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Ablynx

Rapid growth since its foundation in 2001

2001
Foundation

2002
Technology platform
- €5M seed financing
- No products
- No partnerships
- 10 employees

2007
R&D – early stage
- €70M private equity
- €85M IPO (Euronext)
- 11 R&D projects
- 1 Nanobody in the clinic
- 3 partners
- 144 employees

Today
R&D – late stage
- > €370M in equity and debt
- > €400M cash from partners
- > 45 R&D projects
- > 1,500 patients treated
- 8 Nanobodies in the clinic
- 1st Nanobody expected to be launched in 2018
- 8 partners
- ~ 400 employees
- €235M in cash at 31st Dec 2016

Evolving into a commercial stage biotech company
# Broad product pipeline

>45 programmes, 8 Nanobodies in clinical development

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Target</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Filing</th>
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<tbody>
<tr>
<td>caplacizumab</td>
<td>aTTP</td>
<td>vWF</td>
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<tr>
<td>vobarilizumab</td>
<td>RA</td>
<td>IL-6R</td>
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<td></td>
<td>SLE</td>
<td>IL-6R</td>
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<tr>
<td>ALX-0171</td>
<td>RSV</td>
<td>RSV</td>
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<tr>
<td>Up to 17</td>
<td>Immuno-Oncology</td>
<td>Various</td>
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<tr>
<td>programmes</td>
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<tr>
<td>ozoralizumab</td>
<td>RA</td>
<td>TNFα</td>
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<tr>
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<td>RA</td>
<td>TNFα</td>
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<td>ALX-0761/M1095</td>
<td>Psoriasis</td>
<td>IL-17A/IL-17F</td>
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<td>Japan</td>
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<td>BI 836880</td>
<td>Oncology</td>
<td>VEGF/Ang2</td>
<td></td>
<td></td>
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<td>BI 655088</td>
<td>Chronic kidney disease</td>
<td>CX3CR1</td>
<td></td>
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<td>NA</td>
<td>Inflammation</td>
<td>CXCR2</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ALX-0141</td>
<td>Bone disorders</td>
<td>RANKL</td>
<td></td>
<td></td>
<td></td>
<td>Greater China</td>
<td></td>
</tr>
<tr>
<td>&gt;15 wholly-</td>
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<td>Various</td>
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<td>owned and</td>
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<td>programmes</td>
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</tr>
</tbody>
</table>

★ Filing in EU based on Phase II TITAN data
## Four key pillars of value

**First marketed product expected 2018**

<table>
<thead>
<tr>
<th><strong>Caplacizumab</strong> (anti-vWF)</th>
<th><strong>ALX-0171</strong> (anti-RSV)</th>
<th><strong>Vobarilizumab</strong> (anti-IL-6R)</th>
<th><strong>Immuono-oncology</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• First-in-class treatment for acquired thrombotic thrombocytopenic purpura</td>
<td>• Potential breakthrough treatment delivered by inhalation for respiratory syncytial virus infections (RSV)</td>
<td>• Novel potential best-in-class treatment for rheumatoid arthritis (RA); also being studied in systemic lupus erythematosus (SLE)</td>
<td>• Up to 17 programmes partnered with Merck &amp; Co in deal worth up to €5.7Bn in milestones plus royalties</td>
</tr>
<tr>
<td>• Acute, life threatening, ultra-rare blood clotting disorder</td>
<td>• RSV can be very serious in infants, the elderly and the immune-compromised</td>
<td>• Partnership with AbbVie</td>
<td>• First <em>in vivo</em> pre-clinical milestone achieved</td>
</tr>
<tr>
<td>• No indicated therapeutic drug currently available</td>
<td>• No approved therapeutic drug currently available</td>
<td>• RA - two successful Phase IIb studies; preparing for regulatory meetings and potential Phase III; exploring new partnership options</td>
<td>• First clinical studies planned for 2017</td>
</tr>
<tr>
<td>• Filed for approval in Europe in H1 2017</td>
<td>• Phase IIb topline results expected in H2 2018</td>
<td>• SLE – Phase II topline results expected in H1 2018</td>
<td>• Market expected to grow to &gt;$43bn by 2020</td>
</tr>
<tr>
<td>• Wholly-owned; potentially Ablynx’s first marketed product in 2018</td>
<td>• Multi-billion $ market</td>
<td>• Large, multi-billion $ markets</td>
<td>• Self-commercialisation strategy being executed</td>
</tr>
<tr>
<td>• Self-commercialisation strategy being executed</td>
<td>• Wholly-owned</td>
<td></td>
<td>• Peak sales potential of &gt; €400M</td>
</tr>
</tbody>
</table>

