APELLIS R&D DAY
June 30, 2021

AND THEY’RE OFF!
Welcome!

Cedric Francois, M.D., Ph.D.
Chief Executive Officer
Apellis Pharmaceuticals
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. These statements include, but are not limited to, statements relating to the implications of preliminary clinical data. 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 the company’s clinical trials will be fully enrolled and completed when anticipated; 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 pegcetacoplan will successfully advance through the clinical trial process on a timely basis, or at all; whether the results of the company’s clinical trials will warrant regulatory submissions and whether pegcetacoplan will receive approval from the FDA or equivalent foreign regulatory agencies for GA, PNH, CAD, C3G, IC-MPGN, ALS or any other indication when expected or at all; 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 April 28, 2021 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.
<table>
<thead>
<tr>
<th>Name</th>
<th>Disclosures</th>
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<tbody>
<tr>
<td><strong>Bruno Fattizzo, M.D.</strong></td>
<td>Consultancy honoraria: Alexion, Amgen, Apellis, Momenta, and Novartis</td>
</tr>
</tbody>
</table>
| **Angela Genge, M.D.**        | Executive director CRU Montreal Neurological Institute and ALS center of Excellence  
On Advisory boards of following companies: Alexion, Apellis, AL-S Pharma, ArgenX, Biogen, Amylyx, Calico, UCB, Roche, Sanofi, Regeneron, UCB, MTPA  
On DSMB:AZT therapeutics, Clene  
Consulting CMO: Quralis  
Chair Scientific Advisory Committee of CATALIS |
| **Nancy M. Holekamp, M.D.**   | Consultant: Allergan, Acucela, Apellis, Bayer, Lineage Cell Therapeutics, Clearside Biosciences, Gemini, Genentech, Gyroscope, Katalyst Surgical, Nacuity, Notal Vision, Novartis, Polyactiva, Regeneron  
• **Speakers Bureau:** Allergan, Genentech, Novartis, Regeneron, Spark  
• **Contracted Research:** Genentech, Gemini, Gyroscope, Notal Vision  
• **Intellectual Property/Patent:** Katalyst Surgical |
| **Matthew Pickering, Ph.D., M.B., B.S.** | Apellis Pharmaceuticals, Alexion Pharmaceuticals, Gemini Therapeutics, Gyroscope Therapeutics |
| **Ilene Weitz, M.D.**         | Honoraria, consultancy: Alexion, Apellis  
Speakers bureau: Alexion |
Disclosures

**Charles Wykoff, M.D., Ph.D.**


*Research:* Adverum, Aerie Pharmaceuticals, Aldeyra, Alimera Sciences, Allergan, Amgen, Apellis, Asclepix, Bayer, Boehringer Ingelheim, Chengdu Kanghong Biotechnology, Clearside Biomedical, Gemini, Genentech, Graybug Vision, Gyroscope, IONIS Pharmaceutical, iRENIX, IVERIC bio, Kodiak Sciences, LMRI, Neurotech Pharmaceuticals, NGM Biopharmaceuticals, Novartis, Oxurion, RecensMedical, Regeneron, RegenXBio, Roche, SamChunDang Pharm, Taiwan Liposome Company, Xbrane BioPharma

*Ownership/Stock:* ONL Therapeutics, PolyPhotonix, RecensMedical, Visgenx

**Apellis / Sobi Collaboration**

Sobi has global co-development and ex-U.S. commercialization rights for systemic pegcetacoplan
Growing Our Pipeline for Long-Term Leadership in Complement

Transforming Treatment across Rare, Complement-Driven Diseases

Be #1 in the Retina

Building a Portfolio of Brain-Active Complement Therapies

APELLIS: Global Leader in Complement

RARE DISEASE

NEUROLOGY

OPHTHALMOLOGY
Global Leader in Complement, Today and Tomorrow

**RARE DISEASE**

- EMPAVELI™ (pegcetacoplan) launch off to strong start
- Platform potential for EMPAVELI with four new registrational programs
- New molecular entities in development to sustain long-term growth in existing and new indications

**NEUROLOGY**

- C3 plays a key role in a wide range of neurodegenerative conditions
- Apellis to pioneer targeted C3 therapies in neurodegeneration

**OPHTHALMOLOGY**

- Optimistic heading into DERBY and OAKS readout in September 2021
- Significant unmet need and blockbuster opportunity
- New molecular entities in development in GA, wet and intermediate AMD
APPELLIS R&D DAY

Transforming Treatment across Rare, Complement-Driven Diseases

Victoria Brown
Senior Vice President, Rare Disease Program Executive
Apellis Pharmaceuticals

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Transforming Treatment Across Rare, Complement-Driven Diseases
Transforming Treatment Across Rare, Complement-Driven Diseases

Establish EMPAVELI in PNH
- Ensure access for adults with PNH

Expand Rare Disease Portfolio
- Advance four additional registrational programs

Enhance Patient Experience & New Indications
- Launch Enable device
- Develop siRNA + EMPAVELI
- Develop oral alternative pathway inhibitor
Transforming Treatment Across Rare, Complement-Driven Diseases

**Establish EMPAVELI in PNH**
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Paroxysmal Nocturnal Hemoglobinuria (PNH)

David Acheson
Senior Vice President, North America Commercial
Apellis Pharmaceuticals
U.S. Launch Priorities Driving Strategic Activities

- Ensure EMPAVELI commercial supply
- Establish Apellis & the PNH unmet need
- Ensure patient access and reimbursement
- Leverage the clinical data to differentiate the brand
Early Indicators Confirm Unmet Need for PNH Patients

PATIENT SEGMENTS

1/3 of Patients

- Transfusions to address falling hemoglobin
- Hemoglobin below normal and symptoms like fatigue
- Hemoglobin near or at normal levels

1,500 U.S. PNH patients on C5 inhibitors
150 Newly diagnosed eligible PNH patients in the U.S. annually

EARLY POSITIVE INDICATORS

Congratulations to Apellis, I’m excited to start patients on therapy KOL at a major PNH treatment center

I will be following up with my physician, as I was not aware of EMPAVELI until receiving the “Now Approved” email PNH Patient

You guys (Apellis) are the poster child of what good looks like in the pharma/biotech space Lead, Pharmacy Trade Relations at a major pharmacy benefits manager
Market Access Team Having Significant Early Impact

**OUR MARKET ACCESS PRIORITIES**

**CLINICAL EFFICACY**

EMPAVELI demonstrated superior clinical efficacy in improving hemoglobin levels compared to Soliris® (eculizumab) in a head-to-head trial.

**ENSURING ACCESS**

Apellis is committed to ensuring that every eligible patient who wants EMPAVELI will have access regardless of ability to pay.

**REMOVING COSTS**

We expect costs will be reduced to the healthcare system by switching patients to EMPAVELI (e.g., avoidance of transfusions & hospitalizations)\(^1\).

