Orphan Focused
Patient Driven

May 2018
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Vision

- Orphan Drug Company
- Patients in the Center of our Plan
- Retain and Commercialize our factor D Inhibitors
- Laser Focus on Execution
## Complement Factor D Portfolio

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<th>PROGRAM</th>
<th>INDICATION</th>
<th>DELIVERY</th>
<th>PRECLINICAL</th>
<th>CLINICAL</th>
<th>MILESTONES</th>
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<td>ACH-4471</td>
<td>Factor D Inhibitor</td>
<td>Oral</td>
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<td>C3G: 14-day proof-of-concept biomarker trial</td>
<td>Interim 14-day data 3Q18</td>
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<td>C3G: 12-month open-label therapeutic trial</td>
<td>Data in 2019</td>
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<td>C3G: 6-month randomized, double-blind trial</td>
<td>Interim data 4Q18</td>
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<td>PNH: Monotherapy open-label untreated PNH</td>
<td>Interim data 4Q18</td>
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<td>AP-mediated diseases</td>
<td>Interim data in 2H18</td>
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<td>Initiate Ph 1 in 2Q18</td>
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Achillion: Factors for Success

- First-in-class pipeline for complement AP-mediated rare diseases
- Strong market opportunities for fD inhibitor portfolio
- Patient-focused and experienced management team
- $308M at 3/31/18 to support multiple value infection points
ACH-4471 Summary

- C3G Proof of Concept
  - Biomarkers
  - Proteinuria

- PNH Proof of Concept
  - LDH, hemoglobin, and FACIT scores
  - Two patients have been dosed for greater than one year
  - Well-tolerated to date

- Phase I Program
  - Multiple DDI, ADME, and support studies completed
  - >150 healthy volunteers dosed
  - Completing renal-impairment study

- Toxicology Program
  - 6 and 9 month studies completed and support continued development

- Regulatory
  - Support from regulatory agencies for Phase II program in C3G and PNH
Intellectual Property

Broad IP footprint

- IP filings support platform strategy to pursue distinct NCEs for specific drug delivery options and for disease groups
- Currently 9 issued U.S. patents owned solely by Achillion
- 18 additional COM patent applications published March 2017
  - Represent the first three waves of patent applications filed by Achillion to cover new complement factor D inhibitors and uses.
- Aggressively protecting our complement factor D assets
  - Filed multiple additional non-provisional patent applications
Mechanism Matters: Factor D Inhibition

Factor D is a critical control point specifically within the AP (Alternative Pathway). It inhibits the TRIGGER POINT INHIBITOR, preventing amplification and modulating downstream complement cascade.

**Classical Pathway**
- C1q, C1r-C1s
- C4a, C2a, C2b
- C3b
- C3a
- C3bB

**Lectin Pathway**
- MBL, MASP-1-2
- C4b2a
- C3bBb
- C3a

**Alternative Pathway**
- C3b
- C3(H2O) B
- C3b
- C3(H2O) Bb

**Terminal Pathway**
- C5b-9

**FACTOR D**
A critical control point specifically within the AP

**TRIGGER POINT INHIBITOR**
Prevents amplification and modulates downstream complement cascade
C3 Glomerululopathy (C3G)

Rare Kidney Disease Associated with AP Hyperactivity
C3 Glomerulopathy
A Rare Disease with No FDA-Approved Treatment

Significant unmet medical need as nearly half of C3G patients progress to end-stage renal disease

- C3G caused by dysregulation of the complement system, leading to deposition of C3G fragments on the kidney
- 30–50% progress to ESRD within 10 years
- Significant disease burden at onset — inflammation, profound fatigue and weakness
- Greater than 50% of patients experience disease recurrence post renal transplant, with a 50% chance of graft loss
C3 Glomerulopathy

Patients Need Effective Treatments that Address Root Cause

- Significant physical and emotional toll on patients including:
  - Hypertension and edema
  - Susceptibility to infection
  - Anxiety and depression from uncertainty regarding progression

- No approved therapies to treat disease and limited therapies to address edema and fatigue

