Workshop

Efgartigimod Phase 2 Clinical Trial in ITP: Full Data

Cusatuzumab Phase 1/2 Clinical Trial in AML: Proof-of-Biology Data

3 December 2018, San Diego
Forward-Looking Statements

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12:00 – 12:35 PM

**Proof-of-Concept of Efgartigimod (ARGX-113) in Immune Thrombocytopenia (ITP)**

- Full data from Phase 2 clinical trial
- Nicolas Leupin, CMO, argenx
- Guest speaker: Prof. Dr. Adrian Newland, Barts London & Royal London Hospital

12:35 – 1:15 PM

**Advancing Cusatuzumab (ARGX-110) in Acute Myeloid Leukemia (AML)**

- Proof-of-biology data from Phase 1 dose escalation trial
- Hans de Haard, CSO, argenx
- Guest speaker: Prof. Dr. Adrian Ochsenbein, Bern Cancer Center, Inselspital, University of Bern

1:15 – 1:30 PM

**Q&A**
Prof. Dr. Adrian Newland

- Professor of Haematology at Barts and the London NHS Trust
- Expert in haematological malignancy and particular interest in immunohaematology, studying the molecular basis of the autoimmune disease, in particular thrombocytopenia, and piloting the clinical use of novel treatments
- Developed the Leukaemia and Bone Marrow transplant unit in the early 1980s
- Centre Lead for Haematology in the Medical School, Director of Pathology for the Trust and is Clinical Director of the North East Thames Cancer Network

Prof. Dr. Adrian Ochsenbein

- Professor of Bern Cancer Center, Inselspital, University of Bern
- Expert in cancer/leukemia stem cells which are the origin of the disease and responsible for relapse after successful chemotherapy in AML. Studies generate broad understanding of translational research from animal studies to clinical applications
- Member of the National Research Council
- Awarded the Otto Naegeli Prize 2016 in recognition of the excellent scientific work as a clinically active medical oncologist
Efgartigimod: A Pipeline-in-a-Product Opportunity
**Efgartigimod: Human IgG1 Fc Fragment with ABDEG™ Mutations Exploits Natural Fc/FcRn Interaction**

- **IgG antibodies recycle through FcRn**...  
  - Efgartigimod potently blocks FcRn...  
  - Leading to IgG elimination

- Natural ligand binding: complex of efgartigimod and FcRn resides mainly in endosomal recycling compartment avoiding lysosomal degradation
- Improves affinity to FcRn in pH dependent manner thereby providing relatively long half-life of Fc fragment and excellent biodistribution
- Cannot engage FcγReceptors and does not recruit effector cells

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(4) argenx data
### Primary Adult Immune Thrombocytopenia (ITP) – a Severe Autoimmune Disorder

#### What is ITP?

- Rare autoimmune bleeding disease
  - Estimated 69,300\(^{(1)}\) patients in US
  - ~80% diagnosed with primary ITP
    - Newly diagnosed: ~3,000 – 7,500 patients \(^{(1)}\)
    - Persistent: ~4,500 patients \(^{(2)}\)
    - Chronic: ~43,000 patients \(^{(2)}\)
- Symptoms include: mild bruising to severe bleeding, fatigue, fear of bleeding, impact on work and social activities, depression
- Relevance of platelet counts
  - ≤ 30 X 10\(^9\)/L generally accepted trigger for therapy
  - Improvement to ≥ 50 X 10\(^9\)/L considered clinically meaningful

#### Limited treatment options

- Multiple iterations on corticosteroids & IVIg
- TPO-receptor agonists* 
- Splenectomy
- Immunomodulatory agents

* Generated global revenues of $1.5 billion in 2017\(^{(3)}\)\(^{(4)}\)

#### Unmet need in ITP

- Current treatments – limited efficacy and significant side effects
- No real treatment paradigm exists – trial & error
- Patients adapt lifestyle to cope with disease burden and treatment side effects