**100%**

of our “Top 20” payers have received EMPAVELI clinical presentations

**85%**

of PNH patients reside in 20 health plans or PBMs

**4**

Major payers have accelerated EMPAVELI formulary reviews

**1**

Payer has already placed EMPAVELI on formulary

\(^1\) Apellis is committed to ensuring that every eligible patient who wants EMPAVELI will have access regardless of ability to pay.
### Patient Journey & Early Lead Indicators

<table>
<thead>
<tr>
<th>EMPAVELI-Treated Patients by Payer Segment</th>
<th>Early Launch Days from Prescription to First Dose</th>
<th>Physician Enrollment in REMS Since Launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDICAID 25%</td>
<td>7-10</td>
<td>&gt;50</td>
</tr>
<tr>
<td>MEDICARE 25%</td>
<td></td>
<td></td>
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<tr>
<td>COMMERCIAL 50%</td>
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</tbody>
</table>

Have had RXs from all three payer channels submitted & approved
Great Start for EMPAVELI Launch

<table>
<thead>
<tr>
<th>TODAY</th>
<th>Q4 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product in channel within 5 days</td>
<td>90% of payer formulary reviews to be complete</td>
</tr>
<tr>
<td>90% of top payers have received clinical presentations</td>
<td>Engage 100% of priority accounts via Apellis sales organization</td>
</tr>
<tr>
<td>Sales organization live meetings have increased to 38% from 8% post-PDUFA</td>
<td>Engage 85% of priority physicians via Apellis sales organization</td>
</tr>
<tr>
<td>&gt;50 physicians have enrolled in REMS</td>
<td>Maintain &amp; enhance high patient confidence score for self-infusion within 2 weeks on therapy</td>
</tr>
<tr>
<td>ApellisAssist early operational effectiveness is rated high by patients</td>
<td></td>
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</tbody>
</table>

Organization focus is on 2k HCPS & 90 targeted treatment centers
Q&A with Dr. Ilene Weitz

Ilene Weitz, M.D.
Hematology Specialist, Professor of Clinical Medicine
Keck School of Medicine at the University of Southern California

Monica Fay
Senior Vice President, Medical Affairs
Apellis Pharmaceuticals
Transforming Treatment Across Rare, Complement-Driven Diseases

**Establish EMPAVELI in PNH**
- Ensure access for adults with PNH

**Expand Rare Disease Portfolio**
- Advance four additional registrational programs

**Enhance Patient Experience & New Indications**
- Launch Enable device
- Develop siRNA + EMPAVELI
- Develop oral alternative pathway inhibitor
Immune Complex Membranoproliferative Glomerulonephritis (IC-MPGN) / C3 Glomerulopathy (C3G)

Matthew Pickering, Ph.D., M.B., B.S.
Professor of Rheumatology and Wellcome Trust Senior Fellow in Clinical Science
Imperial College London via Imperial Consultants
IC-MPGN and C3G are Rare, Chronic, Complement-Mediated Glomerular Diseases Resulting in Kidney Damage and Failure

- Similar clinical presentation, features, and disease course
- Heterogenous disease pathology (i.e., genetic or acquired)

MPGN
- MPGN pattern of injury
- Complement alternative and classical pathway implicated
- Immunoglobulin deposition dominant or co-dominant with C3

C3 Glomerulopathy
- Complement alternative pathway implicated
- C3-dominant glomerular deposits
- Two subtypes
  - DDD
  - C3GN

Idiopathic Ig-associated MPGN
- Dense deposit disease

C3GN
- FHR5 nephropathy

Overlap of MPGN and C3 Glomerulopathy

Adapted from: JASN January 2018, 29 (1) 9-1

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No Approved Treatments for IC-MPGN or C3G

**Key Clinical Signs and Symptoms**
- Proteinuria and/or hematuria
- Low serum C3
- Decreased GFR
- High blood pressure

**Key Pathological Findings**
- Positive C3 staining
  - C3G and IC-MPGN
- IC-MPGN also has Ig deposition

**No Disease-Modifying Treatments**
IC-MPGN and C3G Represent Areas of High Unmet Need

- ~18,000 patients in US and EU with primary C3G or IC-MPGN
- ~50% of patients progress to ESRD in 5-10 years and require chronic dialysis or transplant
- Kidney transplantation is not curative. Disease recurrence has been reported in as many as 85% transplanted patients
- Proteinuria is an important marker of renal damage and the key clinical marker, along with GFR, used by clinicians to measure progression of the disease

IC-MPGN/C3G Interferes with Life Physically and Emotionally

“Physically, I gained weight in the beginning because of this disease.”

“Mentally, the medication that I was taking made it hard for me to focus.”

“With C3G being such a rare disease, I am often faced with new challenges that do not have solutions.”
EMPAVELI Targets C3 for Comprehensive Control of IC-MPGN and C3G
Phase 2 DISCOVERY Design and Study Goals

Population: Biopsy-confirmed adult or adolescent patients with C3G or biopsy-confirmed adult patients with IgAN, LN, or primary MN

Primary endpoint: Change from baseline in proteinuria as quantified by uPCR

Secondary endpoints include: Change in estimated glomerular filtration rate and serum complement markers, including C3

**EMPAVELI 360 mg QD SC**
Transition to 1080 mg Q2W ≥week 24
N=8 C3G patients

**Screening**
4 weeks

**Long-term extension**
24 weeks

**Primary endpoint readout**
48 weeks

C3G, C3 glomerulopathy; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; Q2W, every 2 weeks; QD, once daily; TEAE, treatment-emergent adverse event; uPCR, urine protein to creatinine ratio.

EMP AVELI Demonstrated 73% Reduction in Mean Proteinuria as Measured by 24h uPCR at Week 48 in DISCOVERY

Treatment with EMP AVELI resulted in proteinuria reduction at week 48

Decreased uPCR, increased serum albumin, and stable renal function were observed at week 48

<table>
<thead>
<tr>
<th>Parameter, mean (SE), [range]a</th>
<th>Baselineb (N=5)</th>
<th>Week 48 (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hour uPCR, mg/mg</td>
<td>3.48 (0.82)</td>
<td>0.93 (0.27)</td>
</tr>
<tr>
<td></td>
<td>[1.74, 6.55]</td>
<td>[0.34, 1.69]</td>
</tr>
<tr>
<td>Percentage CFB in 24-hour uPCR</td>
<td>NA</td>
<td>-67.73 (10.50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[-94.12, -37.31]</td>
</tr>
<tr>
<td>Serum albumin, g/dL</td>
<td>3.50 (0.30)</td>
<td>4.08 (0.24)</td>
</tr>
<tr>
<td></td>
<td>[2.40, 4.10]</td>
<td>[3.30, 4.60]</td>
</tr>
<tr>
<td>eGFRc, mL/min/1.73 m²</td>
<td>88.00 (22.61)</td>
<td>86.60 (20.44)</td>
</tr>
<tr>
<td></td>
<td>[29.00, 138.00]</td>
<td>[41.00, 142.00]</td>
</tr>
</tbody>
</table>

Figure error bars represent standard error. Five patients were included at each time point.
CFB, change from baseline; uPCR, urine protein to creatinine ratio.

a Normal ranges for each parameter: first morning uPCR, <0.200 mg/mg; serum albumin, 3.5-5.50 g/dL;
b Baseline was the most recent result before the first dose.
c eGFR was calculated using the CKD-EPI creatinine equation.
Phase 2 DISCOVERY Study: EMPAVELI Targets Underlying Disease Process of C3G

Serum C3 levels increased after initiation of EMPAVELI

Levels of key complement biomarkers increased from baseline to week 48

<table>
<thead>
<tr>
<th>Biomarker, mean (SD), [range]</th>
<th>Baseline</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum C3, mg/mL</td>
<td>61.60 (20.42) [11.00, 116.00]</td>
<td>252.00 (52.82) [82.00, 407.00]</td>
</tr>
<tr>
<td>Serum C4, mg/dL</td>
<td>19.20 (4.22) [5.00, 31.00]</td>
<td>17.75 (2.17) [14.00, 22.00]</td>
</tr>
<tr>
<td>CH50, U/mL</td>
<td>183.40 (53.17) [23.00, 298.00]</td>
<td>214.00 (12.52) [190.00, 248.00]</td>
</tr>
<tr>
<td>AH50, U/mL</td>
<td>62.00 (25.59) [0.00, 113.00]</td>
<td>60.75 (22.40) [0.00, 96.00]</td>
</tr>
</tbody>
</table>

Graphed error bars represent standard error. Normal ranges are indicated by shading: serum C3, 90-180 mg/dL

Normal ranges for each of the biomarkers: serum C3, 0.94-1.66 mg/mL; CH50, 176-382 U/mL; AH50, 77-159 U/mL. Baseline was the most recent result before the first dose.
EMP AVELI Safety Profile in C3G Cohort of DISCOVERY

There were no discontinuations due to treatment emergent adverse events (TEAEs) and no serious or severe adverse events.

