



ACHILLION

RESEARCH REALIZED

Second Quarter 2017 Results and Pipeline Update

Our Value, Our Science, Our Focus

August 8, 2017

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,” “may” and similar expressions to identify such forward-looking statements. These forward-looking statements are about Achillion Pharmaceuticals, Inc. and its business and prospects, including, without limitation, statements regarding drug discovery, research, clinical development, timing of anticipated clinical trials and clinical data for our product candidates, our expectations regarding the potential safety, efficacy and clinical utility for our product candidates, regulatory approval processes, market opportunities, strategic goals, our collaboration with Janssen in HCV, intellectual property, competition, and financial results. To the extent that statements contained in this presentation are not descriptions of historical facts, they are forward-looking statements reflecting management’s current beliefs and expectations.

Various important factors may cause differences between our forward-looking statements and actual results, including without limitation, unexpected or unfavorable safety or efficacy data, lower than expected enrollment rates in clinical trials, changes in the competitive landscape for our product candidates, changes in the regulatory environment, changes in market conditions or future demand for our drug candidates, the inability to protect our intellectual property, our freedom to operate under third party intellectual property, the risk that Janssen may not advance the HCV program in the time frames projected or at all, our need for future capital, the risk of litigation or other disputes, and general market and economic conditions. These and other risks and uncertainties are described in the reports filed by Achillion with the U.S. Securities and Exchange Commission (“SEC”), including its annual report on Form 10-K and quarterly reports on Form 10-Q, and subsequent filings with the SEC from time to time. You should read these reports, including the Risk Factors contained in these reports with the understanding that our actual future results may be materially different from what we expect.

All forward-looking statements contained in this presentation speak only as of the date hereof, and Achillion undertakes no obligation to update any of these statements, except as required by law.



ACH-4471: First-in-class Complement Inhibitor

GOALS FOR INITIAL CLINICAL DEVELOPMENT

- **Demonstrate proof-of-mechanism with a highly innovative approach**
 - Lack of C3 fragment deposition on PNH red blood cells
 - Reduction in plasma Bb levels
- **Demonstrate proof-of-concept by showing clinical efficacy**
 - Reduction in LDH
 - Increase in hemoglobin
 - Improvement in fatigue score (FACIT score)
 - Increase in PNH RBC clone size
- **Elucidate PK/PD**
 - Understand plasma concentrations of ACH-4471 necessary for potential efficacy
- **Acceptable safety and tolerability profile**

Early development program serves as a gateway to unlock broader potential of ACH-4471



Unlocking the Broader Potential of ACH-4471

PLANS FOR EXPANDING CLINICAL PROGRAM

● PNH

- Phase 2: Expand on-going monotherapy trial in untreated patients
- Phase 2: Add-on trial to support “switch-strategy” for patients with suboptimal response to eculizumab

● C3G & IC-MPGN

- Phase 2: 14-day dosing
- Phase 2: 6-month dosing with long-term dosing extension
- Natural history study: Ongoing study sponsored by Imperial College of London anticipated to enroll up to 400 patients globally

*Pioneer
“best-in-disease”
factor D inhibition
across multiple
indications*



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ACH-4471

Phase 2 PNH Three-month / Long-term Extension Trials

Interim Results and Next Steps



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Study Status and Interim Results

Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Enrollment:
4 to 12 pts

KEY INCLUSION / EXCLUSION CRITERIA

- PNH clone size $\geq 10\%$
- Anemia (Hgb < 12 g/dL)
- LDH $\geq 1.5X$ ULN
- ANC $\geq 1,000/mm^3$
- Platelets $\geq 50,000 \mu/L$
- Normal ALT
- Alk Phos $\leq 1.5X$ ULN

Objectives

- Change in **LDH** from baseline
- Improvements in **Hgb**, **FACIT**
- Increase **PNH RBC clone size**