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\(^{(3)}\) Novartis FY 2017

\(^{(4)}\) Amgen FY 2017
Efgartigimod Targets All Pathogenic AutoAb Actions Simultaneously
Potential to eliminate cycling between therapies based on trial-and-error
**ITP Amended Phase 2 Proof-of-Concept Trial Design**

**Key inclusion criteria:**
- Primary ITP patients
- Platelet levels < 30 \( \times 10^9 \)/L
- On a stable dose of SoC treatment prior to randomization

- **19 study centers from 8 countries**

**Main Study**

<table>
<thead>
<tr>
<th>Screening/Randomization</th>
<th>Treatment Phase</th>
<th>Follow-up Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>SoC + efgartigimod (10 mg/kg) N=13</td>
<td>1 year</td>
</tr>
<tr>
<td>4 doses; N=38</td>
<td>SoC + efgartigimod (5 mg/kg) N=13</td>
<td>SoC + Placebo N=12</td>
</tr>
<tr>
<td>≤2 weeks</td>
<td>SoC + Placebo N=12</td>
<td>21 weeks</td>
</tr>
<tr>
<td></td>
<td>3 weeks</td>
<td>1 year</td>
</tr>
</tbody>
</table>

**Open Label Extension (OLE)**

- SoC + efgartigimod (10 mg/kg) N = 12
- 33% of OLE patients come from placebo arm

**Primary endpoint**

- Safety & Tolerability

**Secondary endpoints**

- Efficacy
- PK
- PD
- Immunogenicity
### Key Inclusion Criteria:
- Primary ITP patients
- Platelet levels < 30 × 10^9/L
- On a stable dose of SoC treatment prior to randomization

### Secondary Endpoints
- **Primary Endpoint:** Efficacy (platelet counts, rescue therapy, and bleeding)
- **Safety & Tolerability:** PK, PD total IgG, pathogenic IgG, Immuno-genicity

### Main Study

<table>
<thead>
<tr>
<th>Screening/Randomization</th>
<th>Treatment Phase</th>
<th>Follow-up Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>SoC + efgartigimod (10mg/kg) N=13</td>
<td>SoC + efgartigimod (10mg/kg) N=13</td>
<td></td>
</tr>
<tr>
<td>SoC + efgartigimod (5mg/kg) N=13</td>
<td>SoC + efgartigimod (5mg/kg) N=13</td>
<td></td>
</tr>
</tbody>
</table>

### Open Label Extension (OLE)
- SoC + efgartigimod (10 mg/kg) N = 12
- 33% of OLE patients come from placebo arm

### Key Considerations
- Initiated OLE halfway through the study
- Some of best responders did not enroll because still in response at end of study
- 33% (N = 4) of OLE patients come from placebo arm
ITP Phase 2 Clinical Trial: Results
### ITP Phase 2 Baseline Population and Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 12)*</th>
<th>Efgartigimod: 5 mg/kg (n = 13)</th>
<th>Efgartigimod: 10 mg/kg (n = 13)**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median (range)</strong></td>
<td>38.5 (19 - 69)</td>
<td>41.0 (22 - 77)</td>
<td>46.0 (29 - 62)</td>
</tr>
<tr>
<td><strong>Gender, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>5 (41.7)</td>
<td>4 (30.8)</td>
<td>9 (69.2)</td>
</tr>
<tr>
<td>• Female</td>
<td>7 (58.3)</td>
<td>9 (69.2)</td>
<td>4 (30.8)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• White</td>
<td>11 (91.7)</td>
<td>12 (92.3)</td>
<td>13 (100)</td>
</tr>
<tr>
<td>• Not reported</td>
<td>1 (8.3)</td>
<td>1 (7.7)</td>
<td></td>
</tr>
<tr>
<td><strong>ITP Classification, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Newly diagnosed (≤3 months)</td>
<td></td>
<td>2 (15.4)</td>
<td></td>
</tr>
<tr>
<td>• Persistent (&gt;3 and &lt;12 months)</td>
<td></td>
<td>1 (7.7)</td>
<td>4 (30.8)</td>
</tr>
<tr>
<td>• Chronic (≥12 months)</td>
<td>9 (75.0)</td>
<td>10 (76.9)</td>
<td>9 (69.2)</td>
</tr>
<tr>
<td><strong>Duration of ITP, median years (range)</strong></td>
<td>3.5 (0.3 - 47.8)</td>
<td>4.5 (0.1 - 34.2)</td>
<td>5.4 (0.7 - 28.7)</td>
</tr>
<tr>
<td><strong>Baseline platelet count, mean, k/µL (range)</strong></td>
<td></td>
<td>15 (5 - 35)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline platelet count of &lt;15k/µL, N (%)</strong></td>
<td></td>
<td>7 (53.8)</td>
<td></td>
</tr>
<tr>
<td><strong>SoC at baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Corticosteroids n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• TPOs n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Immunosuppressants n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Watch &amp; Wait n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Other n (%)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- Four placebo patients were discontinued before the end of the main study
- **Two 10mg/kg patients were discontinued before receiving all 4 infusions argenx data