- **Immuno-oncology**
  - Up to 17 programmes partnered with Merck & Co in deal worth up to €5.7Bn in milestones plus royalties
  - First *in vivo* pre-clinical milestone achieved
  - First clinical studies planned for 2017
  - Market expected to grow to >$43bn by 2020
**Ablynx**

**Diversified shareholder base – as of January 2017**

- Ordinary shares listed on Euronext Brussels (ABLX)
- Sponsored Level I ADRs on the US OTC market (ABYLY)
- 61.1M shares outstanding
- 2.5M outstanding warrants (in number of shares)

**Breakdown of share capital**

- 64% Other shareholders
- 10% Van Herk Investments B.V. (NL)
- 9% Fidelity Management Research LLC (FMR LLC) (US)
- 5% Bank of America (US)
- 5% Perceptive Advisors (US)
- 5% GAM International (UK)
- 4% Boehringer Ingelheim (DE)

**% of Institutional Shareholders by Geography**

- US 38%
- UK 21%
- Belgium 20%
- France 2%
- Scandinavia 2%
- The Netherlands 14%
- Other 4%

*based on public filings*
Nanobodies

Derived from heavy-chain only antibodies

- *Camelid* heavy-chain only antibodies are stable and fully functional
- Nanobodies represent the next generation of antibody-derived biologics

Ablynx’s Nanobody
- small and robust
- easily linked together
- sequence homology comparable to humanised/human mAbs
- nano- to picomolar affinities
- able to bind and block challenging targets
- multiple administration routes
- manufactured in microbial cells
Ablynx’s Nanobody drug discovery engine

Rapid generation of novel biologics

Immunise llamas with antigen

and/or

Use proprietary synthetic Nanobody phage libraries

Wide range of highly diverse Nanobodies with 0.1-10nM affinities

Formatted Nanobodies

Cloned into microbial systems and produced through fermentation

~12-18 months
Ablynx’s Nanobodies
Platform advantages

Mix and match
Multi-specific/multivalent Nanobodies that address multiple targets in a single drug molecule – flexible GS linker lengths

Multiple delivery routes
- Inhalation
- Ocular
- Oral-to-topical

Manufacturing
- High-yield, high-concentration, low-viscosity, microbial production

Able to bind and block challenging targets
- Nanobodies against ion channels and GPCRs

Customised half-life extension
- Albumin-binding Nanobody
- Fc
Caplacizumab (anti-vWF) – wholly-owned

Potential first-in-class treatment of acquired thrombotic thrombocytopenic purpura (aTTP)
Caplacizumab – anti-vWF Nanobody

First-in-class potential for the treatment of aTTP

- Total annual market potential ~€800M\(^1\)
- Feb 2017: filed in Europe for approval
- Phase III HERCULES topline results in H2 2017
- Phase I results in Japanese subjects in H2 2017
- 2018: anticipated first launch in Europe and BLA submission in USA
- 2019: anticipated launch in USA
- Forecast peak sales of >€400M\(^1\)
- Ablynx to lead commercialisation in USA, Canada and Europe
- Orphan Drug Status (EU/USA) – Patent protection to 2035

\(^1\) USA, Canada, EU and Japan
Caplacizumab unique mode of action

Rapidly stops formation of microclots

Caplacizumab blocks the platelet – ULvWF interaction

Ex vivo assay for platelet string formation
Fluorescence microscopy image of platelets adhering to UL-vWF in plasma of an aTTP patient