Three-month Dose Finding

PATIENT D

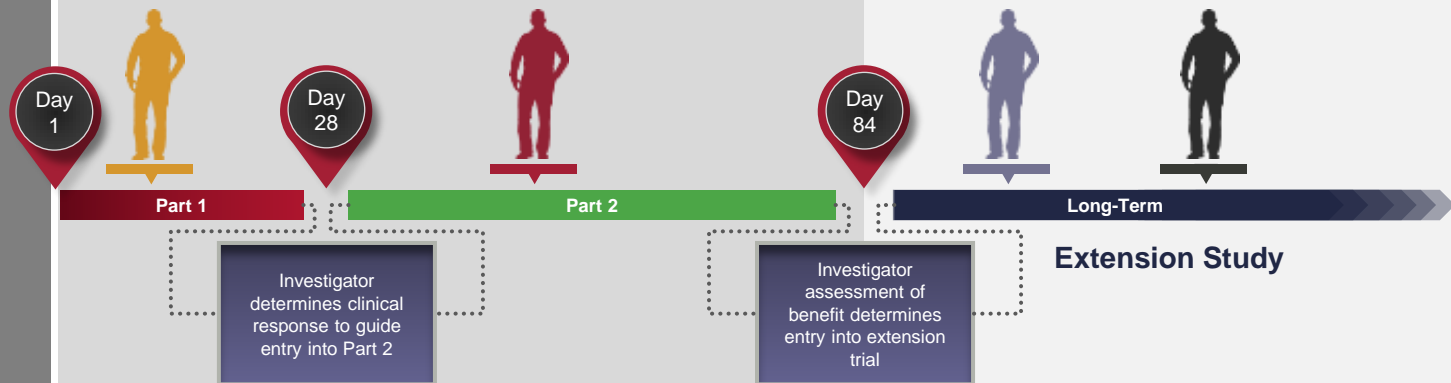
Classic PNH

Total days on therapy: 9
Days on 200mg TID: --

PATIENT C

Classic PNH

Total days on therapy: 44
Days on 200mg TID: 14



Long-term Extension

PATIENT B

Aplastic Anemia / PNH

Total days on therapy: 126
Days on 200mg TID: 33

PATIENT A

Classic PNH

Total days on therapy: 132
Days on 200mg TID: 40

Initial dose 100 mg TID. Protocol subsequently amended to allow:

- Newly enrolled patients to start at 150 mg TID
- Intra-patient dose escalation throughout both studies

Available data as of August 8, 2017.

Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Patient A: Classic PNH



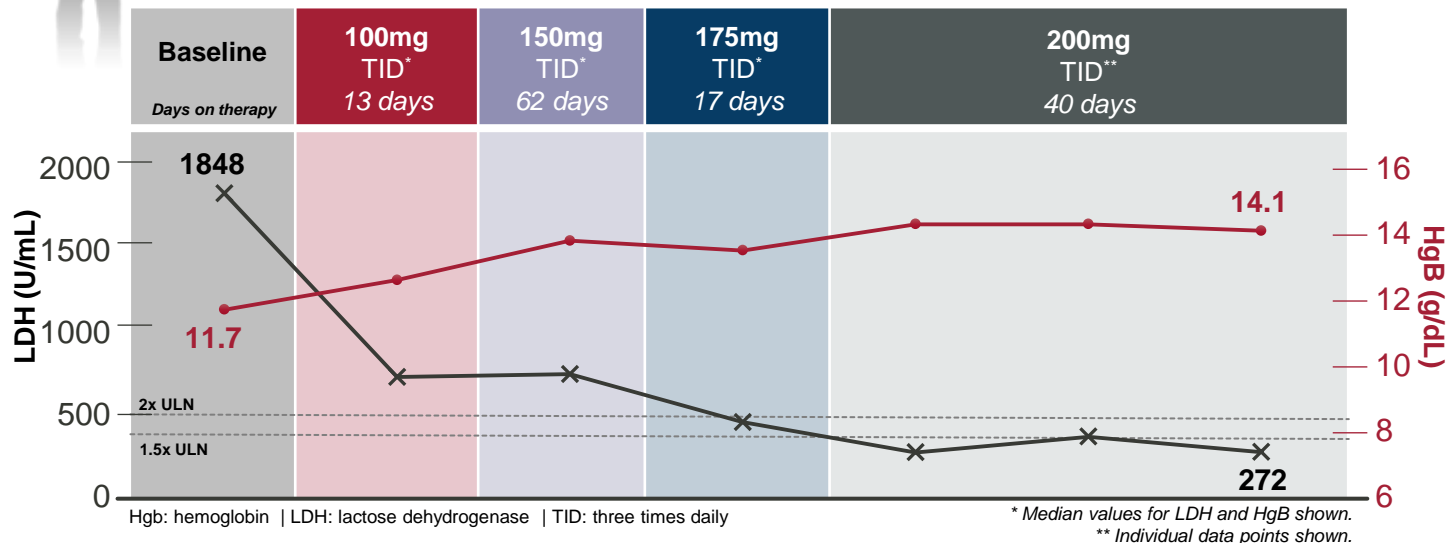
36-year-old male; diagnosed with PNH in 2011 after presentation with dermal thrombosis and hemolytic anemia