**Very refractory population**

50% of patients with baseline platelet counts below 15k/µL
Favorable Tolerability Profile Consistent with Previous Studies

Treatment-emergent adverse events balanced between active and placebo arms

- Tolerability profile consistent with Phase 2 myasthenia gravis (MG) and Phase 1 healthy volunteer (HV) trials
- TEAEs mostly mild in severity (grade 1)
- No deaths or TEAEs leading to discontinuation of treatment reported*

Bleeding TEAEs not included

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (TEAEs) Reported in ≥ 2 subjects</th>
<th>Placebo (N = 12)</th>
<th>Efgartigimod 5 mg/kg (N = 13)</th>
<th>Efgartigimod 10 mg/kg (N = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Most common TEAEs N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Headache</td>
<td>2 (16.7)</td>
<td>1 (7.7)</td>
<td>-</td>
</tr>
<tr>
<td>• Hypertension</td>
<td>1 (8.3)</td>
<td>-</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>• Vomiting</td>
<td>-</td>
<td>1 (7.7)</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>• Cystitis</td>
<td>-</td>
<td>1 (7.7)</td>
<td>-</td>
</tr>
<tr>
<td>• Rash</td>
<td>1 (8.3)</td>
<td>1 (7.7)</td>
<td>-</td>
</tr>
<tr>
<td>• Productive cough</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>TEAEs deemed related to study intervention N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Headache</td>
<td>1 (8.3)</td>
<td>-</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>• Vomiting</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>• Pubic pain</td>
<td>1 (8.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>• Vaginal discharge</td>
<td>1 (8.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>• Amenorrhoea</td>
<td>1 (8.3)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* One thrombocytopenia downgraded per protocol after database lock

argenx data: Table 14.3.1.2a & 14.3.1.5a - Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug - Main Study
Efgartigimod Leads to Lasting IgG Reduction Across Studies

Total IgG levels in efgartigimod studies to date (Healthy Volunteers, MG, ITP)

- Pharmacodynamics (PD) closely align with Phase 1 trial in HV and Phase 2 trial in MG
- IgM, IgA and albumin levels not affected (data not shown)
- Half-life: approx. 5 days
- Pharmacokinetics (PK) very similar to Phase 1 trial in HV and Phase 2 trial in MG (data not shown)
- Low titer of anti-drug antibodies (ADA) seen in 16.7% placebo patients vs. 30.8% efgartigimod patients (10 mg/kg) with no apparent effect on PK/PD
• IgG subtypes reduced in all patients in active arms (auto-antibodies in ITP are IgG1/3)
• Relatively small differences observed between 5 and 10 mg/kg cohort
• Similar reduction levels achieved with 10 mg/kg dose compared to previous studies
• All patients tested positive for platelet associated auto-antibodies (GP IIb/IIIa; GP Ib/IX; GP Ia/IIa)
• Platelet associated auto-antibody signal reduced by maximally 53-97% in 8/12 efgartigimod responders
Clinically Meaningful Improvements in Platelet Counts in Active Arms
Separation from placebo starts at maximum PD and lasts through study follow-up

Mean platelet count ± SEM (x10^9/L)