The majority of TEAEs were considered unrelated to study drug.
Phase 2 Study in Post-Transplant Recurrence Is Ongoing and Phase 3 Study Is Expected to Initiate in 2H21

**Phase 3 IC-MPGN / C3G Study Goals:**

1. Evaluate efficacy through proteinuria
2. Evaluate impact on key disease parameters
3. Assess functional outcomes
4. Evaluate safety and tolerability

**IC-MPGN / C3G Patient Journey**

- **Mild**
  - Ph 3 study population
- **Severe**
  - ESRD & Kidney Transplant
- **Post-Transplant Recurrence**
  - Ph 2 and Ph 3 study population
Key Takeaways

IC-MPGN and C3G are rare, chronic, complement-mediated diseases resulting in kidney damage and failure with no approved therapies.

Excessive deposition of C3 breakdown products in the kidney is the primary driver of kidney damage in patients with IC-MPGN and C3G.

EMPAVELI achieved proof of concept in C3G by demonstrating a 73% reduction in mean proteinuria at 48 weeks.

Phase 2 study ongoing; Phase 3 expected to initiate in 2H21.
Amyotrophic Lateral Sclerosis (ALS)

Angela Genge, M.D., FRCP(C)
Executive Director, Clinical Research Unit & Director of ALS Center of Excellence
Montreal Neurological Institute
Significant Unmet Need for People Living with ALS

ALS is a fatal neurodegenerative disorder, characterized by progressive loss of upper and lower motor neurons\(^1\).

2/3 initially present with muscle weakness of the limbs\(^2\)

1/3 initially present with difficulty with speech and swallowing\(^2\).

ALS affects 225,000 people globally. ~90% of cases are sporadic and death typically occurs 3-5 years from disease onset\(^1,2\).

Currently, no treatment targets the neuroinflammation caused by an overactive immune response.

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Extensive evidence suggests that complement activation plays a role in disease progression:

- Disease progression is correlated with elevated C3
- Complement C3 is elevated in the serum, brain, and spinal cord compared to nonaffected controls
- Individuals with ALS have high levels of activated C3 at the neuromuscular junction where neurons communicate directly to muscle cells
Complement C3 and its Breakdown Products Are Deposited at the Neuromuscular Junctions of People with ALS
EMPAVELI Targets C3 to Slow Disease Progression in ALS

- Classical Pathway
- Lectin Pathway
- Alternative Pathway

EMPAVELI Controls all downstream effects

C3a → C3b → C5

- C5a → Neuroinflammation
- C5b → MAC

C3a → C3b → Neurodegeneration

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MERIDIAN: Phase 2 Study in ALS Expected to Complete Enrollment by End of 2021

Population: Adult patients with sporadic ALS

Primary endpoint: Combined Assessment of Function and Survival (CAFS) rank scores

Secondary endpoints include: Measures of lung function, muscle strength, and quality of life

Screening
52 weeks

Open-label extension
52 weeks

2:1 RANDOMIZATION

EMPAVELI
1080mg SC twice weekly
N=152

Placebo SC twice weekly
N=76

APL2-ALS-206; NCT04579666
Key Takeaways

- Urgent and significant need for treatments for ALS, a fatal neurodegenerative disorder
- Evidence suggests complement activation and elevated levels of C3 play a role in disease progression
- Controlling complement activation centrally at C3 with EMPAVELI may have the potential to slow the progression of ALS
- Phase 2 enrollment completion expected by the end of 2021
Cold Agglutinin Disease (CAD)

Bruno Fattizzo, M.D.
Professor, Consultant Hematologist and Clinical Researcher
Fondazione IRCCS Ca' Granda Policlinico Hospital, Milan, Italy
Cold Agglutinin Disease (CAD) Is a Chronic and Severe Blood Disorder with No Approved Therapies

**Disease Background:**

- Chronic and severe red blood disorder
- Exacerbation of the condition in a cold environment
- Primarily affects older adults (age 50+)
- Symptoms include
  - Hemolytic anemia and fatigue
  - Transfusion requirements
  - Cold-induced circulatory symptoms
  - Increased risk of thrombotic events like stroke or heart attack
Phase 2 PLAUDIT Study Design

**Population:** CAD patients with hemoglobin (Hb) levels <11 g/dL, signs of hemolysis, and positive direct antiglobulin test (DAT) for IgG and/or complement C3

**Primary endpoints:**
- Safety
- Change in hematologic and blood chemistry parameters and FACIT

PLAUDIT study also includes a parallel cohort of patients with warm antibody autoimmune hemolytic anemia (wAIHA)

**Screening**
All subjects

**Randomized 1:1**
48 weeks

- **EMPANELI Daily 270mg QD SC**
  - N=7

- **EMPANELI Daily 360mg QD SC**
  - N=6
PLAUDIT: Efficacy and Safety Results Support Further Clinical Development of EMPAVELI in CAD

EMP AVELI Increased Hemoglobin within the First Weeks of Treatment with Sustained Benefit with Longer Exposure

Additional Efficacy Outcomes
- 77% (n=10) patients were transfusion free at month 12
- FACIT score increased by 7.7 points from baseline to week 24

Safety Profile Was Generally Consistent with Other Studies
- All 13 CAD subjects experienced ≥1 treatment-emergent adverse event (TEAE), mainly mild to moderate in severity
- Five subjects reported 13 serious adverse events (SAEs) unrelated to EMPAVELI
- EMPAVELI was generally well tolerated

*FACIT- Clinically significant increase is 3 or more points
APL2-CP-AIHA-208; NCT03226678
Key Takeaways

- CAD is a chronic and severe blood disorder with no approved therapies
- EMPAVELI may be able to control hemolysis in CAD by controlling complement
- EMPAVELI demonstrated meaningful efficacy results across multiple hematologic parameters and was well tolerated in PLAUDIT study
- Sobi expects to initiate a Phase 3 study in H2 2021
Hematopoietic Stem Cell Transplant Thrombotic Microangiopathy (HSCT-TMA)

Bruno Fattizzo, M.D.
Professor, Consultant Hematologist and Clinical Researcher
Fondazione IRCCS Ca' Granda Policlinico Hospital, Milan, Italy
C3 Plays a Critical Role in HSCT-TMA, a Multi-System Disease

- Multi-system disease characterized by microangiopathic hemolytic anemia, consumptive thrombocytopenia and microvascular thrombosis

- Patients who develop organ damage as a result of HSCT-TMA are associated with high mortality rates