- Otherwise healthy with active lifestyle; no transfusion requirements at baseline

	HgB (g/dL)	LDH (U/L)	FACIT	PNH clone size (%)	C3 fragment deposition
Current Value	14.1	272	49	43	Negative
Baseline	11.7	1848	32	11	Negative

Status:

- Patient remains on 200 mg TID



Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Patient C: Classic PNH

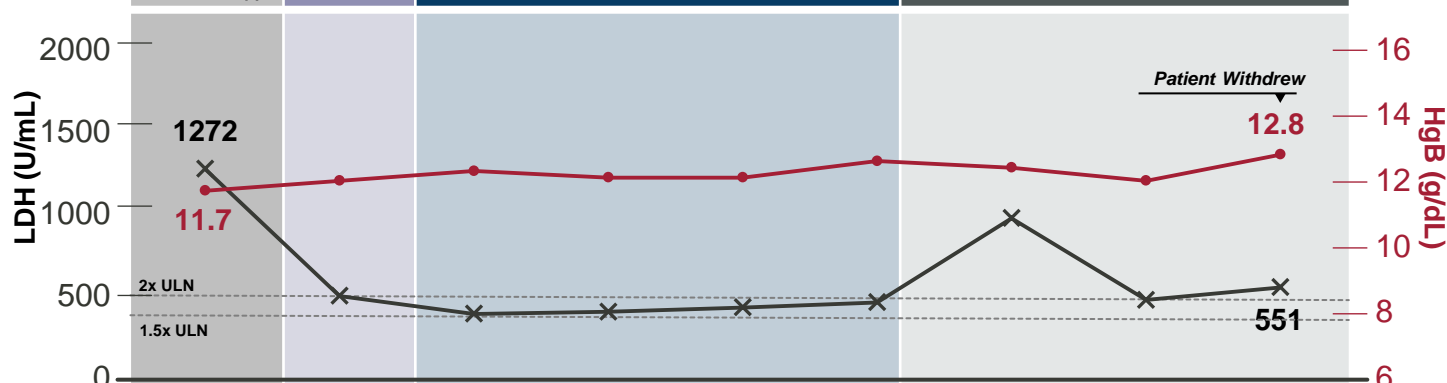


34-year-old male; diagnosed with PNH in 2003

- Otherwise healthy with active lifestyle; no transfusion requirements at baseline (BL)

	HgB (g/dL)	LDH (U/L)	FACIT	PNH clone size (%)	C3 fragment deposition
Current Value	12.8	551	36	43	Negative
Baseline	11.7	1272	23	24	Negative

Baseline	150mg TID* 13 days	175mg TID** 14 days	200mg TID** 14 days†
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Hgb: hemoglobin | LDH: lactose dehydrogenase | TID: three times daily
 † Patient began taper on day 41 following withdrawn consent.

* Median values for LDH and HgB shown.
 ** Individual data points shown.

Status:

- Patient reported non-compliance after initiation of 200 mg TID dose
- Patient voluntarily withdrew consent for reasons unrelated to safety on day 41



Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Patient D: Classic PNH

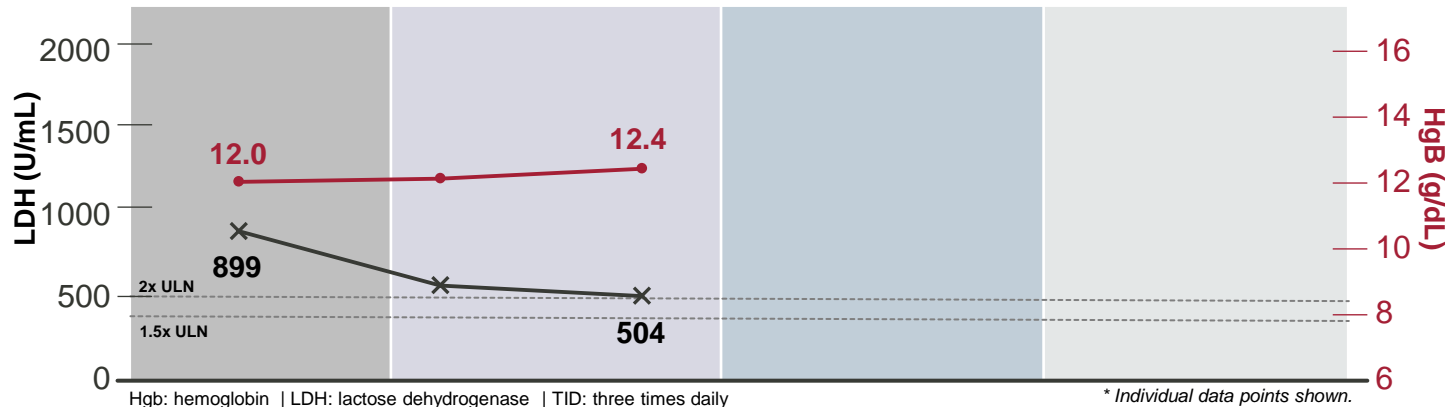


54-year-old male; diagnosed in 2012 with PNH

- No history of transfusion-dependence

	HgB (g/dL)	LDH (U/L)	FACIT	PNH clone size (%)	C3 fragment deposition
Current Value	12.4	504	n/a	n/a	n/a
Baseline	12.0	899	n/a	36	Negative

Baseline	150mg TID* 9 days	175mg TID --	200mg TID --
<i>Days on therapy</i>			



Hgb: hemoglobin | LDH: lactose dehydrogenase | TID: three times daily

* Individual data points shown.

Status:

- Patient recently enrolled
- Currently receiving 150 mg TID dose and will be evaluated for intra-patient dose escalation



Patient B: Aplastic Anemia PNH



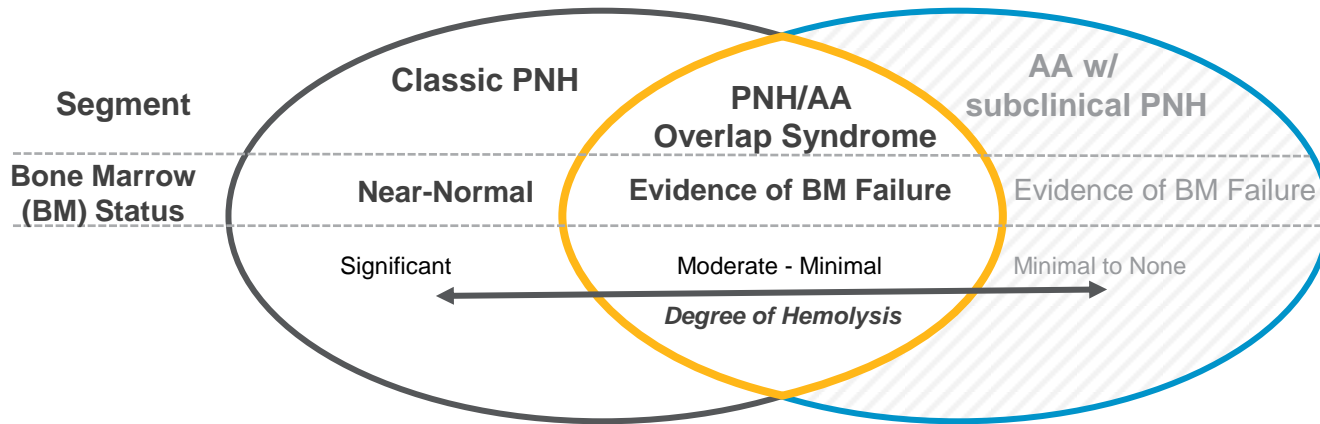
41-year-old male; diagnosed with AA in 2008; subsequently diagnosed with PNH in 2016

- Treated with ATG, oral prednisone and cyclosporine; ending in 2012
- Baseline marrow function: platelets range 30-60K, ANC 0.7-1.5 and requires Q3-4 weekly RBC transfusions to maintain HgB \geq 8 g/dL

	HgB (g/dL)	LDH (U/L)	FACIT	PNH clone size (%)	C3 fragment deposition
Current Value					
Baseline	7.5	941	22	20	Negative

Understanding PNH Classifications

Classic PNH vs. PNH + Aplastic Anemia (AA)