- Placebo
- 5 mg/kg efgartigimod
- 10 mg/kg efgartigimod

Days

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80
Strong Improvement of Platelet Counts Across Doses

46-67% of patients exceeded platelet counts ≥ 50×10⁹/L during at least two visits

- OLE acts as true fourth cohort since patients’ platelets had to fall below 30×10⁹/L to be eligible for a treatment cycle; patients still in response from primary study were not eligible
- Responses seen across newly diagnosed (in 5mg/kg arm), persistent and chronic ITP patients

Patients achieving platelet counts of ≥ 50×10⁹/L at least two times

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% of patients with an improvement of platelet counts ≥ 50×10⁹/L for at least two visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo + SOC</td>
<td>25% (N=3)</td>
</tr>
<tr>
<td>efgartigimod 5 mg/kg + SOC</td>
<td>46% (N=6)</td>
</tr>
<tr>
<td>efgartigimod 10 mg/kg + SOC</td>
<td>46% (N=6)</td>
</tr>
</tbody>
</table>

OLE (1st treatment cycle)

- 67%* (N=8) after cut-off date not QC-ed

*After cut-off date not QC-ed
Robust Improvement of Platelet Count with Durability
Increasing differentiation from placebo for increasing efficacy hurdle

Post-hoc analysis of increasing thresholds of efficacy

<table>
<thead>
<tr>
<th>Response Rate (%)</th>
<th>placebo + SOC (N=12)</th>
<th>efgartigimod + SOC (pooled N=26)</th>
<th>P* = 0.03</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 50×10⁹/L (≥50×10⁹/L)</td>
<td>0% (N=0)</td>
<td>38% (N=10)</td>
<td>38%</td>
</tr>
<tr>
<td>≥ 100×10⁹/L</td>
<td>8% (N=1)</td>
<td>42% (N=11)</td>
<td>42%</td>
</tr>
<tr>
<td>≥ 50×10⁹/L (at least two visits)</td>
<td>25% (N=3)</td>
<td>46% (N=12)</td>
<td>46%</td>
</tr>
<tr>
<td>≥ 30×10⁹/L</td>
<td>58% (N=7)</td>
<td>73% (N=19)</td>
<td>73%</td>
</tr>
</tbody>
</table>

- Efgartigimod generated therapeutic activity at multiple relevant thresholds of efficacy
- Duration of platelets remaining ≥50×10⁹/L ranged from 1 - 20 weeks, with five patients above that platelet threshold for more than a month
- ≤ 30 X 10⁹/L generally accepted trigger for therapy with improvement to ≥ 50 X 10⁹/L considered clinically meaningful

Note: Increasing threshold analysis based exact logistic regression model with the baseline result as a factor
Responses in First Cycle of Open Label Extension

**Responders in main study**
Patients achieving platelet counts of ≥ 50×10⁹/L at least two times

- Placebo
- 5 mg/kg
- 10 mg/kg

**Roll-over in OLE (N=12)**

- Placebo
- 5 mg/kg
- 10 mg/kg

**Responders in OLE (8/12)**
Patients achieving platelet counts of ≥ 50×10⁹/L at least two times

- 10 mg/kg
- 10 mg/kg
- 10 mg/kg

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**Open Label Extension study**

**1st Cycle Analysis:**

8 patients responded on efgartigimod (10 mg/kg):

- 3 Non-responders from placebo started to respond
- 2 Non-responders from 5 mg/kg treatment arm started to respond
- 3 Responders from 10 mg/kg treatment arm continued to respond
Validated Bleeding Assessment Measures

Bleeding events are hallmark of ITP and were not an exclusion criterion to study entry

**Bleeding events**

- **Mild**: Transient or mild discomfort & no medical intervention required
- **Moderate**: Mild to moderate limitation in activity & no or minimal medical intervention required
- **Severe**: Marked limitation in activity, some assistance usually required & medical intervention required, hospitalization possible
- **Life-threatening**

