ESBATech case story

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Advancing antibody fragment therapeutics

Antibodies are the most successful drugs

Average annual sales [M$]

Source: CMR Database

Source: Datamonitor
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Formats of antibody fragments

- Antibody
- Fab Fragment
- Single-chain antibody fragment

ESBA105
ESBA1008

Lucentis
Cimzia
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Local therapy for safe and effective treatment

Eye
CNS
Lung
GI-Tract
Skin
Joint

- Serum conc. following i.v. injection
- Local conc. following i.v. injection
- Local conc. following local application
- Serum conc. following local application

Drug concentration vs. time graph with different tissues highlighted.
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Fragments lacking drug like properties

Classical scFv

- Low yield
- Strong aggregation
- Low stability
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ESBATech’s unique approach

IgG gene segments

<table>
<thead>
<tr>
<th></th>
<th>Human</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_H$</td>
<td>1200</td>
</tr>
<tr>
<td>$V_L$</td>
<td>$\kappa$ 850</td>
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<tr>
<td></td>
<td>$\lambda$ 400</td>
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</table>

> 1.5 Mio fully human frameworks
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Drug-like properties of ESBATech frameworks

Size-exclusion chromatography:

Mouse scFv:
- Low yield
- Strong aggregation

Humanized scFv:
- High yield
- Low aggregation
<table>
<thead>
<tr>
<th>Indications</th>
<th>Target</th>
<th>Research</th>
<th>Preclinic</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tbody>
<tr>
<td>ESBA105 Uveitis</td>
<td>TNF</td>
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<td>ESBA105 PK and post surgical inflammation</td>
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<td>ESBA105 Osteoarthritis</td>
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Anatomy of the eye

Anterior
- Oil layer
- Aqueous layer
- Mucin layer
- Corneal epithelium: Cut-off: 40kDa

Posterior
- Sclera
- Descemet's membrane: Cut-off: 60kDa

Cross section of human cornea at 160X (from: Anant Mathur, Univ. of Rochester, 2005)

Optic Nerve
Cornea
Retina
Sclera
Topical ESBA105 reaches therapeutic levels

- Aqueous humour
- Vitreous
- Neuroretina
- Serum
- RPE-choroid

TNF level in AU

Topical treatment

Furrer et al. IOVS 2009
Phase I of ESBA105

- 27 healthy volunteers
- Randomized, vehicle-controlled, double-masked
- Single and repeat dose
- Dose escalation (up to 4 weeks, up to 16 daily topical dosings)
ESBA105: Phase II in progress

Regulatory clearance to start two phase Ib/IIa clinical trials:

- **Human PK in cataract and vitrectomy surgery, post-surgical inflammation**
  - Examining human PK in anterior/ posterior chamber
  - Early PD/ efficacy readout in post-surgical inflammation
  - Total 90 patients, different dosing, PD part double-blind, placebo controlled

- **Acute anterior uveitis**
  - Proof of clinical concept in AAU patients
  - Changes in the level of intraocular inflammation (anterior chamber cell count according to SUN Working group criteria)
  - Enrollment of 25 patients
  - Open-label
## Capital need

<table>
<thead>
<tr>
<th>Date</th>
<th>Series</th>
<th>Investors</th>
<th>Capital raised [CHF]</th>
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<tbody>
<tr>
<td>April 2000</td>
<td>Seed</td>
<td>Novartis Venture Fund</td>
<td>1M</td>
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<tr>
<td>Sept 2001</td>
<td>Series A</td>
<td>Lombard Odier Credit Suisse BSI Novartis Venture Fund BioMedinvest VI Partners</td>
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<td>Aug 2006</td>
<td>Series B</td>
<td>Clarus Ventures HBM Partners SV Life Sciences Novartis Venture Fund VI Partners ZKB</td>
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<td>Aug 2007</td>
<td>Series B2</td>
<td>Same syndicate</td>
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<td></td>
<td>TOTAL</td>
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<td><strong>88.5M</strong></td>
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</table>
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Franchise deal

- Ophthalmology
- Virology
- Cardiovascular
- Auto immune disease
- Cancer
ESBATech, an Alcon Biomedical Research Unit

Advancing antibody fragment therapeutics

ESBATech, an Alcon Biomedical Research Unit LLC
### Acquisitions of antibody fragment companies

<table>
<thead>
<tr>
<th>Company</th>
<th>Acquirer</th>
<th>Date</th>
<th>Stage</th>
<th>Valuation</th>
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<tbody>
<tr>
<td>ESBATech</td>
<td>Alcon</td>
<td>09 / 2009</td>
<td>Phase II</td>
<td>USD 589M 1)</td>
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<tr>
<td>Adnexus</td>
<td>BMS</td>
<td>09 / 2007</td>
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<td>USD 430M</td>
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<td>Domantis</td>
<td>GSK</td>
<td>12 / 2006</td>
<td>Preclinic</td>
<td>USD 454M</td>
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<td>Avidia</td>
<td>Amgen</td>
<td>09 / 2006</td>
<td>Phase I</td>
<td>USD 290M</td>
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<tr>
<td>NeuTec</td>
<td>Novartis</td>
<td>06 / 2006</td>
<td>Phase III</td>
<td>USD 575M</td>
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1) Ophthalmology franchise only
• Franchise deal of platform
• De-merger allows further maximizing platform value
• Alcon / Novartis resource to maximally develop platform
• Ophthalmology acquisition as validation for Delenex