- Two most clinically overt presentations of PNH are:
 - Classic PNH: > hemolysis without bone marrow failure
 - AA: Overlap of both PNH and bone marrow failure
 - Both are associated with elevated risk of thrombosis, chronic kidney disease, and fatigue
 - Estimated 25% PNH patients have overlap



Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Patient B: Aplastic Anemia PNH

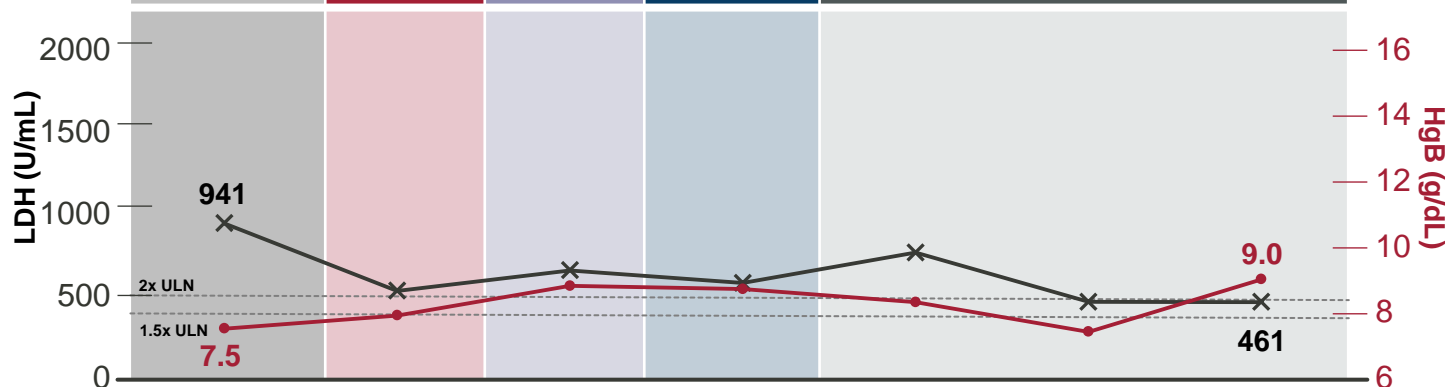


41-year-old male; diagnosed with AA in 2008; subsequently diagnosed with PNH in 2016

- Treated with ATG, oral prednisone and cyclosporine; ending in 2012
- Baseline marrow function: platelets range 30-60K, ANC 0.7-1.5 and requires Q3-4 weekly RBC transfusions to maintain Hgb \geq 8 g/dL

	Hgb (g/dL)	LDH (U/L)	FACIT	PNH clone size (%)	C3 fragment deposition
Current Value	9.0	461	31	36	Negative
Baseline	7.5	941	22	20	Negative

Baseline	100mg TID*	150mg TID*	175mg TID*	200mg TID**
Days on therapy	13 days	58 days	22 days	33 days



AA: Aplastic Anemia | Hgb: hemoglobin | LDH: lactose dehydrogenase
 ANC: absolute neutrophil count | TID: three times daily

* Median values for LDH and Hgb shown.
 ** Individual data points shown.

Status:

- Patient remains on 200 mg TID
- Patient continued to receive RBC transfusions during therapy



Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Summary of Interim Data

- ACH-4471 has been well tolerated with no SAEs. No clinically significant elevations in liver enzymes
- At 200 mg TID, clinically significant improvements observed include:
 - Improvements in hemoglobin:
 - 2.4 g/dL increase and a 1.1g/dL increase for the 2 classic PNH patients at dose of 200mg TID
 - Increase in PNH type III RBC clone size
 - Clinically meaningful reductions in LDH
 - Patient interviews and increase in objective fatigue scores show meaningful improvements in well being
- No evidence of C3 fragment deposition on PNH RBCs
- Increases in clone size demonstrated PNH RBC protection from hemolysis
- Sustained decreases in plasma Bb level indicated targeted inhibition of factor D (data not shown)



Unlocking the Broader Potential of ACH-4471

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● PNH

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● C3G & IC-MPGN

- Phase 2: 14-day dosing
- Phase 2: 6-month dosing with long-term dosing extension
- Natural history study: Ongoing study sponsored by Imperial College of London anticipated to enroll up to 400 patients globally

Interim results generated with ACH-4471 have been shared with regulatory agencies in order to support planned expansion of PNH and C3G programs