Without treatment, fluorescently labelled platelets adhere to UL-vWF, observed as string-like structures

Caplacizumab inhibits the formation of platelet strings and potentially the associated microvascular thrombi in many organs
Acquired TTP

Acute, life-threatening, ultra-rare blood clotting disorder

- **aTTP** is an acute disease leading to extensive morbidity and mortality
  - causes extensive micro clot formation in small blood vessels throughout the body
  - leads to tissue ischemia, organ dysfunction, and major thromboembolic events (stroke, myocardial infarction, thrombosis)
  - up to 20% mortality rate in the acute phase\(^1\) and \(~36\%\) of patients suffer from further disease recurrences\(^2\)

- We estimate a total of \(~7,500\) patients present p.a. in North America, Europe and Japan

- High unmet medical need with no approved therapeutic drug currently available

---

\(^1\) Allford et al, BJH 2003, Kremer Hovinga, Blood 2010; Benhamou, Haematologica 2012; \(^2\) George et al, EJH 2008
Acquired TTP

Current standard-of-care – high unmet medical need

There is a high unmet need for a novel treatment option that would result in:

- faster resolution of the acute episode of aTTP and related resulting organ damage
- reduction in risk of mortality and thromboembolic events
- prevention of recurrences while on treatment
- reduction in risk of refractoriness to treatment
- reduction in dependency on PEX
Caplacizumab
Addressing the unmet need in aTTP

TITAN Phase II study of caplacizumab¹
• 39% reduction in time to platelet normalisation
• 71% fewer patients with recurrences during treatment

Post-hoc analysis²
• 74% reduction in the frequency of major thromboembolic events (11% vs 43%)
• dramatic reduction in refractoriness to treatment (6% vs 22%)

Caplacizumab is expected to become a key component of the new standard-of-care

¹ Publication in the NEJM – 11 February 2016
² Publication in the Journal of Thrombosis and Haemostasis – 26 April 2017
Caplacizumab Phase II TITAN data

Post-hoc analysis of TTP related clinically relevant adverse events

- Post-hoc analysis of data from the TITAN study
- TTP related clinically relevant adverse events during study drug treatment

<table>
<thead>
<tr>
<th>Event</th>
<th>Caplacizumab (N=35)</th>
<th>Placebo (N=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Subjects</td>
<td>% of subjects</td>
</tr>
<tr>
<td>Embolic and thrombotic events (SMQ)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>(2.9%)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura</td>
<td>3 [2]</td>
<td>(8.6%)</td>
</tr>
<tr>
<td>TTP-related mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths related to TTP</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>4 [3]</td>
<td>(11.4%)</td>
</tr>
</tbody>
</table>

[1] This preferred term consisted of recurrences of TTP during the treatment period, defined in the protocol as exacerbations of TTP
[2] One adverse event reported as ‘Thrombocytopenia’ was not considered in this analysis, as this event was reported as part of the presenting disease
[3] A subject may have experienced more than one event:
   - ischemic and hemorrhagic stroke occurred in the same subject;
   - AMI and exacerbation occurred in the same subject;
   - pulmonary embolism and 2 exacerbations occurred in the same subject;
   - venous thrombosis and exacerbation occurred in the same subject

1 Publication in the Journal of Thrombosis and Haemostasis – 26 April 2017
# Caplacizumab Phase II TITAN data

## Post-hoc analysis on refractoriness to treatment

- Data published in a “letter to the editor” in the NEJM, issue 23 June 2016

<table>
<thead>
<tr>
<th>Refractoriness to treatment, n (%)</th>
<th>Caplacizumab N=35</th>
<th>Placebo N=37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure of platelet response after 7 days despite daily PEX treatment$^1$</td>
<td>2 (5.7)</td>
<td>8 (21.6)*</td>
</tr>
<tr>
<td>Absence of platelet count doubling after 4 days of standard treatment, and LDH&gt;ULN$^2$</td>
<td>0 (0)</td>
<td>4 (10.8)</td>
</tr>
</tbody>
</table>