- C3 is believed to play a critical role in TMA based on proinflammatory and procoagulant properties of C3a and C3b

- sC5b9 is a high-risk feature of HSCT-TMA
HSCT-TMA Is Associated with Very Poor Outcomes

- ~9,000 and ~18,000 allogeneic transplants conducted in U.S. and EU+ annually.\(^1,2\)

- TMA incidence can be up to ~40% of allogenic transplants\(^3\)

- ~50% of HSCT-TMA cases can be severe\(^3\)

- ~90% or more of severe HSCT-TMA is fatal\(^3\)

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**Overall survival**

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>HSCT without TMA</th>
<th>HSCT with TMA (HSCT-TMA): Median survival 5.8 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
<td><strong>P=9.82E-16</strong></td>
</tr>
<tr>
<td>12</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>72</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>84</td>
<td>0</td>
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<tr>
<td>96</td>
<td>0</td>
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<tr>
<td>108</td>
<td>0</td>
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</table>

**Median survival**

- HSCT without TMA: Median survival 79.7 months
- HSCT with TMA (HSCT-TMA): Median survival 5.8 months

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Extremely High Levels of Complement Activation Post-Transplant Leads to Severe Complement Dysregulation in HSCT-TMA

- Classical Pathway
- Lectin Pathway
- Alternative Pathway

**Endothelial Damage**

**Amplification Loop**

*Loss of Control & Detrimental Effects*

- C3
- C3a
- C3b
- C3a
- C5
- C5a
- C5b
- MAC
- Blood Clots/Organ Damage
- Inflammation
EMPAVELI Targets C3 to Control Complement Activation in HSCT-TMA

Classical Pathway

Lectin Pathway

Alternative Pathway

EMPAVELI

C3

Inflammation

C3a

STOP

C3b

Blood Clots/Organ Damage

C5

Inflammation

C5a

STOP

C5b

MAC

Blood Clots/Organ Damage

Controls all downstream effects
Key Takeaways

- HSCT-TMA is a multi-system disease associated with high mortality rates
- EMPAVELI has the potential to control the extremely high levels of complement activation associated with HSCT-TMA
- Sobi expects to initiate a potentially registrational Phase 2 study in H2 2021
# EMPAVELI: Comprehensive Control of Complement with Broad Platform Potential

<table>
<thead>
<tr>
<th>Disease</th>
<th>EMPAVELI Ambition</th>
<th>U.S. Patients Needing Treatment</th>
<th>Key Upcoming Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNH</td>
<td>The new standard of care</td>
<td>~1,500*</td>
<td>U.S. launch is ongoing</td>
</tr>
<tr>
<td>IC-MPGN / C3G</td>
<td>Best-in-class therapy for late-stage and transplant patients</td>
<td>~5,000**</td>
<td>First patient dosed in Phase 3 study in 2H21 (Apellis)</td>
</tr>
<tr>
<td>ALS</td>
<td>Increase survival and slow the progression of symptoms</td>
<td>~19,000***</td>
<td>Complete enrollment by end of 2021 (Apellis)</td>
</tr>
<tr>
<td>CAD</td>
<td>Improve hemoglobin levels and reduce transfusion dependency</td>
<td>~5,000**</td>
<td>Initiate Phase 3 trial in 2H21 (Sobi)</td>
</tr>
<tr>
<td>HSCT-TMA</td>
<td>Protect organ function and prevent mortality</td>
<td>~4,000****</td>
<td>Initiate potentially registrational Phase 2 study in 2H21 (Sobi)</td>
</tr>
</tbody>
</table>

*Based on complement-treated patient population  
**Based on severe patient population  
***Based on sporadic only, patients seeking treatment, and non-monotherapy patients  
****Based on high-risk patients for developing TMA

Sobi has global co-development and ex-U.S. commercialization rights for systemic pegcetacoplan

# EMPIAVELI Ambition


---

**U.S. Patients Needing Treatment**

- PNH: ~1,500*
- IC-MPGN / C3G: ~5,000**
- ALS: ~19,000***
- CAD: ~5,000**
- HSCT-TMA: ~4,000****

*Based on complement-treated patient population  
**Based on severe patient population  
***Based on sporadic only, patients seeking treatment, and non-monotherapy patients  
****Based on high-risk patients for developing TMA
Transforming Treatment Across Rare, Complement-Driven Diseases

**Establish EMPAVELI in PNH**
- Ensure access for adults with PNH

**Expand Rare Disease Portfolio**
- Advance four additional registrational programs

**Enhance Patient Experience & New Indications**
- Launch Enable device
- Develop siRNA + EMPAVELI
- Develop oral alternative pathway inhibitor
Launch Enable Device

Victoria Brown
Senior Vice President, Rare Disease Program Executive
Apellis Pharmaceuticals

Enhance Patient Experience & New Indications
- Launch Enable device
- Develop siRNA + EMPAVELI
- Develop oral alternative pathway inhibitor
Advancing Patient-Centered Device Innovation for 2022

Patients responded positively to a next-generation device:

- Administers with a few simple steps
- Alleviates needle fear
- Allows discreet self-administration
- Increases mobility and independence

Source: Consultant analysis of PNH focus groups unique
Develop siRNA + EMPAVELI for Less-Frequent Dosing

Lukas Scheibler, Ph.D.
Chief Innovation Officer
Apellis Pharmaceuticals
Silencing C3 Expression Could Reduce EMPAVELI Posology

- EMPAVELI dose and posology is driven by high C3 concentration in blood

- Silencing C3 expression in the liver with siRNA reduces circulating C3 concentration

- GalNAc-conjugated siRNAs have been shown to target the liver and are approved in variety of indications
  - Patisiran, givosiran, inclisiran are approved
  - 19 GalNAc-siRNA development programs exist
Apellis siRNA Silenced 90% of C3

<table>
<thead>
<tr>
<th></th>
<th>3 mg/kg</th>
<th>10 mg/kg</th>
<th>30 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA Day 15 KD</td>
<td>89%</td>
<td>97%</td>
<td>99%</td>
</tr>
<tr>
<td>Protein max KD</td>
<td>77%</td>
<td>85%</td>
<td>94%</td>
</tr>
</tbody>
</table>

NHP Liver Biopsy C3 mRNA

NHP Serum C3 Protein to Day 172
Complement Targets Require Silencing & Inhibition

**C5 siRNA in monotherapy does not control PNH in Phase 1 study**

- “Maximal reductions in LDH, an exploratory objective, of 37-50% were observed in eculizumab-naïve patients, and LDH levels remained above the goal of <1.5xULN.” – Badri et al 2020
- “... residual levels of C5 ... were sufficient to cause intravascular hemolysis.” - Harris et al 2018

**C5 siRNA in combination with eculizumab controls PNH with less-frequent dosing in Phase 1 study**

- “All patients receiving cemdisiran achieved LDH <1.5xULN on reduced doses and/or frequency of eculizumab.” – Badri et al 2020
- “In combination with Cemdisiran, the total cumulative yearly maintenance dose of eculizumab can potentially be reduced to approximately 70%.” – Badri et al 2020

**siRNA enables less frequent dosing:**

- Single dose ALN-CC5 reduced classical pathway hemolytic activity by 65-70% to day 71 in nonhuman primates. – Badri et al 2020; Kusner et al 2019
Apellis siRNA + EMPAVELI: Improving Treatment Experience with Less-Frequent Dosing