- Urgent need for disease-modifying treatment to maintain kidney function in native or transplanted kidneys, not just address symptoms
Pillars of Achillion’s Patient-Focused Support
Moving beyond the Pill

C3G Patient-focused Drug Development
• First PFDD meeting focused on a renal disease led by the NKF with FDA participation
• Sponsored by Achillion
• Goal was to understand the patient experiences and perspective

WeC3G patient support initiative
• Unites voices of community impacted by disease
• Connects patients and caregivers to each other and to information, support and resources that can shine the light on C3G
• Raises awareness and understanding

Natural history study:
• Ongoing study conducted by Imperial College of London in up to 400 patients globally
• Tracks natural course of disease over 4 years

Achillion is a uniting force working to expand our awareness and understanding of C3G and patient needs

May 2018
**NORMAL KIDNEY HISTOLOGY**

**NORMAL GLOMERULAR FUNCTION**
- No Proteinuria
- Normal GFR
C3G DISEASE HISTOLOGY

C3G is a DISEASE of DEPOSITION
Results in abnormal glomerular function
- Proteinuria
- Reduced GFR

C3G DISEASE HISTOLOGY
ACH-4471
C3G: Phase 2 Clinical Development Program

Interim Data and Next Steps
C3 Glomerulopathy

Phase 2 14-Day Trial in Patients with C3G

Clinical Trial Design

**Group 1:** 2 patients received ACH-4471 100mg TID x 14 days followed by 7-day taper.

**Group 2:** Up to 8 additional patients to receive ACH-4471 200mg TID x 14 days followed by 7-day taper.

Criteria

Must have confirmed diagnosis of C3G

C3 must be <50% LLN with C4 >90% LLN

Estimated glomerular filtration rate cannot be < 45 ml/min/1.73m²

Outcome Measures

Changes in biomarkers of alternative pathway activity (AP) including:

- C3 fragments and intact C3 levels, Bb, and Ba

Proteinuria

Pharmacokinetic profiles

Clinical Trial Status

✓ Group 1: Complete
○ Group 2: Ongoing
Phase 2 14-day Trial in Patients with C3G

**Baseline Characteristics**

**Patient A: Adult male with C3G; diagnosed in March 2017**

- **Key concomitant medications**
  - Prednisolone
  - Mycophenolate
  - Enalapril
  - Spironolactone

- **Disease characteristics at baseline:**
  - Proteinuria: Albumin to Creatinine ratio (ACR) 259.3 mg/mmol
    (ref range: 0 – 2.5)
  - Fragment: Intact C3 ratio: 0.1692
    (ref range: 0.0085 – 0.0949)

**Patient B: Adult male with nephrotic syndrome; diagnosed with C3G in November 2016**

- **Key Concomitant medications:**
  - Irbesartan
  - Spironolactone

- **Disease characteristics at baseline:**
  - Proteinuria: Albumin to Creatinine ratio (ACR) 580.3 mg/mmol
    (ref range: 0 – 2.5)
  - Fragment: Intact C3 Ratio: 0.1775
    (ref range: 0.0085 – 0.0949)
Phase 2 14-day Trial in Patients with C3G

Patient A: Biomarker Improvements

- Improvement in fragment:intact C3 ratio observed during dosing
- Mechanistic approach facilitates ability to address root cause of AP-mediated diseases

Additional biomarkers improvements observed:
- 30% reduction in Bb level as compared to baseline
- Improvement in complement proteins in the kidney
- 4.4-fold improvement in Ba:creatinine ratio over baseline

- Decreased Ba levels, resulting from inhibited cleavage of factor B by factor D
- Lower levels of Ba suggest lower levels of C3 convertase that would result in fewer C3 fragments
Phase 2 14-day Trial in Patients with C3G

Patient A: Significant Reduction in Proteinuria Observed

Time-dependent decrease observed in proteinuria as measured by ACR

Greater than 50% reduction achieved during 14 days of treatment

ACH-4471 demonstrated potential early signs of clinical benefit
Phase 2 14-day Trial in Patients with C3G

Patient B: Biomarker Improvements

- Improvement in fragment:intact C3 ratio observed during dosing
- Mechanistic approach facilitates ability to address root cause of AP-mediated diseases