* 2 patients in the placebo group who discontinued the study prematurely (before 7 days) without reaching the platelet count criteria (i.e. platelet count <150x10$^9$/l) were counted as refractory to treatment

---


HERCULES Phase III and follow-up study

Phase III topline results expected in H2 2017

145 patients

1st PEX

Daily PEX

Placebo* N=66

30 days

28 days max

28 days

TREATMENT** PERIOD // EXTENSION

Daily PEX

Caplacizumab* N=66

Extension based on ADAMTS13 <10%

FOLLOW-UP

HERCULES 3-year follow-up study

Primary endpoint: time to confirmed normalisation of platelet count

Secondary endpoints: composite efficacy endpoint; recurrence of TTP during the study period; refractory TTP; time to normalization of organ damage markers

* iv bolus (10mg) followed by daily sc (10mg) ** including corticosteroids at start of daily PEX until underlying disease activity resolved

- Successfully completed patient recruitment in HERCULES study
- HERCULES study will be used to support European filing and BLA submission in the USA
Commercialising caplacizumab for aTTP

Potentially Ablynx’s first marketed product

Strategic opportunity to self-commercialise in USA, Canada and Europe

- Concentrated patient presentation
- Established KOL network and reference centres
- Modest commercial infrastructure requirements
- Contract sales, distributors and/or commercial partners in other territories

Market opportunity

- High unmet medical need
- Strong product profile with compelling clinical data
- No direct competition in aTTP
- Orphan Drug status with patent protection to 2035
- Peak sales potential in aTTP of >€400M
## Preparing the market for caplacizumab

**Planned launch in 2018**

### Medical Marketing
- Medical Science Liaisons (MSLs)
- Key centres & stakeholders
- Advisory boards
- Diagnostic & Treatment guidelines
- Registries
- Patient advocacy

### Pricing & Access
- Payor landscape
- Value proposition
- Health economic model
- Early access programmes
- First launch in Germany

### Commercial Operations
- Key Account Managers (KAMs)
- Contract Sales Organisation
- USA office
- Stock in reference centres
- Next day delivery (24/7)
# Caplacizumab

## Key potential milestones

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HERCULES and 3-year follow-up</strong></td>
<td></td>
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<tr>
<td>Top line results</td>
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<tr>
<td><strong>Regulatory EMA</strong></td>
<td>⭐️</td>
<td>⭐️</td>
<td>⭐️</td>
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<tr>
<td>MAA submission</td>
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<tr>
<td>conditional MA</td>
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<tr>
<td>full MA</td>
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<tr>
<td><strong>Regulatory FDA</strong></td>
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<td>⭐️</td>
<td>⭐️</td>
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<tr>
<td>BLA submission</td>
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<tr>
<td>BLA approval</td>
<td></td>
<td></td>
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<tr>
<td><strong>Operations</strong></td>
<td></td>
<td>⭐️</td>
<td>⭐️</td>
<td>⭐️</td>
</tr>
<tr>
<td>First sales EU</td>
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<td>First sales USA</td>
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<tr>
<td>MSL</td>
<td></td>
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<tr>
<td>KAM</td>
<td></td>
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</tr>
</tbody>
</table>

**MAA**: marketing authorization application; **MA**: marketing authorization; **BLA**: biologic license application; **MSL**: medical science liaison; **KAM**: key account manager
Inhaled ALX-0171 (anti-RSV) – wholly-owned

Potential first-in-class treatment for RSV infections
ALX-0171 – inhaled anti-RSV Nanobody

Potential breakthrough for the treatment of RSV infections

- Multi-billion dollar market
- Administered by inhalation
- Infants – important pre-clinical and clinical milestones achieved; started Phase IIb study (Jan 2017); preparations underway to start clinical development in Japan (H2 2017)
- Adults – preparations underway to start clinical development of ALX-0171 in haematopoietic stem cell transplant (HSCT) patients (H2 2017)
- Patent protection to 2035
RSV infections – vulnerable populations