Silencing C3 expression in the liver may reduce treatment frequency of EMPAVELI

Apellis siRNA silenced C3 expression >90% over 3+ months in NHP and significantly reduced complement activity

Results support potential to reduce dosing frequency of EMPAVELI

IND for siRNA program anticipated in 2022
Oral Alternative Pathway Inhibitor

Lukas Scheibler, Ph.D.
Chief Innovation Officer
Apellis Pharmaceuticals
Alternative Pathway Inhibitor Where Comprehensive Control of Complement Is Not Needed and/or Classical Pathway Is Not Involved

**Table: Alternative Pathway Inhibition**

<table>
<thead>
<tr>
<th></th>
<th>IC&lt;sub&gt;50&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apellis</td>
<td>29 nM</td>
</tr>
<tr>
<td>LNP023 (Iptacopan)</td>
<td>162 nM</td>
</tr>
</tbody>
</table>

**Diagram:**
- Classical Pathway
- Lectin Pathway
- Alternative Pathway

**Graph:**
- **RAT PK**
- Concentration (ng/mL) vs. Time (h)
  - IV
  - PO

STOP
Oral Alternative Pathway Inhibitor for Indications Where Comprehensive Control of Complement Is Not Needed

C3G

MILD
Oral alternative pathway inhibitor target

SEVERE

ESRD & KIDNEY TRANSPLANT

POST-TRANSPLANT RECURRENT

EMPANELI target

EMPANELI target
Transforming Treatment Across Rare, Complement-Driven Diseases
AND THEY’RE O F F !

Rare Disease Q&A
Lunch Break

Boxed lunches are in the lobby. The presentation will resume in 20 minutes.
Building a Portfolio of Brain-Active Complement Therapies

Lukas Scheibler, Ph.D.
Chief Innovation Officer
Apellis Pharmaceuticals
The Retina as a Window to the Brain
C3 Therapy for Neurodegeneration Is an Extension of the Neuroprotective Effects of Pegcetacoplan in the Retina

Geographic Atrophy Is a C3-Dependent Neuropathology

Phase 2 FILLY Study: Pegcetacoplan Reduced GA Lesion Growth

*Square root. Modified intention-to-treat (mITT) population was used for the efficacy analysis; defined as all patients who received at least 1 injection and underwent at least 1 follow-up examination at month 2 or later at which primary efficacy data were collected. 2-sided t tests at the alpha = 0.1 level.

Role of C3 in Neurodegeneration

Angela Genge, M.D., FRCP(C)
Executive Director, Clinical Research Unit & Director of ALS Center of Excellence
Montreal Neurological Institute
Multiple Preclinical Studies Demonstrate that C3 Inhibition Is Neuroprotective in Aging and Neurodegenerative Diseases
Aberrant C3-Mediated Pruning Leads to Synaptic and Cognitive Dysfunction in Multiple Neurologic Diseases

Stephen, Barres and Stevens, Annu Rev Neurosci 2012

C3 Protein Is Elevated in Alzheimer’s Disease Patient CSF; C3 Knockout Is Synaptoprotective in AD Animal Models

**AD PATIENTS**

C3 and Processed C3 Protein (C3b, iC3b and C3c) Is Increased in AD Patient CSF

**MOUSE MODEL OF AD**

C3 Knockout Is Protective of Synapses in an Amyloid Mouse Model

Wu, 2019

Wu, et al 2019

Apellis proprietary information / for Apellis use only
C3 Is Upregulated in Rapidly Progressing Tauopathies such as PSP, CBD and FTD

C3 mRNA Is Elevated in CBD and PSP Patient Brains

C3 KO Prevents Cortical Atrophy in a Mouse Tauopathy Model

CBD – Corticobasal Degeneration
PSP – Progressive Supranuclear Palsy
FTD – Frontotemporal Dementia

Litvinchuk et al., 2018

Wu et al., 2019
C3 Protein Is Correlated with Cognitive Decline in Patients with Demyelinating Disease

C3 Is Increased in MS Patient Brain and CSF

Neuroinflammation Leads to Cortical Atrophy and Cognitive Decline in MS

Aeinheband et al., 2017; Xin & Chan 2020

Damjanovic et al., 2017
Rationale for C3 Inhibition as a Treatment for Neurodegenerative Diseases

**C3 regulation** is required for synaptic refinement, learning, and memory in neural development and throughout life.

**C3 dysregulation** results in synaptic loss and dysfunction, a primary cause of cognitive decline in aging and many neurologic diseases including ALS, Alzheimer’s disease, multiple sclerosis, and tauopathies.

**Restoring C3 regulation** with Apellis’ proprietary molecules aims to improve cognitive function in multiple neurodegenerative diseases.
Pioneering C3 in Neurodegeneration

David Eyerman, Ph.D.
Vice President, Translational Neurology
Apellis Pharmaceuticals
A Large Challenge in Treating CNS Diseases Is Getting Pharmacologic Treatment Across the Blood Brain Barrier
Building a Portfolio of Brain-Active Complement Therapies

First-in-Class Brain-Active C3 Inhibitor
- Intrathecal APL-1030

Next-Gen Brain-Active C3 Inhibitors
- Brain-shuttle enabled biologic inhibitors

Gene Therapies
- Brain-delivered APL-1030 secretors
- Brain-delivered C3 gene knockdown
Building a Portfolio of Brain-Active Complement Therapies

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APL-1030: A Novel Molecular Entity C3 Inhibitor

- 64 amino acids, highly water soluble
- Binds to same epitope of C3/C3b as pegcetacoplan
- Binding affinity and inhibition equal to pegcetacoplan
- High thermal stability
- Recombinant and synthetic manufacture is feasible
- C- and/or N-terminus accessible to modification without impact on function

![Diagram of the Classical, Lectin, and Alternative Pathways with C3, C3a, C3b, C5, C5a, C5b, and MAC](image)

Controls all downstream effects
APL-1030 is a novel C3 & C3b inhibitor for intrathecal delivery to the brain.

- Good tolerability and high brain concentrations following 5-day intrathecal pump infusion in rats.
- Enters brain interstitial fluid in rats.
- Enters brain and inhibits C3 in human primates (NHPs).
High CSF Concentrations and Good Tolerability in NHPs Following Intrathecal Administration of APL-1030

- Dose escalating exposure in CSF up to ~500µg/mL
- SS CSF achieved within 8-24 hours of infusion
- T1/2 of APL-1030 post-pump shutoff = 3-6h in CSF and ~20h in plasma
- Plasma concentrations are 10-15X lower than CSF
APL-1030 Distributes Across the Brain of NHPs Following 5 Days of Intrathecal Administration

Brain Tissue Concentrations of APL-1030

**APL-1030 (2 mg/day)**

<table>
<thead>
<tr>
<th>Target Tissue</th>
<th>Concentration (ug/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortex</td>
<td>100</td>
</tr>
<tr>
<td>Hippocampus CA1</td>
<td>100</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>100</td>
</tr>
<tr>
<td>Other</td>
<td>100</td>
</tr>
</tbody>
</table>

**APL-1030 (20 mg/day)**

<table>
<thead>
<tr>
<th>Target Tissue</th>
<th>Concentration (ug/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortex</td>
<td>1000</td>
</tr>
<tr>
<td>Hippocampus CA1</td>
<td>1000</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>1000</td>
</tr>
<tr>
<td>Other</td>
<td>1000</td>
</tr>
</tbody>
</table>