Additional biomarkers improvements observed:
- 50% reduction in Bb as compared to baseline
- Improvement in complement proteins in the kidney after dosing with ACH-4471
- Observed an 18.6-fold improvement in Ba:creatinine ratio over baseline

- Decreased Ba levels, resulting from inhibited cleavage of factor B by factor D
- Lower levels of Ba suggest lower levels of C3 convertase that would result in fewer C3 fragments
Phase 2 14-day Trial in Patients with C3G

Patient B: Significant Reduction in Proteinuria Observed

Time-dependent decrease observed in proteinuria as measured by ACR

Greater than 50% reduction achieved during 14 days of treatment

ACH-4471 demonstrated potential early signs of clinical benefit
Clinical Efficacy & Safety for C3G

<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>Description</th>
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<tbody>
<tr>
<td>Proteinuria</td>
<td>Reduced by over 50%</td>
</tr>
<tr>
<td>Inhibition of C3 Cleavage</td>
<td>Reduced Fragment vs Intact C3 Ratio</td>
</tr>
<tr>
<td>Inhibit AP C3 Convertase Formation</td>
<td>In vivo Bb Reduction in Plasma</td>
</tr>
<tr>
<td></td>
<td>Ex vivo Inhibition of Ba production</td>
</tr>
<tr>
<td>Safety</td>
<td>Well-tolerated – No SAEs, discontinuations due to AEs</td>
</tr>
</tbody>
</table>

- **PoC established with 100 mg TID**
  - Preliminary POC established with 50% improvement in proteinuria
  - AP inhibition confirmed based on changes in complement biomarkers

- **Next steps**
  - Evaluating 200 mg TID ACH-4471 in Group 2
  - Actively screening to enroll up to eight patients with C3G

Clinical data generated to date highlight the potential role of factor D inhibition in C3G
C3G Program Accomplishments

ACH-4471 was safe and well-tolerated
• No SAEs or AEs of note. Well tolerated both on-treatment and post-cessation.

Established PoC
• POC established with 50% improvement in proteinuria
• AP inhibition confirmed based on changes in complement biomarkers

Regulatory Status
• Open U.S. FDA INDs for C3G and PNH
• Orphan drug designation for C3G
• Regulatory discussions for Ph 2 design and potential pivotal endpoints

Ongoing Clinical Studies
Phase 2: Evaluating 200 mg TID ACH-4471 for 14-days – Data 3Q18
Phase 2: 12-month Open Label Trial – Data 4Q18
Phase 2: 6-month Randomized Double-Blind Trial – Data 2019
Paroxysmal Nocturnal Hemoglobinuria (PNH)

Rare Disease Characterized by Destruction of Red Blood Cells by the AP
Achillion PNH Strategy

Patient Perspective
- 25% to 40% of PNH patients still experience a sub-optimal response on standard of care
- Market research shows
  - Strong desire for oral therapy
  - 20% of patients currently decline therapy

PNH Strategy
- Evaluate data from naïve and sub-optimal C5 responders in 4Q 2018
- Determine go-forward development plan post data

Sources: Achillion. Data of file.
PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)
Factor D and Potential Protection from Intra- & Extra-vascular Hemolysis

Type III PNH erythrocytes

No treatment

Intra-vascular hemolysis

Anti-C5 therapy
C3 fragment deposition

Breakthrough and Extra-vascular hemolysis
C3 fragment opsonization via RES macrophages (liver, spleen)

Protected Type III PNH erythrocytes

PNH RBCs treated with a fD inhibitor may be protected from both intra- and extra-vascular hemolysis

Adapted from Luzzatto L, Risitano AM, Notaro R. Haematologica 2010;95(4):523–526.
Study Status and Interim Results
Phase 2 Trial of ACH-4471 in Untreated PNH Patients

Enrollment: 4 to 12 pts

Three-month Dose Finding

Day 1

Part 1

Day 28

Part 2

Day 84

Long-term Extension

Investigator determines clinical response to guide entry into Part 2

Investigator assessment of benefit determines entry into extension trial

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

Trial Summary to Date

- Two patients on therapy for greater than one year, one patient beyond eight months
- Well-tolerated to date
- Continue to screen and enroll untreated PNH patients