**Adverse events**

**WHO scale**

General bleeding assessment widely used in clinical development

- **Grade 0**: No bleeding
- **Grade 1**: Petechial bleed
- **Grade 2**: Mild blood loss (clinically significant)
- **Grade 3**: Gross blood loss requires transfusion (severe)
- **Grade 4**: Debilitating blood loss, retinal/cerebral bleed (associated with fatality)

**ITP-BAT scale**

Consistent description of the bleeding phenotype in ITP in 3 domains: Skin, Mucosa and Organ grade (SMOG)

- **Grade 0**: No bleeding
- **Grade 1**: Reported without medical documentation
- **Grade 2 → 4**: Increasing severity, number and surface area
- **Grade 5**: Fatal bleeding
No Adverse Event Reports of Severe Bleeding

All bleeds in 10 mg/kg were mild

- Bleeding is hallmark of ITP disease; low platelet counts correlate with higher incidence of bleeding events
- No bleeding events deemed study drug related by investigator
- No severe bleedings in any patient
- No moderate bleeds occurred in 10 mg/kg arm; bleeds were all mild
- 5 patients in each treatment arm experienced at least one bleeding TEAE, compared to 3 in placebo cohort
- 35 bleeding events reported in 13/38 patients; 15 bleeds (37%) in 1 non-responder (data not shown)
Efgartigimod Reduces Incidence of Bleeding Compared to Placebo

Bleeding events in 10 mg/kg arm steadily decline and stay low following treatment.

WHO scale in placebo versus 5 mg/kg and 10 mg/kg efgartigimod

* Severity is graded from 0 to 4 – Only grade 1 and 2 were observed
Fewer Patients with Bleeds in Active Arms Versus Placebo Over Time

ITP-BAT/SMOG scale in placebo versus 5 mg/kg and 10 mg/kg efgartigimod

- **Skin**
- **Mucosa**
- **Organ**

*Severity is graded from 0 to 5 – Only grade 1, 2 and 3 were observed*
Reduction of Total IgGs Correlates with Increased Platelet Counts and Reduced Bleeding Events

Mean platelet counts versus total WHO scale versus total IgGs

**Placebo**

**10 mg/kg efgartigimod**

- Mean platelet counts (x10^9/L)
- % patients with total WHO scale >0
- % total IgGs

Days
Favorable and consistent safety and tolerability profile
- No trends seen for infections or headaches across all studies
- No decreases in IgM, IgE, IgA or albumin

Robust efficacy signal in relapsed/refractory population after short drug exposure
- Clinically meaningful increase in platelet counts over placebo
- 50% of patients came on study with platelets <15x10⁹

Strong correlation between IgG reduction, platelet count improvement and reduction of bleeding events

Data enable Phase 3 in ITP (IV) and launch of Phase 2 in ITP (SC)
Cusatuzumab: Selectively Targeting LSCs
**Cusatuzumab: Unique MOA Targeting Acute Myeloid Leukemia (AML) Leukemic Stem Cells (LSCs) and Blasts**

- First-in-class anti-CD70 ADCC enhanced SIMPLE Antibody™ which selectively targets LSCs and blasts in AML and other hematological indications
- CD70 expressed on ~86-100% of AML blasts; majority of malignant cells are CD70/CD27 double-positive

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**Cusatuzumab induces LSC differentiation**

1. **Induce myeloid differentiation**
   - LSC
   - Differentiated cell
   - CD27, CD70

2. **Kill LSCs**
   - LSC
   - CD27, CD70

**Cusatuzumab kills blasts**

3. **Kill Blasts**
   - Blast
   - CD27, CD70

4. **Block proliferation & survival signal**
   - Activation of the pathway leads to release of sCD27, which is a biomarker

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Selective Targeting of CD70 Expressed on Leukemic Stem Cells
Unifying rationale across risk and age classes in AML

Elevated sCD27 serum levels correlate with poor prognosis

- Elevated serum sCD27 in all newly diagnosed AML patients, regardless of risk category or age
- sCD27 levels are an independent negative prognostic marker in all newly diagnosed AML patients
- CD70 selectively overexpressed on LSCs, not on hematopoietic stem cells (HSCs)

Legend: OS, overall survival.
Statistics: left: one-way ANOVA; middle: log-rank test. ***, P < 0.001.