Target Tissue Concentration
Functional Inhibition of C3 Breakdown in Cognition-Relevant Brain Regions of NHPs Treated with APL-1030

Brain Tissue Levels of the C3 Breakdown Product C3a Following Intrathecal Infusion with APL-1030 for 5 Days

- Prefrontal Cortex
- Entorhinal Cortex
- Hippocampus CA1
- Hippocampus CA3

LOD (0.12 ng/mL)
APL-1030: Advancing First-in-Class, Brain-Active C3 Inhibitor

- Distributes throughout the brain
- Inhibits C3 breakdown in brain of nonhuman primates
- Potential to treat multiple neurodegenerative disorders
- IND planned in H1 2022
Building a Portfolio of Brain-Active Complement Therapies

First-in-Class Brain-Active C3 Inhibitor
- Intrathecal APL-1030

Next-Gen Brain-Active C3 Inhibitors
- Brain-shuttle enabled biologic inhibitors

Gene Therapies
- Brain-delivered APL-1030 secretors
- Brain-delivered C3 gene knockdown
Small Biological Building Blocks Replicating Pegcetacoplan Pharmacology Will Yield New Therapies for Neurologic Diseases

Salvia et al., 2016

C3/C3b Complement Inhibitors and Bifunctional NBES

Brain Shuttle Mediated Delivery via Systemic ROA

Gene Therapy Secretion in Brain with Long Durability of Effect


APELLIS PROPRIETARY INFORMATION / FOR APELLIS USE ONLY
Brain-Shuttle Enabled C3 Inhibitor to Treat CNS Indications

Brain Shuttle
Brain delivery via trojan horse

C3/C3b
Pharmacologically-active moiety

Brain-Shuttle Enabled C3 Inhibitor in Rat Brain Following a Single IV Administration

Data on file

Target Concentration

10mg/kg; IV route of administration; 24 hours post dose
Building a Portfolio of Brain-Active Complement Therapies

First-in-Class Brain-Active C3 Inhibitor
- Intrathecal APL-1030

Next-Gen Brain-Active C3 Inhibitors
- Brain-shuttle enabled biologic inhibitors

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Small Biological Building Blocks Replicating Pegcetacoplan Pharmacology Will Yield New Therapies for Neurologic Diseases

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C3/C3b Complement Inhibitors and Bifunctional NBEs

Gene Therapy Secretion in Brain with Long Durability of Effect

Salvia et al., 2016

Lipid Nanoparticles and APL-1030 Plasmids Distribute to Brain and Secrete Protein *In Vitro* and *In Vivo*

**APL-1030 Secretion in hIPSC Derived Brain Cells**

- **Sham Injection**
- **Lumbar Intrathecal (IT)**
- **Cisternal Intrathecal (ICM)**

**Protein in Rat Brain 28-Days Post Single ICM Dose**

- **Active**
- **PBS**

**APL-1030 (ng/mL)**

- **3022**
- **3027**

**Time point**

- 72H
- 96H
- 120H
- 144H

**Units**

- 10X
- 20X
Building a Portfolio of Brain-Active Complement Therapies

- Potential to treat multiple neurodegenerative diseases by targeting C3
- APL-1030 is a first-in-class, brain-active C3 inhibitor
  - Preclinical pharmacodynamic response at dose levels expected to translate to humans
  - IND submission in H1 2022

<table>
<thead>
<tr>
<th>TECHNOLOGY</th>
<th>DRUG CANDIDATE</th>
<th>DISCOVERY</th>
<th>IND ENABLING</th>
<th>EARLY CLINICAL</th>
</tr>
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<tbody>
<tr>
<td>Biologic</td>
<td>APL-1030 - IT</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C3/C3b Brain Shuttle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gene therapy</td>
<td>C3/C3b Secretor</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Be #1 in the Retina

Cedric Francois, M.D., Ph.D.
Chief Executive Officer
Apellis Pharmaceuticals
Apellis: Be #1 in the Retina

Geographic Atrophy and Intermediate AMD
- Pegcetacoplan

Next-Gen Wet AMD
- APL-2006: anti-VEGF plus anti-C3

Gene Therapy
- Gene therapies for all forms of AMD
Apellis: Be #1 in the Retina

- Geographic Atrophy and Intermediate AMD
  - Pegcetacoplan

- Next-Gen Wet AMD
  - APL-2006: anti-VEGF plus anti-C3

- Gene Therapy
  - Gene therapies for all forms of AMD
We believe that GA is the consequence of a failure to clean up C3 deposition in the retina.

Single pathway inhibitors are insufficient to correct this failure.

Pegcetacoplan, a targeted C3 therapy, has the potential to accomplish this with its broad, multi-point control of complement across all three pathways.

• Visual acuity charts don't reflect the real impact of GA in vision due to foveal sparing.
• GA is a relentless, progressive disease that severely impairs patients’ visual function and quality of life.
• A leading cause of blindness, GA has no approved treatments and remains the most significant unmet need in the retina.
• The need and desire for treatment was reflected in the speed of enrollment in DERBY and OAKS.
The FILLY study met its primary endpoint, demonstrated a dose response, and the sham group progressed at the expected rate.

Dropouts were in line with other GA trials. 242 out of 246 patients (modified intent-to-treat: mITT) were included in the primary analysis population, which accounted for missing data with the well-established mixed-effect model for repeated measures (MMRM).

All sensitivity analyses confirmed the efficacy results.

Post hoc analyses also showed that lesion growth slowed in treated eyes vs. contralateral eyes in patients with bilateral GA and that pegcetacoplan slowed progression from intermediate AMD to GA.

The FILLY trial had no safety findings that limited DERBY and OAKS, which studies the same broad patient population.

Exudations are an expected occurrence in GA. No classical CNV was detected and there was no clinically significant impact on vision.

FILLY was single-masked, which may have led to greater reporting of exudations in subjects randomized to pegcetacoplan than in subjects randomized to sham. DERBY and OAKS are double masked to further minimize potential bias.

Two cases of infectious endophthalmitis out of ~1,500 intravitreal injections are consistent with reported incidence rates in published studies involving intravitreal injection.
Geographic Atrophy Is a Leading Cause of Blindness Impacting 5M Patients Worldwide

Current global prevalence

Global Prevalence

5,000,000

Estimated future commercial opportunity across US and Europe

Prevalent Patients

4,037,000

2,741,000

1,296,000

Diagnosed Patients

2,942,000

907,000

2,035,000

Treated by any DMT

845,000

257,000

588,000

US

Europe

Europe includes 31 countries in southern, northern, and western Europe. US and EU figures represent future years. DMT: Disease Modifying Therapies

What Is the Unmet Need in Geographic Atrophy?