High unmet medical need and no approved therapeutic

**INFANTS**

- out-patient and hospitalized settings

- 33.8 million episodes globally p.a.\(^1\)
- 3.4 million hospital admissions globally p.a.\(^1\)
- 66,000-199,000 deaths globally p.a.\(^1\)
- Long-term disease burden \(^2,3\)

**ELDERLY**

- out-patient and hospitalized settings

- Serious health risk for elderly \(^4\)
- Infection rates up to 10% p.a. with up to 20% hospitalised and 2-8% deaths p.a.
- US: 177,000 hospital admissions and 14,000 deaths p.a.
- High disease burden in nursing homes

**IMMUNOCOMPROMISED**

- hospitalized HSCT patients

- 50,000 haematopoietic stem cell transplant (HSCT) procedures globally p.a.\(^5\)
- 30-40% of patients with RSV progress to lower respiratory tract infection (LRTI) and pneumonia \(^6\)
- mortality rates of up to 30% in RSV-infected HSCT patients with LRTI and pneumonia

---

## Anti-RSV Nanobody – ALX-0171

### Incorporating unique Nanobody platform advantages

<table>
<thead>
<tr>
<th>Platform advantage</th>
<th>Product features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivalent formatting</td>
<td>• 3 Nanobodies linked together that bind to the F-protein of RSV</td>
</tr>
<tr>
<td></td>
<td>• 7,000 fold increase in potency over monovalent construct</td>
</tr>
<tr>
<td></td>
<td>• 10,000 fold reduction in viral titres <em>in vitro</em></td>
</tr>
<tr>
<td></td>
<td>• Neutralises 87% of a broad range of clinical RSV isolates</td>
</tr>
<tr>
<td>Delivery via inhalation</td>
<td>• Biological activity maintained after nebulisation</td>
</tr>
<tr>
<td></td>
<td>• Delivered directly to the site of infection</td>
</tr>
<tr>
<td></td>
<td>• Very encouraging efficacy in neonatal lamb model for infant RSV infection</td>
</tr>
<tr>
<td></td>
<td>• Safe and well-tolerated in healthy adults and adults with hyperreactive airways</td>
</tr>
<tr>
<td></td>
<td>• Well-tolerated in hospitalised RSV infected infants</td>
</tr>
</tbody>
</table>
### Inhaled ALX-0171

Successfully completed Phase I/IIa study in 53 infants with a RSV infection

- Recruitment from Q4 2014 to Q1 2016
- Study centres in Europe and Asia-Pacific region
- Adapted infant inhalation device (vibrating mesh)
- Inhaled ALX-0171 administered once/day, for 3 consecutive days

**Primary endpoint:**
Safety and tolerability of ALX-0171

**Secondary endpoints:**
Assessment of clinical effect (feeding, respiratory rate, \( \text{O}_2 \) saturation, wheezing, coughing, general appearance), PD, PK and immunogenicity

**RANDOMISATION**

<table>
<thead>
<tr>
<th>Open-label lead-in ( N=5 )</th>
<th>( 2:1 )</th>
<th>ALX-0171 ( N=20 )</th>
<th>Placebo ( N=10 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalised infants aged 5-24 months</td>
<td>ALX-0171</td>
<td>Hospitalised infants aged 3-24 months</td>
<td></td>
</tr>
<tr>
<td>Hospitalised infants aged 1-5 months</td>
<td>Placebo</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>( N=12 )</td>
<td>( N=6 )</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
First-in-infant Phase I/IIa study

Safety and tolerability

<table>
<thead>
<tr>
<th>Adverse events (AEs)</th>
<th>Open-label group ALX-0171 (N=5)</th>
<th>Randomised group ALX-0171 (N=30)</th>
<th>Randomised group Placebo (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- number (%) of subjects with an AE</td>
<td>4 (80.0)</td>
<td>9 (30.0)</td>
<td>4 (25.0)</td>
</tr>
<tr>
<td>- number (%) of subjects with a treatment-related AE</td>
<td>1 (20.0)</td>
<td>2 (6.7)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serious adverse events (SAEs)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- number (%) of subjects with an SAE</td>
<td>3* (60.0)</td>
<td>1** (3.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>- number (%) of subjects with treatment-related SAEs</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