Cusatuzumab + Hypomethylating Agents Work Synergistically

- HMAs upregulate CD70 on AML leukemic stem cells – NOT on hematopoietic stem cells
- *Ex vivo*: HMA/cusa variant synergistically reduces colony formation
- *In vivo*: Transient treatment by HMA/cusa variant eradicates human LSCs in therapeutic model (not shown)


Hinterbrander ASH 2017: Blocking CD70/CD27 signaling in combination with hypomethylating agents eradicates human CD34+ AML stem and progenitor cells; manuscript in preparation
Ongoing Phase 1/2 Trial in Newly Diagnosed AML: Update Phase 1
Ongoing Phase 1/2 Combination Trial
Newly diagnosed AML patients unfit for intensive chemotherapy

Phase 1 – Dose Escalation
- 1 mg/kg, N = 3+3
- 3 mg/kg, N = 3+3
- 10 mg/kg, N = 3+3
- 20 mg/kg, N = 3+3

Endpoints
• Safety, tolerability
• Clinical outcome
• Translational data

Phase 2 – Proof of Concept at 10 mg/kg
Currently enrolling Phase 2

- Efficacy seen across doses in Phase 1 dose escalation
- Up to 21 patients to enroll in initial Phase 2 study with potential to expand enrollment to 40
- 10 mg/kg selected for Phase 2 to saturate bone marrow and maintain clean tolerability profile
Ongoing Phase 1/2 Combination Trial

Two weeks cusatuzumab monotherapy to assess impact on LSC biology

Key inclusion criteria
- Newly diagnosed AML patients
- Unfit for intensive treatment or stem cell transplantation
- ≥20% blasts in the bone marrow by cytomorphology
# Phase 1 Dose Escalation Population

Newly diagnosed patients with intermediate or adverse risk profiles

<table>
<thead>
<tr>
<th></th>
<th>1 mg/kg (N=3)</th>
<th>3 mg/kg (N=3)</th>
<th>10 mg/kg (N=3)</th>
<th>20 mg/kg (N=3)</th>
<th>Total (N=12)</th>
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</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
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<tr>
<td>Median</td>
<td>77</td>
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<td>Range</td>
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<td>64-75</td>
<td>72-77</td>
<td>64-84</td>
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<td>Male</td>
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<td><strong>AML Classification (WHO 2016)</strong></td>
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<td>NOS*</td>
<td>0</td>
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<td>With myelodysplasia-related changes</td>
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<td>2</td>
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<td><strong>Time since diagnosis (days)</strong></td>
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<td>Median</td>
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<td>17</td>
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<td>0-29</td>
<td>0-61</td>
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<td><strong>Risk categories</strong></td>
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<tr>
<td>Adverse</td>
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<td>1</td>
<td>2</td>
<td>6</td>
</tr>
</tbody>
</table>

* NOS: not otherwise specified; # ELN 2017

- Median age: 75 years
- Balanced distribution of intermediate or adverse risk profiles between different cohorts
Vidaza Monotherapy Provides Limited Overall Response Rate
ORR in 30-35% range with significant side effects

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (N)</th>
<th>ORR (%)</th>
<th>Adverse events (G3-G4)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falantes et al. 2017</td>
<td>710</td>
<td>35.5*</td>
<td>Pancytopenia</td>
<td>8 – 75</td>
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<td>Febrile neutropenia</td>
<td>11 – 50</td>
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<tr>
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<td>Infections</td>
<td>6 – 30</td>
</tr>
<tr>
<td>Dombret et al. 2015</td>
<td>231</td>
<td>31.1**</td>
<td>Febrile neutropenia</td>
<td>28</td>
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<tr>
<td></td>
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<td></td>
<td>Neutropenia</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thrombocytopenia</td>
<td>24</td>
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<td></td>
<td></td>
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<td>Pneumonia</td>
<td>24</td>
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<td></td>
<td>Anemia</td>
<td>19</td>
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<td></td>
<td>Leukopenia</td>
<td>16</td>
</tr>
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<td></td>
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<td></td>
<td>Hypokalemia</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infections</td>
<td>5</td>
</tr>
</tbody>
</table>