Charles Wykoff, M.D., Ph.D.
Director of Research
Retina Consultants of Texas
There are 5 million people living with GA worldwide; 1 million are in the US\(^1\)

GA accounts for 20% of all legal blindness attributed to AMD\(^2,3\)

There is no approved treatment for GA\(^1\)

---

2. Ferris FL 3rd et al., *Arch Ophthalmol.* 1984

Image from Holz FG et al., *Ophthalmology* 2014.
VisuAl SymPtoms\(^1\)

- Loss of ability to see objects clearly (especially in dim light conditions)
- Straight lines appear to be wavy or distorted
- Loss of color vision
- Dark areas of gray and white spots may appear in the center of vision

In a natural history study, among patients who had visual acuity sufficient to drive at baseline, \(\frac{2}{3}\) progressed to vision loss that left them ineligible to drive over a median time of 1.6 years\(^2\)

---


Images: NIH National Eye Institute video on AMD
Living with GA:
Q&A with Rob
Pegcetacoplan: Phase 2 FILLY Results

Charles Wykoff, M.D., Ph.D.
Director of Research
Retina Consultants of Texas
Phase 2 FILLY Study: Design

**Population:** patients with geographic atrophy* secondary to AMD

**Design:** single masked, randomized 2:1:2:1

**Duration:** 18 months

---

**Sham groups were pooled for all analyses**

**PEGCETACOPLAN 15 mg/0.1 mL monthly** (n=86)

**PEGCETACOPLAN 15 mg/0.1 mL every other month** (n=79)

**SHAM monthly** (n=41)

**SHAM every other month** (n=40)

---

*Confirmed by the central reading center using fundus autofluorescence images. †Not counting the 3 satellite sites


---

ELIGIBLE PATIENTS WITH GA*

246 subjects in 43 sites†
Phase 2 FILLY Study: Timeline and Endpoints

Primary efficacy endpoint
Change in geographic atrophy (GA) lesion size from baseline at month 12

Primary safety endpoint
Number and severity of local and systemic treatment emergent adverse events (TEAEs)

Images taken at

0 months
2 months
6 months
12 months
18 months

Treatment period
No injections

Phase 2 FILLY Study: Pegcetacoplan Met Primary Endpoint, Reducing GA Lesion Growth

Chroma and Spectri Phase 3 Trials

<table>
<thead>
<tr>
<th>Change from baseline in square root of GA area at 48 wk, mm</th>
<th>Sham Pooled (n=598)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted mean (SE)</td>
<td>0.342 (0.007)</td>
</tr>
</tbody>
</table>

* \( p = 0.067 \) vs sham  
† \( p = 0.008 \) vs sham

LS Mean (±SE) Change from Baseline in Square Root GA Lesion (mm)

Month 0 6 12

Sham injections (N=80)  Pegcetacoplan every other month (n=78)  Pegcetacoplan monthly (N=84)

\( * p = 0.067 \) vs sham  
\( † p = 0.008 \) vs sham


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Phase 2 FILLY Study: Impact of Pegcetacoplan on Absolute GA Lesion Growth Is Consistent with the Primary Endpoint

**Primary Endpoint**
(Square Root Transformed Lesion Growth)

- Sham injections (N=80)
- Pegcetacoplan every other month (n=78)
- Pegcetacoplan monthly (N=84)

**Absolute (Untransformed) Lesion Size**

- Nominal p values
- mITT, Observed, Mixed-Effect Model
- A mixed effect model with main effects of treatment, visit and GA lesion at baseline, and interactions of treatment × visit, visit × baseline.

M12DBL Data

APELLIS PROPRIETARY INFORMATION / FOR APELLIS USE ONLY
Exudations at 12 Months (treatment period):

- 16% monthly, 6% every other month, 1% sham
- 0 cases of classical CNV
- No clinically significant impact on vision
- Patients discontinued pegcetacoplan; most treated with anti-VEGF therapy

Safety in line with other studies of intravitreally administered agents

Serious adverse events in the study eye were reported in 4 of 86 (4.7%) (2 endophthalmitis, 1 IOP increase, 1 retinal detachment), 2 of 79 (2.5%) (endophthalmitis, IOP increase), and 1 of 81 (1.2%) (dry AMD) of patients in the pegcetacoplan monthly, pegcetacoplan every other month, and sham groups, respectively.
Intermediate AMD (iAMD) is characterized by the presence of large drusen and pigmentary abnormalities in the macula.

- Associated with visual impairment, especially in low-light condition.
- Similar to Geographic Atrophy (GA), dysregulation of the complement system is implicated in iAMD.
- No approved therapy to prevent the progression of iAMD to advanced AMD.
Earlier Endpoints for Retinal Atrophy

- Therapeutic trials for geographic atrophy are focused on the end-stage (complete RPE and outer retinal atrophy or cRORA); e.g., GA lesions

- Earlier endpoints in the atrophy pathway have been defined: incomplete RPE and outer retinal atrophy (iRORA); e.g., consistent with intermediate AMD
Phase 2 FILLY Post Hoc Analysis: Pegcetacopoplan Slowed Progression from Intermediate AMD to GA

**PROGRESSION FROM iRORA TO cRORA**

- **Month 6**
  - Pegcetacoplan Monthly (n=18): 27.8%
  - Pegcetacoplan Every Other Month (n=33): 40.6%
  - Sham (33): 53.1%
  - Pearson Chi-Square: *P=0.02*

- **Month 12**
  - Pegcetacoplan Monthly (n=18): 50.0%
  - Pegcetacoplan Every Other Month (n=33): 57.6%
  - Sham (33): 81.8%
  - Pearson Chi-Square: *P=0.03*

**Relative risk:**
- Month 6: 0.61 (0.37–1.00) for PM; 0.70 (0.50–0.98) for PEOM
- Month 12: 0.02 for PM; 0.03 for PEOM
Key Takeaways

- Urgent and significant need for treatments for GA, a disease that leads to blindness
- Pegcetacoplan met the primary endpoint in the Phase 2 FILLY study, reducing GA lesion growth with benefit shown across GA phenotypes
- Demonstrated a dose response with sham group progressing at expected rate
- Slowed progression from intermediate AMD to GA; potential for earlier intervention in the course of GA
- Phase 2 FILLY safety in line with other studies of intravitreally administered agents
Pegcetacoplan: Advancing the First Potential Treatment for GA

Jeffrey Eisele, Ph.D.
Executive Vice President, Ophthalmology Program Lead
Apellis Pharmaceuticals
Retina Specialists Are Enthusiastic About the Prospect of Pegcetacoplan as the First-Ever GA Therapy

94% believe that GA poses a significant burden to patients’ quality of life†

84% believe that slowing lesion growth is the most important goal for preserving vision in GA†

“I think APL-2 is the most promising of any of the agents in development so far.” – Retina KOL²

“All three complement pathways converge on C3, which makes APL-2 much more promising than lampalizumab’s factor D inhibitor.” – Retina Specialist²

“Apellis designed these trials really well. If it shows benefit, I think APL-2 will get a lot of uptake pretty quickly.” – Retina Specialist²

“Anything over 20% [reduction in lesion growth rate] would be significant in my mind.” – Retina Specialist²

†BEESY Strategy Global GA ECP ATU (n=488) | *Rating 5, 6 and 7-point scale where 1= completely disagree and 7= completely agree
²Health Advances Commercial Assessment & Analysis (n=31) These statements include only the opinions of a limited sample of retina specialists and do not necessarily reflect the opinions of all retina specialists.
DERBY and OAKS: Two Phase 3 Studies of Pegcetacoplan in Patients with GA (n=1,258)

Same study population and trial design as FILLY

Population: patients with geographic atrophy* secondary to AMD

Primary endpoint: change in total area of GA lesion(s) based on fundus autofluorescence (FAF) at month 12

Design: single masked, randomized 2:1:2:1

Duration: 2 years

ELIGIBLE PATIENTS WITH GA*
>600 subjects from approx. 100 multinational sites per study