* 1 of whom discontinued ** subject discontinued

- Most common AEs were infections and respiratory disorders
- 3 AEs related to ALX-0171: mild cough, mild rhinorrhoea, mild fever 11 days after last dose
- 5 SAEs reported: hypo-responsiveness, hypotonia, pneumonia (2) and atelectasis

Excellent safety and tolerability profile confirmed in the target population
First-in-infant Phase I/IIa study

Key secondary objectives

- Treatment with inhaled ALX-0171 had an immediate and significant impact on viral replication
- Encouraging initial indication of therapeutic effect was demonstrated

"median time to undetectable virus was >24 hours quicker with ALX-0171”
nominal p-value=0.014

"difference in effect on clinical score is statistically significant”
nominal p-value=0.0092

* Overall disease severity assessment including feeding intolerance, medical intervention, respiratory difficulty, respiratory frequency, apnoea, general condition and fever
Inhaled ALX-0171

Phase IIb RESPIRE clinical efficacy study in 180 hospitalized infants

- Study start: Q1 2017; expected results: H2 2018
- Study centres in Europe, Asia-Pacific and the USA
- Adapted infant inhalation device (vibrating mesh)
- Infants: 28 days to <2 years of age
- Inhaled ALX-0171 (3 doses) administered once/day, for 3 consecutive days

**Primary endpoint:** Anti-viral effect

**Secondary endpoints:**
Assessment of clinical effect over time (feeding, respiratory rate, O₂ saturation, wheezing, coughing, general appearance), time to clinical response, effect on composite clinical scores, PD, PK and immunogenicity; safety

*DMC: data monitoring committee*
ALX-0171 development plan

Key potential near term milestones

- **Phase IIb - ongoing**
  - 180 RSV-infected infants, 3 doses,
  - Primary endpoint: anti-viral effect

- **Japan**
  - RSV-infected infants
  - Start clinical development

- **Phase IIa**
  - RSV-infected haematopoietic stem cell transplant (HSCT) patients
  - Start clinical development

- **2017 - 2018**
  - Topline results

- **2018**
  - Start clinical development
Vobarilizumab (anti-IL-6R) – partnering opportunities being explored

Novel potential best-in-class treatment for RA
Vobarilizumab – anti-IL-6R Nanobody

Novel potential best-in-class treatment for RA

• RA – excellent results from 2 Phase IIb RA studies in a total of ~600 patients; open-label extension study ongoing
• AbbVie declined to opt-in for RA and Ablynx now preparing for regulatory meetings and exploring potential new partnerships
• SLE – Phase II study ongoing (312 patients) with results expected in H1 2018
• Opportunity in multi-billion dollar markets

RA: rheumatoid arthritis
SLE: systemic lupus erythematosus
Vobarilizumab (225mg every 2 weeks)

Excellent Phase IIb study results reported in July/August 2016

<table>
<thead>
<tr>
<th>Combination therapy (+MTX) 24 weeks (across studies)</th>
<th>DAS28\textsubscript{CRP} remission</th>
<th>ACR 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>vobarilizumab</td>
<td>49%</td>
<td>43%</td>
</tr>
<tr>
<td>tocilizumab</td>
<td>32%</td>
<td>20%</td>
</tr>
<tr>
<td>adalimumumab</td>
<td>23%</td>
<td>21%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Monotherapy 12 weeks (head-to-head study)</th>
<th>DAS28\textsubscript{CRP} remission</th>
<th>ACR 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>vobarilizumab (6 doses)</td>
<td>41%</td>
<td>21%</td>
</tr>
<tr>
<td>tocilizumab (~ 12 doses) open-label</td>
<td>27%</td>
<td>23%</td>
</tr>
</tbody>
</table>

tocilizumab: BREVACTA PhIII (sc) 162mg Q2W + MTX (Kivitz et al., Arthritis Care & Research, Nov 2014); note: remission is based on ESR (no CRP data available)
adalimumab: Weinblatt et al, Arthritis & Rheumatology, Sept 2015 (Phase IIb head-to-head adalimumab 40mg Q2W + MTX vs clazakizumab + MTX)
**Vobarilizumab + MTX (placebo-adjusted)**