Measures of Clinical Efficacy & Safety in PNH

✓	Lactose dehydrogenase (LDH)	GOAL Clinically meaningful reduction in LDH
✓	Hemoglobin (Hgb)	GOAL Stabilize / increase hemoglobin
✓	C3 fragment deposition	GOAL Observe no C3 fragment deposition on PNH RBCs
✓	Fatigue (FACIT scale)	GOAL Improvement over time in objective measures of patient fatigue
✓	PNH RBC Clone Size	GOAL Increase percentage of PNH RBC clones from baseline
✓	Safety	GOAL Good tolerability profile

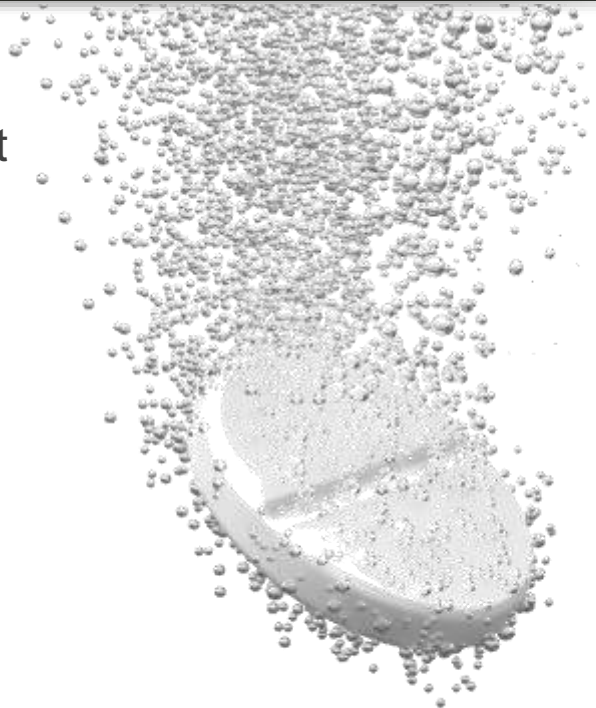
Clinical data generated to date highlight the potential role of factor D inhibition in PNH



Extended-Release Activities for ACH-4471

ONGOING EXTENDED-RELEASE (XR) FORMULATION

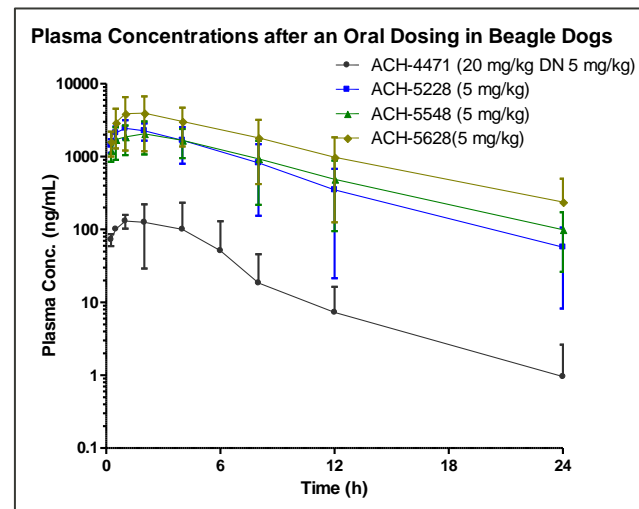
- **Objective** Develop an extended release tablet formulation to allow for:
 - Optimized trough exposures
 - Reduced dosing frequency
- ACH-4471 has high permeability with animal and modeling data reporting good absorption throughout the GI tract
- Human bioavailability study for extended release tablet is planned for 4Q 2017



ACH-5228: Next-Generation Oral Factor D Inhibitor

- Next-generation factor D inhibitor platform can be leveraged to create additional strategic options for value creation
- Structure alteration in next-generation factor D inhibitors target improvements in potency and pharmacokinetic properties
- ACH-5228: GLP studies are on-going with goal of initiating clinical studies in 4Q17

Compound ID	AP Hemolysis	
	IC ₅₀ (nM)	IC ₉₀ (nM)
ACH-4471	22	90
ACH-5228	9	34
ACH-5548	5	14
ACH-5628	17	75
ACH-5931	7	17