**PEGCETACOPLAN**
15 mg/0.1 mL monthly (n=200)

**PEGCETACOPLAN**
15 mg/0.1 mL every other month (n=200)

**SHAM INJECTIONS**
pooled (n=200)
DERBY and OAKS: Key Efficacy Endpoints

**PRIMARY**
- Change from baseline to Month 12 in total area of GA lesion(s) in the study eye (in mm²) based on FAF

**SECONDARY**
- BCVA, LL-BCVA
- Reading speed
- Microperimetry (OAKS study only) — Macular Integrity Assessment (MAIA) device
- National Eye Institute Visual Functioning Questionnaire 25-Item Version (NEI VFQ-25)
- Functional Reading Independence Index (FRI) composite score

BCVA=best-corrected visual acuity; FAF=fundus autofluorescence; LL-BCVA=low-luminance BCVA.
NCT03525600, NCT03525613

APELLIS PROPRIETARY INFORMATION / FOR APELLIS USE ONLY
DERBY and OAKS: Top-Line Results Expected in September

**PRIMARY ENDPOINT**
Change in lesion growth

- Monthly treatment with pegcetacoplan
- Every-other-month treatment with pegcetacoplan

**SAFETY**

- Safety profile including rate of exudations and intraocular inflammation
Advancing Pegcetacoplan into Intermediate AMD for Earlier Treatment of AMD

**Intermediate AMD**
- Presence of drusen
- No therapy to prevent progression to advanced AMD

**Advanced AMD**

**Geographic Atrophy**

- Positive post-hoc analysis from FILLY showed a treatment effect on biomarkers of intermediate AMD
- Pivotal study in intermediate AMD planned for 2022 following a positive GA readout
- Study to assess potential of pegcetacoplan to delay or prevent progression to advanced AMD

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

1 Rofagha et al. Ophthalmology 2013
Next-Gen Wet AMD

Lukas Scheibler, Ph.D.
Chief Innovation Officer
Apellis Pharmaceuticals
Apellis: Be #1 in the Retina

- Geographic Atrophy and Intermediate AMD
  - Pegcetacoplan

- Next-Gen Wet AMD
  - APL-2006: anti-VEGF plus anti-C3

- Gene Therapy
  - Gene therapies for all forms of AMD
US and Europe Prevalence of Patients with AMD

C3 + Anti-VEGF Therapy May Be Superior to Anti-VEGF Alone

Wet AMD patients treated with anti-VEGF therapy develop GA

Complement levels increase after anti-VEGF therapy in eyes with wet AMD

Visual function outcome declines over time despite anti-VEGF treatment

https://www.aaojournal.org/article/S0161-6420(19)31954-2/fulltext

https://doi.org/10.1038/s41598-021-87340-6

https://www.aaojournal.org/article/S0161-6420(18)30947-3/fulltext
APL-2006: Potential to Be Best-in-Class Treatment for Patients with Wet AMD

TREATMENT GOALS

- Non-inferior BCVA outcome to Eylea® (aflibercept) and/or Lucentis® (ranibizumab) in year one
- Lower rate of GA leading to superior outcome to Eylea and/or Lucentis in the long term
- Re-treatment interval > 3 months
- Similar safety as established therapies
APL-2006: Next-Generation Wet AMD Therapy

- Potential to provide superior treatment for patients with wet AMD and GA
- Less frequent dosing
- IND anticipated late 2022

Ranibizumab – VEGF inhibitor

Long Acting – 2x half-life over Lucentis in NHP

APL-1030 – C3 / C3b inhibitor
APL-2006: Potent Bispecific C3 and VEGF Inhibitor

**Complement Inhibition Potency**

**CP Inhibition**

<table>
<thead>
<tr>
<th>Inhibitor</th>
<th>CP IC$_{50}$</th>
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<tr>
<td>APL-2</td>
<td>116 nM</td>
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<tr>
<td>APL-2006</td>
<td>46 nM</td>
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**VEGF Inhibition vs. Lucentis**

- **Abs. (690nm – 570 nm)**
  - **Lucentis**
  - **APL-2006**

**HUVEC Proliferation Assay**
Apellis: Be #1 in the Retina

Geographic Atrophy and Intermediate AMD
- Pegcetacoplan

Next-Gen Wet AMD
- APL-2006: anti-VEGF plus anti-C3

Gene Therapy
- Gene therapies for all forms of AMD

APELLIS PROPRIETARY INFORMATION / FOR APELLIS USE ONLY
Goal: Develop Gene Therapy to Secrete APL-1030 or APL-2006 in the Retina

In vitro data in ARPE19 cells

APL-1030 protein in media of transfected ARPE19 cells

In vivo / rabbit study

Plasmid copy number GC/ng DNA

APELLIS PROPRIETARY INFORMATION / FOR APPELLIS USE ONLY
Be #1 in the Retina
Neurology/Ophthalmology Q&A
Cedric Francois, M.D., Ph.D.
Chief Executive Officer
Apellis Pharmaceuticals
EXCLUSIVE RESEARCH COLLABORATION
to apply base editing to discover novel therapies for complement-driven diseases
EXCLUSIVE RESEARCH COLLABORATION

- 6 research programs over 5 years: vision for one-time, curative therapies
- Base editing technology to discover precision medicines for diseases of the eye, liver, and brain
- Focused on C3 and other complement targets
- Modulating a complex biological system

POSITIONS APELLIS FOR LONG-TERM LEADERSHIP IN COMPLEMENT

Apellis

Beam Therapeutics
**BASE EDITING IS A NEW APPROACH TO GENE EDITING**

**Nuclease editing**
Creation of double-stranded breaks in DNA at a target location to **disrupt, delete, insert, or modify genes**

**Base editing**
Direct conversion of one base pair to another at a target location, without double-stranded breaks

**Two components fused as a single protein:**

**CRISPR** → Guide RNA-driven targeting
- Leverages established DNA targeting ability of CRISPR
- Modified to not cause double-stranded breaks

**Deaminase** → Single base editing
- Completes predictable chemical modification at target DNA base
- Adenine Deaminase for A-to-G editor (“ABE”)
- Cytidine Deaminase for C-to-T editor (“CBE”)
Beam Collaboration Q&A
Global Leader in Complement, Today and Tomorrow

**RARE DISEASE**

- **EMPAVELI** launch off to strong start
- **Platform** potential for EMPAVELI with four new registrational programs
- **New molecular entities** in development to sustain long-term growth in existing and new indications

**NEUROLOGY**

- **C3 plays a key role** in a wide range of neurodegenerative conditions
- Apellis to **pioneer targeted C3 therapies** in neurodegeneration

**OPHTHALMOLOGY**

- Optimistic heading into DERBY and OAKS readout in September 2021
  - **Significant unmet need** and blockbuster opportunity
- Data from monthly dosing believed to be sufficient for **NDA submission**
  - Primary endpoint on monthly dosing minimally affected by missed visits due to COVID-19
  - Primary endpoint on every-other-month dosing may be affected by missed visits due to COVID-19
- **New molecular entities** in development in GA, wet and intermediate AMD
## Growing Pipeline in Rare Disease, Ophthalmology, and Neurology

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<tr>
<th>PRODUCT</th>
<th>DISEASE</th>
<th>PRECLINICAL</th>
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<td>EMPAVELI™ (systemic pegcetacoplan)*</td>
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<td>siRNA + EMPAVELI**</td>
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*Sobi has global co-development and ex-U.S. commercialization rights for systemic pegcetacoplan. **Initial IND for siRNA. *** Pending regulatory feedback.
APELLIS R&D DAY

AND THEY’RE OFF!

THANK YOU!
APPELLIS R&D DAY
June 30, 2021
AND THEY’RE OFF!