Impressive efficacy* compared with other leading commercial biologicals

---

**Placebo-adjusted DAS\textsubscript{28}_{ESR} remission**

- **Vobarilizumab** 225mg, Q2W
- **Tocilizumab** 162mg, Q2W (Roche)
- **Adalimumab** 40mg, Q2W (AbbVie)

- 43% better than tocilizumab
- 233% better than adalimumab

**Placebo-adjusted ACR70 response**

- **Vobarilizumab** 225mg, Q2W
- **Tocilizumab** 162mg, Q2W (Roche)
- **Adalimumab** 40mg, Q2W (AbbVie)

- 73% better than tocilizumab
- 116% better than adalimumab

---

* 24-week data from similar RA combination therapy studies reported in listed publications, not resulting from head-to-head studies

---

1. Phase IIb + MTX (August 2016); 2. BREVACTA Phase III + MTX (Kivitz et al., Arthritis Care & Research, Nov 2014); 3. Phase IIb (Weinblatt et al., Arthritis & Rheumatology, Sept 2015) (note: remission based on CRP, no data on ESR available)
Vobarilizumab (Q2W) as monotherapy

Impressive efficacy* after 12 weeks vs anti-IL-6R drugs in development after 24 weeks

* data from RA most recent monotherapy studies reported in November 2016; not resulting from head-to-head studies

Vobarilizumab (Q2W) + MTX (placebo-adjusted)

Impressive efficacy* vs anti-IL-6R drugs in development (week 24)

* data from most recent RA combination therapy studies reported in November 2016; not resulting from head-to-head studies

Vobrilizumab + MTX (placebo-adjusted)

Impressive efficacy compared to oral anti-RA drugs in development*

Placebo-adjusted DAS28$_{\text{CRP}}$ remission

- **Vobrilizumab**
  - 225mg, Q2W
  - 30% better than Filgotinib
  - 100% better than ABT-494

- **ABT-494**
  - 24mg, oral 1x/day (AbbVie)$^2$

- **Filgotinib**
  - 100mg, oral 1x/day (GLPG/Gilead)$^3$

* Data from similar studies reported in listed publications, not resulting from head-to-head studies

1 Phase IIb + MTX at week 12 and 24 (August 2016; LOCF imputation); 2 Phase IIb + MTX at week 12 (EULAR 2016) 3 Phase IIb + MTX (LOCF imputation) at week 12 and 24 (April 2015; July 2015)
Vobarilizumab + MTX

Favourable safety and immunogenicity profile

<table>
<thead>
<tr>
<th>Drug</th>
<th>% pts with ≥ 1 SAEs</th>
<th>% pts with grade 3 toxicity for neutrophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>vobarilizumab, 225mg Q2W&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1.4%</td>
<td>0.0%</td>
</tr>
<tr>
<td>tocilizumab, 162mg Q2W&lt;sup&gt;2&lt;/sup&gt;</td>
<td>4.6%</td>
<td>3.5%</td>
</tr>
<tr>
<td>adalimumab, 40mg Q2W&lt;sup&gt;3&lt;/sup&gt;</td>
<td>5.1%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

• Anti-vobarilizumab antibodies
  - develop in up to 31% of patients
  - BUT have no effect on PK, efficacy or safety

• Anti-adalimumab antibodies<sup>4</sup>
  - develop in ~30% of patients
  - AND are associated with loss of efficacy and an increased risk of adverse events
  - 1/3<sup>rd</sup> of patients become resistant to adalimumab as a result of ADAs (with a strong signal occurring early in the treatment cycle)