• 60% of newly diagnosed AML patients are more than 60 years old
• Hypomethylating agents (HMA) have no documented effect on leukemic stem cells responsible for relapse

* ORR defined as CR + CRi + PR
** ORR defined as CR + CRi + CRc-20 + PR

Dombret et al. 2015, Blood; Falantes et al. 2017, Leuk & Lymphoma.
Phase 1 Dose Escalation: No Obvious Toxicity on Top of Known Vidaza Toxicity

- No dose-limiting toxicity observed
- Grade 3 and 4 hematological toxicities in line with expected Vidaza toxicities in 6 patients (50%), predominantly reported in 1 mg/kg and 3 mg/kg cohorts
- Other single cases of Grade 3 events were reported: Constipation, Arthritis, Proctitis, Epistaxis, Tooth Infection, Vulvovaginal Inflammation, Anal Abscess, Agitation, Lung infection, Pleuro-pericarditis, Lung infiltration
- Multi-Organ failure (Grade 5) was due to disease progression

<table>
<thead>
<tr>
<th>Treatment Emerging Adverse Events (TEAEs)</th>
<th>Grade 3* events (N)</th>
<th>Grade 4 events (N)</th>
<th>Grade 5 events (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>16 (5)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>6 (4)</td>
<td>7 (4)</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>3 (2)</td>
<td>3 (3)</td>
<td></td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>4 (4)</td>
<td></td>
<td>2 (2)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td></td>
<td></td>
<td>1 (1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (1)</td>
<td></td>
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</tr>
<tr>
<td>Multi-Organ Failure</td>
<td></td>
<td></td>
<td>1 (1)</td>
</tr>
<tr>
<td>Atrial Flutter</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Grade 3: only if reported in at least 2 cases
92% (11/12) Response Rate – CR/CRi/PR

Three patients on study for more than 12 months
11 (92%) patients responded to the combination therapy:

- Including 10/11 patients reaching complete remission (8 with hematologic recovery and 2 without)
- Mean reduction of bone marrow blasts:
  - 30% after cusatuzumab monotherapy that reduced down to 86% at best response
Rapid Onset of Response with 3 Patients Reaching First Response After Single Dose

- **Median time to first response**
  - **All patients**: 14.0/3.3 weeks/months
  - 1 mg/kg: 17.6/4.0 weeks/months
  - 3 mg/kg: 14.7/3.4 weeks/months
  - 10 mg/kg: 13.9/3.2 weeks/months
  - 20 mg/kg: 10.0/2.3 weeks/months

- **3 (25%) patients reached a first response after a single dose of cusatuzumab**
Duration of Response – Ongoing Analysis

3/12 patients event free survival > 1 year; 6/12 patients still on study

- Median duration of response: 5.5 months
- Median event free survival: 8.1 months (range: 2 months – 17.4 months)
- 9 (75%) patients event free survival for > 6 months
- 6 (50%) patients still on trial:
  - 3 patients more than 1 year on trial
  - 1 patient more than 17 months on trial
Recommended Phase 2 Dose Is 10 mg/kg
Saturating serum level at this dose maintained in bone marrow

- RP2D was established at 10 mg/kg based on safety data, pharmacokinetics and saturation of cusatuzumab in blood
- Similar levels of cusatuzumab observed in blood and bone marrow
Patient Case Studies
Case 10: Complete Remission after Lowering Vidaza Concentration

Cusatuzumab monotherapy

Time to response (weeks)

- Partial remission (PR)
- Complete remission (CR)
- Complete remission with incomplete recovery (CRi)
- MRD - BM by flow and molecular genetics
- EOT due to PD
- EOT due to AE (IRR)
- EOT due to transplant
- Transplant

