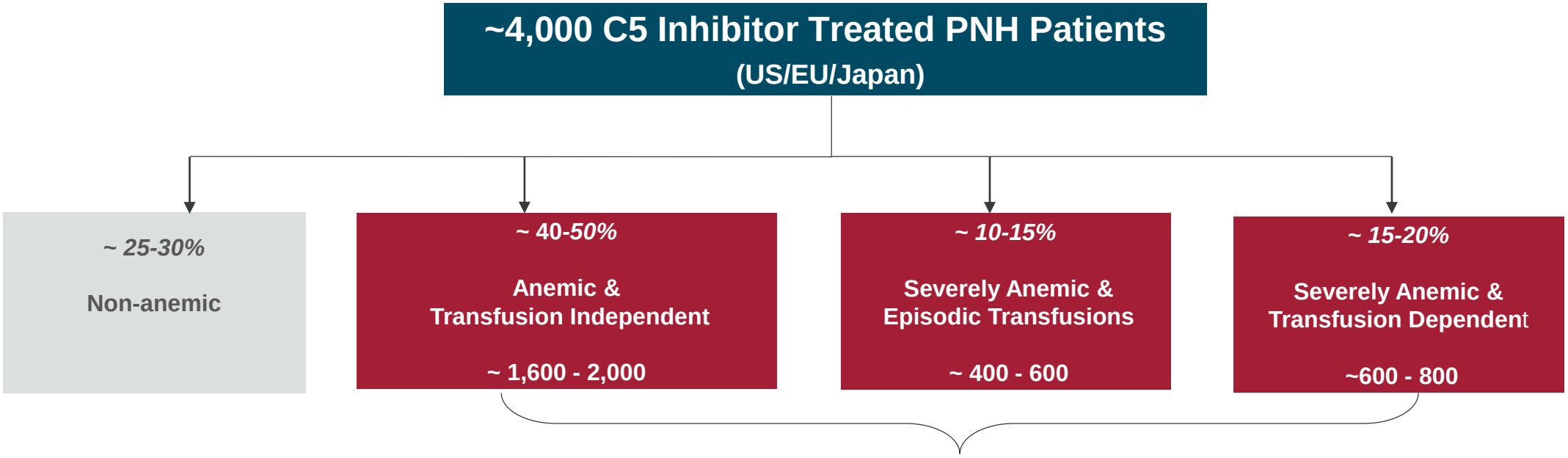
Market Opportunity for ACH-4471 Combination Therapy

PNH C5 Inhibitor Clinical Segmentation[1]



Up to 75% of patients remain anemic or severely anemic on C5 inhibition therapy.

Research shows C5 inhibitor PNH patients had variable amounts of C3 on their red cells demonstrating that some degree of extravascular hemolysis is seen.[2]

1. Source: ACHN Physician Interviews of 14 KOLs in US/EU 2018, McKinley et al, ASH Dec. 2017, Risitano et al: Blood 2009, Alexion SEC Filings & Wall St. Research
2. McKinley et al. ASH Dec. 2017

ACH-4471 Combination Therapy: Readily Accessible Market

- **Established market of C5 inhibitor patients identified in the US, EU and Japan**
  - Current C5 inhibitor treatment is an established approach to treatment

- **An Unmet Need: Blood transfusions and anemia are burden to patients**
  - Factor D inhibition plus C5 inhibition has the potential to significantly reduce the need for blood transfusions
  - Transfusions can have acute and long term risks including iron overload and red cell antibody production
  - Anemia can impact PNH patient's ability to carry out everyday activities due to fatigue, shortness of breath and exercise intolerance

- **Innovative approach to treat PNH patients on C5 inhibitors**
  - Impact of extravascular hemolysis is known: hemoglobin levels, reticulocyte counts, and fatigue scores
  - Combination development approach: possibility of improving outcomes where current treatment falls short

- **Oral 4471 combination treatment: minimal disruption to current C5 inhibitor administration**
  - Shown to address EVH while continuing to focus on IVH: potential complete treatment approach for PNH

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Our Planned Path Forward in PNH Therapy

1H 2019

- ✓ ACH-4471 PNH combination study w/eculizumab complete enrollment & targeting interim data for May 17, 2019 (n=11)
- ACH-4471 Study in Untreated PNH Patients Accepted for Oral Presentation at the 24th Congress of the European Hematology Association - June 15th 2019

2H 2019

- ACH-4471 PNH combination study w/eculizumab end of Phase 2 FDA meeting 2H 2019
- Targeting ACH-4471 PNH combination study w/eculizumab complete data set for Fall 2019 conference submission
- ACH-5228 submit IND in Q4 2019

1H 2020

- Target initiation of ACH-5228 PNH monotherapy switch extension study n=7 ex-US patients Q1 2020
- Target initiation of Phase 3 ACH-4471 PNH combination with C5 inhibitors

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