KEY INCLUSION / EXCLUSION CRITERIA
- PNH clone size ≥ 10%
- Anemia (Hgb < 12 g/dL)
- LDH ≥ 1.5X ULN
- ANC ≥ 1,000/ mm³
- Platelets ≥ 50,000 μL
- Normal ALT
- Alk Phos ≤ 1.5X ULN

Objectives
- Reduction in LDH from baseline
- Improvements in Hgb, FACIT
- Increase PNH RBC clone size

Hgb: hemoglobin  | LDH: lactose dehydrogenase|
ANC: absolute neutrophil count | ALT: alanine aminotransferase | TID: three times daily

Corporate Overview
Clinical Efficacy & Safety Data for PNH

<table>
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<tr>
<th></th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Lactose dehydrogenase (LDH)</strong></td>
<td>Clinically meaningful reduction in LDH</td>
</tr>
<tr>
<td><strong>Hemoglobin (Hgb)</strong></td>
<td>Stabilize / increase hemoglobin</td>
</tr>
<tr>
<td><strong>C3 fragment deposition</strong></td>
<td>Observe no C3 fragment deposition on PNH RBCs</td>
</tr>
<tr>
<td><strong>Fatigue (FACIT scale)</strong></td>
<td>Improvement over time in objective measures of patient fatigue</td>
</tr>
<tr>
<td><strong>PNH RBC Clone Size</strong></td>
<td>Increase percentage of PNH RBC clones from baseline</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>Favorable tolerability profile</td>
</tr>
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</table>

Clinical data generated to date highlight the potential role of factor D inhibition in PNH.
Phase 2 Trial of ACH-4471 with eculizumab in PNH Sub-optimal Responders

Clinical Trial Design
Open-label study of ACH-4471 with eculizumab

Duration: Six-months of combination treatment

Criteria
Confirmed diagnosis of PNH and on stable dose of eculizumab
Persistent anemia and continued transfusion requirements

Outcome Measures
Change in hemoglobin compared to baseline
Number of units of RBCs during treatment period
Change in LDH compared to baseline

Clinical Trial Status
- Enrollment beginning 1H18
- Interim data targeted 4Q18
Next-Generation fD Inhibitors

An Expanding Portfolio of Candidates for Complement-mediated Diseases
Advancing additional fD inhibitors in the clinic

Creating strategic options for value creation

Structural alterations designed to achieve significant improvements in potency and pharmacokinetic properties

**ACH-5228**
Phase I single-ascending dose HV study initiated in December 2017

**ACH-5548**
Phase I single-ascending dose HV study targeted for initiation 2Q 2018
First-in-class pipeline for complement AP-mediated rare diseases

Strong market opportunities for fD inhibitor portfolio

Patient-focused and experienced management team

$308M at 3/31/18 to support multiple value infection points
## 2018 Goals and Milestones

### Near-term ACH-4471 Clinical Development Plan

<table>
<thead>
<tr>
<th>Compound</th>
<th>Indication</th>
<th>Anticipated Next steps</th>
</tr>
</thead>
</table>
| ACH-4471 | C3G        | • 14-day Ph 2 Group 2 interim data 3Q18  
            |            | • 12-month open label Ph 2: Interim data targeted 4Q18  
            |            | • 6-month randomized double-blind C3G Ph 2: Full enrollment anticipated YE18  |
| PNH      |            | • Monotherapy Ph 2: Interim data targeted 4Q18  
            |            | • Add-on trial Ph 2: Interim data targeted by 4Q18  |

<table>
<thead>
<tr>
<th>Next-Gen Compound</th>
<th>TBD</th>
<th>Interim Ph 1 data targeted 2H18</th>
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</thead>
</table>

| ACH-5548 | TBD | Initiate Ph 1 in 2Q18 |

$308$ million in cash, cash equivalents, and interest receivable at 3/31/18 to support execution on factor D inhibitor program
Corporate Overview

May 2018