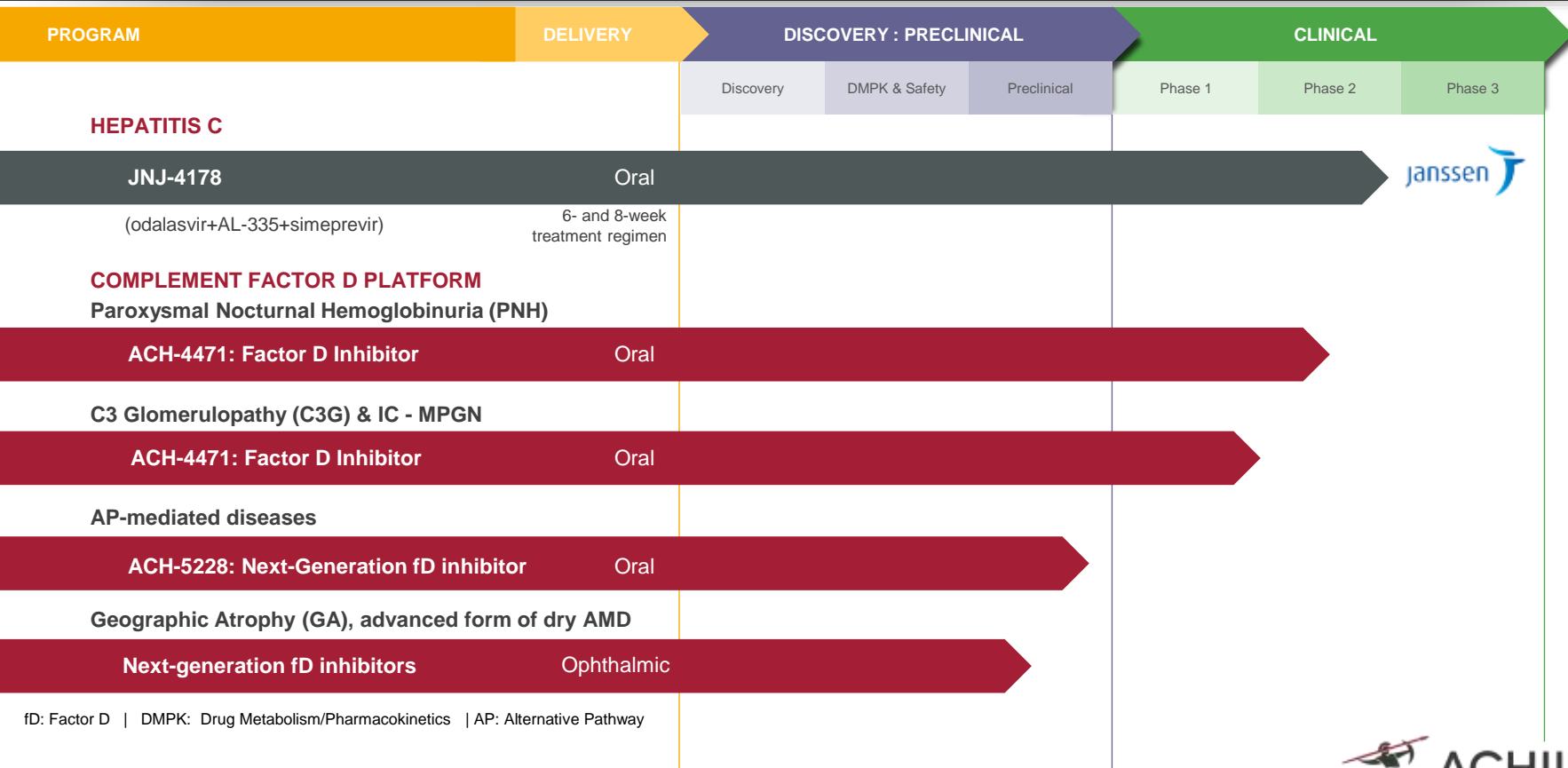


Factor D Inhibitors in Ophthalmological Disease



- Geographic Atrophy (GA) is an advanced form of dry Age-related Macular Degeneration (dry AMD)
- GA is a leading cause of impaired vision and blindness that affects more than 2.6 million people in US & EU and more than 5 million world-wide
- Factor D is a validated target as demonstrated by Genentech's lampalizumab program
 - Phase 3 trial with lampalizumab underway evaluating intra-vitreous injections every 4 or 6 weeks
- Achillion is targeting treatment duration of 3 months or longer with diverse small molecule factor D inhibitors
 - Four diverse compounds and distinct delivery approaches are advancing this year with the goal of initiating IND enabling studies in 2018

