Caplacizumab

Wholly-owned anti-vWF Nanobody

- First-in-class bivalent Nanobody with Orphan Drug Status and patent protection up to 2035
- Developed for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP)
- Phase II (75 patients) successfully completed; Phase III (92 patients) on-going with results expected by end of 2017
- Planned filing for conditional approval in Europe (H1 2017) and BLA submission in USA (2018)
- Ablynx to lead commercialisation in Europe and USA
- Anticipated first launch in 2018
- Peak sales potential of ~€300M

1 US, EU, Japan, other major markets
Caplacizumab unique mode of action

Rapidly stops formation of micro-clots

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 (aTTP)

Life-threatening ultra-rare acute blood clotting disorder

- aTTP is caused by impaired activity of ADAMTS13 (<10% of that in normal plasma\(^1\))
  - extensive micro-clot formation in small blood vessels throughout the body
  - leads to tissue ischemia and damage to vital organs

- Ultra-rare indication with incidence estimated at up to 11 per million\(^2\)

- High unmet medical need with no approved therapeutic drug currently available
  - high acute mortality (10-20%)\(^3\), vast majority within 2 weeks post diagnosis, and ~ 36% of patients with recurrences\(^2\)
  - major morbidities, including brain (e.g. stroke), heart and kidney damage
  - impacts life expectancy and quality of life

\(^{1}\) Scully et al, BJH 2012; \(^{2}\) George et al, EJH 2008; \(^{3}\) Alford et al, BJH 2003, Kremer Hovinga, Blood 2010; Benhamou, Haematologica 2012
Caplacizumab (anti-vWF) proven clinical benefit

TITAN Phase II study – achieved clinical proof-of-concept

- **Primary endpoint** met with high statistical significance ($p=0.005$)
  - 40% reduction in time to platelet normalisation
    - faster reversion of thrombocytopenia and reduced use of plasma exchange (PEX)
- 71% fewer patients with recurrences during caplacizumab treatment
  - potential prevention of organ damage

**Randomisation**

<table>
<thead>
<tr>
<th>Group</th>
<th>Timepoints</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo N=39</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>PEX Caplacizumab N=36</td>
<td>30 days</td>
<td></td>
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</tbody>
</table>

**Primary endpoint:**

time to confirmed normalisation of platelet count

**Secondary endpoints:**
recurrences; PEX parameters; mortality; major clinical events

PEX = plasma exchange
Caplacizumab (anti-vWF)

Hercules Phase III study (Q3 2015 to Q4 2017)

**Primary endpoint:** time to confirmed normalisation of platelet count

**Secondary endpoints:** recurrences; mortality rate; severe morbidity; organ damage biomarkers (troponin, creatinine, LDH); PEX parameters; days in ICU/hospital; AEs; PD; PK; immunogenicity

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

PEX = plasma exchange
Caplacizumab positioning

Potential new component in standard of care for aTTP

Future standard of care could be based on three pillars

Caplacizumab
- Rapid inhibition of platelet aggregation, micro-clot formation and small blood vessel occlusion
- Reduction in duration of PEX treatment
- Protection during the acute phase of the disease
- Prevention of organ damage
- Reduction in recurrences

Daily PEX
- Removal of ULvWF & auto-antibodies
- Replenishment of ADAMTS13

Immunosuppression
- Reduces activity of immune system to resolve the underlying cause of aTTP

Caplacizumab may become the first approved product for the treatment of aTTP
Caplacizumab (anti-vWF)

Potentially Ablynx’s first marketed product

Strategic opportunity

- Concentrated patient presentation
- Established KOL network and reference centres
- Modest commercial infrastructure requirements
- Retain direct control over commercialisation in EU5 and USA
- Contract sales, distributors and/or commercial partners in other territories

Market potential

- No direct competition in aTTP
- Potential key component in future standard of care
- Orphan Drug status with patent protection to 2035
- Peak sales potential in aTTP of ~€300M

Potential launch in 2018