A Nanobody class advantage

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Vobarilizumab

Novel best-in-class drug candidate for the treatment of RA

- Rapid, strong and sustained effect on signs and symptoms of disease
- As a monotherapy, >50% more patients in clinical remission as compared to tocilizumab
- Powerful effect as a combination therapy on the most stringent efficacy parameters compared to leading commercial biologicals and oral anti-RA drugs in development
- Potential for effective monthly administration
- Class advantage of vobarilizumab vs antibodies demonstrated: anti-Nanobody antibodies had no effect on PK, efficacy or safety
- Very encouraging safety profile compared to other biological anti-RA drugs

Ablynx is now preparing for end-of-Phase II meetings with regulators whilst exploring partnering opportunities
### Vobarilizumab

#### Key potential near term milestones

<table>
<thead>
<tr>
<th>RA</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory consultations</td>
<td></td>
<td>★ FDA and EMA</td>
</tr>
<tr>
<td>Phase III – depending on partnering support</td>
<td></td>
<td>★ start clinical development</td>
</tr>
<tr>
<td>Open-label extension study</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SLE</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase II</td>
<td></td>
<td>★ topline results</td>
</tr>
</tbody>
</table>

opt-in decision for SLE
Immuno-oncology

Major collaboration with Merck & Co, Inc. and wholly-owned programmes
Immuno-oncology

Changing the cancer treatment paradigm

Huge market potential

• Market expected to grow to >$43bn by 2020*
• I/O drugs expected to treat 60% of cancers*
• Proven substantial survival impact

Multiple targets

• Increasing number of targets
• Combination therapies are the future

Multi-specific Nanobodies - the next wave!

• Bind multiple targets (2, 3, 4 or 5) with one Nanobody molecule
• Potential to increase efficacy and avoid escape mechanisms
• Technology allows rapid exploration of combinations
• Manufacturing simplicity and cost-effectiveness

*NbL Merrill Lynch July 2015
Immuno-oncology

Multi-specific Nanobodies versus combination mAbs

More difficult for mAbs to bind to different targets simultaneously

One tri-specific Nanobody is 4x smaller than a mAb

Multi-specific Nanobodies may block multiple targets simultaneously
Immuno-oncology (IO)

Up to 17 programmes with Merck & Co., Inc.

- ~80% of total R&D budget* invested in IO
- First IO drug, Keytruda®, approved in 2014
- Sales of Keytruda® estimated to reach $6Bn by 2020**
- >160 clinical studies for Keytruda® in >30 tumor types

First in vivo preclinical milestone (€3.5M) achieved and first clinical studies planned to start in 2017

* Bryan Garnier Oct 2015  ** Leerink August 2015
2017 outlook
## 2017 outlook

### Focus on sustainable value creation

<table>
<thead>
<tr>
<th>Corporate</th>
<th>Pipeline</th>
<th>Potential study results</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Filing for approval of caplacizumab in Europe ✔️</td>
<td>• Continue recruitment in the Phase IIb RSV study with ALX-0171 in 180 hospitalised infants</td>
<td>• HERCULES Phase III results for caplacizumab in H2</td>
</tr>
<tr>
<td>• Further develop commercial organisation in preparation for caplacizumab launch</td>
<td>• Complete Phase II study in ~300 SLE patients with vobarilizumab</td>
<td>• Phase Ib results for ALX-0761/M1095 (anti-IL17A/F) in psoriasis with Merck KGaA in H1</td>
</tr>
<tr>
<td>• End-of-Phase II meetings for vobarilizumab</td>
<td>• Start clinical development for Japan with both caplacizumab and ALX-0171</td>
<td>• Phase Ib results for anti-VEGF-Ang2 with BI in H2</td>
</tr>
<tr>
<td>• Explore partnering opportunities for vobarilizumab in RA</td>
<td>• Start pre-clinical and clinical development in new indications for caplacizumab and ALX-0171 respectively</td>
<td></td>
</tr>
</tbody>
</table>
Questions

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