Achillion Development Portfolio



fD: Factor D | DMPK: Drug Metabolism/Pharmacokinetics | AP: Alternative Pathway



Financial Summary: Capitalization and Ownership

Balance Sheet Metrics	As of 6/30/2017
Cash, cash equivalents, marketable securities and interest receivable	\$369.9 million
Debt obligations	\$0.5 million
Shares outstanding	136.8 million
Top Shareholders†	Position
Johnson & Johnson Development Corp.	18.4 million (13%)
RA Capital	13.6 million (10%)
Orbimed Advisors	13.1 million (10%)
Blackrock, Inc.	9.9 million (7%)
Vanguard Group	9.6 million (7%)
Janus Capital Management	4.4 million (3%)
State Street Global Advisors	4.3 million (3%)
Goldman Sachs & Co.	3.7 million (3%)
Biotechnology Value Fund (BVF)	3.3 million (2%)
Numeric Investors	3.0 million (2%)

† Based upon most recent SEC filings.



Strength to Achieve our Goals

Near-term Development Plan

Compound	Indication	Next steps
ACH-4471	PNH	Phase 2: Expand on-going monotherapy Phase 2: Add-on trial to support “switch strategy” for suboptimal responders
	C3G & IC-MPGN	Phase 2: 14-day dosing Phase 2: Long-term (6-month dosing)
	Extended Release Tablet	Phase 1 Bioavailability
ACH-5228	AP-mediated diseases <i>(acute/chronic)</i>	Phase 1 SAD/MAD
Ophthalmology	Geographic Atrophy	Complete Preclinical Assessment



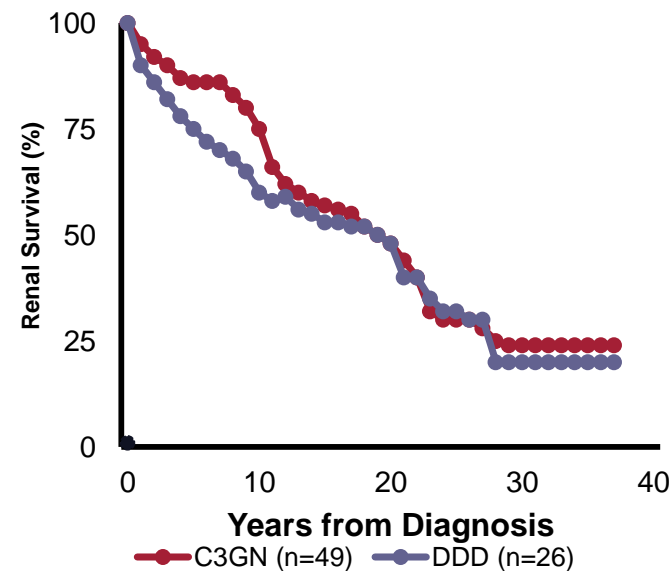
\$369.9 million in cash, cash equivalents, and interest receivable to support expansion

HCV: worldwide collaboration with Janssen for JNJ-4178

A Rare Disease with No Available Treatment

- C3G includes both **Dense Deposit Disease (DDD)** and **C3 glomerulonephritis (C3GN)**
- Estimated prevalence of **8–12 people affected per million in major markets**
 - Incidence rate of 1–2 per million patients diagnosed with C3G on an annual basis
- There are **no approved treatments** for patients with C3G
 - Non-specific treatment approaches include blood pressure control and broad immunosuppression
- Significant unmet medical need as nearly half of **C3G patients progress to end-stage renal disease**
 - 30-50% progress to ESRD within 10 years
 - ~70% of patients experience disease recurrence post renal transplant, with a 50% chance of graft loss

DDD AND C3GN
IMPACT ON RENAL SURVIVAL



Barbour et al. (2015); NICE C3G Evidence Summary (2015);

Patient-Focused Drug Development (PFDD) Meeting

- Achillion was lead sponsor of externally-led PFDD meeting focused on C3G
 - First renal disease discussed at a PFDD meeting on August 4, 2017
- Led by the National Kidney Foundation
- Goal is to understand the patient perspective of their disease
 - PFDD meeting provides an important opportunity to us and to the FDA to hear directly from patients / caregivers
 - Understand the impact of the disease on patients' daily lives
 - Input may inform FDA's decisions throughout the drug development process
- Patient experiences shared at the meeting highlight the unmet need and the urgency to develop transformative therapies



Q&A



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