Cohort 1 (1 mg/kg)
- Adv CR: 1
- Int CR: 2
- Adv CR: 3

Cohort 2 (3 mg/kg)
- Int CR: 4
- Int CR: 5
- Adv PR: 6

Cohort 3 (10 mg/kg)
- Int CR: 7
- Int CR: 8
- Adv CRi: 9

Cohort 4 (20 mg/kg)
- Adv CR: 10
- Adv CR: 11
- Int: 12

Best response

EOT due to 15Oct18

6 months

12 months

Ongoing

MRD - BM by flow and molecular genetics
Case 10: Complete Remission after Lowering Vidaza Concentration

- 77 year old male; AML with myelodysplasia related changes, M2; BM 50% blasts
- Molecular genetics: ASXL1 mutated, RUNX1 mutated, EZH2 mutated, ZRSR2 mutated, SH2B3 mutated; cytogenetics: Deletion 1p; Deletion 7q – Adverse risk profile

Complete remission with incomplete hematological recovery at C3 and MRD negativity by flow cytometry

Complete remission at C4D17

Vidaza reduced by 50% due to Vidaza hematoxicity (C3); cusatuzumab maintained at 20 mg/kg

Still on study

Source: argenx data – patient anecdotes – uncleaned data
Case 10: Complete Remission after Lowering Vidaza Concentration

<table>
<thead>
<tr>
<th>Cohort 1 (1 mg/kg)</th>
<th>Cohort 2 (3 mg/kg)</th>
<th>Cohort 3 (10 mg/kg)</th>
<th>Cohort 4 (20 mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adv CR 1</td>
<td>Int CR 2</td>
<td>Adv CR 3</td>
<td>Adv PR 6</td>
</tr>
<tr>
<td>Int CR 4</td>
<td>Int CR 5</td>
<td>Int CR 7</td>
<td>Int CR 8</td>
</tr>
<tr>
<td>Adv PR 10</td>
<td>Adv CR 11</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

Cusatuzumab monotherapy

- Transplant
- MRD - BM by flow and molecular genetics

Time to response (weeks)
- 6 months
- 12 months
- EOT due to PD
- EOT due to AE (IRR)
- Complete remission (CR)
- Complete remission with incomplete recovery (CRi)
- Partial remission (PR)
- EOT due to transplant

Cohort cut off: 15 Oct 18

Case 10: Complete Remission after Lowering Vidaza Concentration

Ongoing

Partial remission (PR)
Case 11: Complete Remission in a TP53 Mutant AML Patient

- 72 year old female; AML with myelodysplasia related changes; BM 22% blasts CM

**Partial remission at C1 after one dose of 20 mg/kg cusatuzumab monotherapy**

**Complete remission at C5 with MRD negativity by flow cytometry**

**Still on study**
<table>
<thead>
<tr>
<th>Cohort</th>
<th>Case</th>
<th>Response</th>
<th>MRD flow BM*</th>
<th>MRD mol BM</th>
<th>MRD flow PB*</th>
<th>MRD mol PB</th>
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</thead>
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<tr>
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<tr>
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<td>2</td>
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<tr>
<td>3 mg/kg</td>
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<td>6</td>
<td>PR</td>
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<td>10 mg/kg</td>
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<td>9</td>
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<td>20 mg/kg</td>
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<td>11</td>
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</tbody>
</table>

* MRD negativity threshold = 10E-4
Overall Conclusions Phase 1 Dose Escalation

Favorable tolerability profile
- No obvious toxicity on top of Vidaza toxicity
- No dose-limiting toxicity observed

Encouraging proof-of-biology data in 12 patients (4 dose cohorts; 3 pts each)
- 92% response rate (11/12) mainly CR/CRi
- 3 patients responded after cusatuzumab monotherapy
- Significant blast reduction in bone marrow after cusatuzumab monotherapy
- MRD negativity in 42% (5/12) treated patients

Supported by translational dataset
- Decreased sCD27 levels
- Reduced LSC colony formation
- Increased myeloid differentiation – asymmetric division

Recommended Phase 2 dose: 10 mg/kg
Acknowledgement

T. Pabst & A. Ochsenbein,
U. Bacher, U. Novak, C. Riether,
S. Höpner, E. Gfeller

Thank you to the study teams, the patients and their families
Thank you!