Creating innovative antibodies for cancer & auto-immune diseases

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Creating superior, differentiated antibodies

Focus on cancer & severe autoimmune diseases
- Highly differentiated products
- Orphan and large indications

Rich pipeline approaching major value inflection points
- ARGX-110 in Ph1/2 (oncology): first-in-class; clinical activity demonstrated
- ARGX-111 in Ph1 (oncology): best-in-class; clinical activity demonstrated
- ARGX-113 in preclinical (autoimmune): breakthrough concept for crisis management
- ARGX-115 in preclinical (oncology): novel immune checkpoint

Strategic alliances with premier partners
- Strategic partnerships fuelled by consistent success
- Cash funding, milestone & royalty payments and product rights
- Strong cash position (~€52m March 2015)

Powerful technology suite
- Highly productive platform generates multiple leads
- SIMPLE Antibody™: llama immune systems cracks complex/novel targets
- NHance®, ABDEG™, POTELLIGENT® Fc engineering enables multiple MoA’s
- IP protection until 2028-2032
Highly productive discovery engine

- **SIMPLE Antibody™**: Unlock novel and complex targets
- **NHance®, ABDEG™, POTELLIGENT®**: Enhance SIMPLE Antibody™ leads
- Multiple layers of IP protection in place until 2028-2033 (excluding any PTE)

**Powerful technology suite: multiple modes of actions**

- Extend half-life
- Boost cell killing
- Clear autoantibody/disease target, Sweeping concept
Sweeping concept delivers active target clearance

- Clinical potential for indications:
  - with high circulating target concentrations
  - which require fast target clearance
  - e.g. Inflammatory cytokines (receptors)

**NHance® /'ABDEG™**
*FcRn modulation*

**SIMPLE ANTIBODY™**
*pH-dependent target binding*
Recognized promise of arGEN-X technology

The strength of arGEN-X' technology suite is recognized by its partners

"We look forward to collaborating with arGEN-X and exploring the potential of SIMPLE Antibody™ technology to complement Bayer’s efforts in the discovery and development of first-in-class therapeutic antibodies”

Dr. Harald Dinter, Head of Global Biologics

"One cannot engineer such diversity"

Dr. Wolfgang Glaesner, CSO Lilly

"Our collaboration has exceeded our expectations in delivering highly differentiated antibody programs within our therapeutic focus. The time is right to commit more significantly to the company through a longer term investment in its unique, world class technologies”.

Dr. Philip J. Vickers, Global Head of Research and Development
## Rich pipeline approaching major value inflection points

<table>
<thead>
<tr>
<th>Drug Candidate</th>
<th>Indication</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 1/2</th>
<th>Ownership</th>
<th>Proposition</th>
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<tbody>
<tr>
<td>ARGX-110</td>
<td>Heme malignancies</td>
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<td>Wholly owned</td>
<td>Immune checkpoint inhibition (CD70) Enhanced cell kill</td>
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<td>ARGX-110</td>
<td>Solid tumors</td>
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<td>Wholly owned</td>
<td>Complete c-Met blocking Enhanced cell kill</td>
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<td>Potent FcRn blocking Clears auto-antibodies</td>
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<td>ARGX-111</td>
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<td>Wholly owned</td>
<td>Potent GARP blocking</td>
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<tr>
<td>ARGX-113</td>
<td>Autoimmunity Myasthenia gravis</td>
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<td>Wholly owned</td>
<td>Novel complex targets</td>
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<td>ARGX-115</td>
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<td>Discovery</td>
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<td>Wholly owned</td>
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<tr>
<th>Company</th>
<th>Indication</th>
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<th>Phase 1</th>
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<td>RuiYi</td>
<td>Autoimmunity Cancer</td>
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<td>Novel, complex targets</td>
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<td>Novel skin targets</td>
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<td>LEO</td>
<td>Chronic inflammation</td>
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<td>Bayer</td>
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<td>Novel, complex targets</td>
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ARGX-110: Pioneering intervention in CD70 biology

First-in-class human mAb
- Targets CD70 involved in broad range of blood & solid tumors
- 3 modes of action using SIMPLE Antibody™ and POTELIGENT®
- Optionality in niche and major indications

Clinical activity & safety demonstrated
- Biological activity in 3/4 TCL patients in Ph 1
- PFS benefit in RCC, ovarian cancer, mesothelioma,...
- Outstanding safety profile: no dose-limiting tox, no auto-immune AE’s

Development plan
- Hematological tumors
  - T-Cell Lymphoma (TCL)
  - Leukemia (CML & AML)
- Solid tumors: Nasopharyngeal Carcinoma (NPC)
ARGX-110: Potential cancer therapy for CD70+ T-Cell Lymphoma’s with elevated sCD27 levels

- 71% CTCL & 22% PTCL patients have >50% CD70+ tumor cells
- 7 out of 13 patients show elevated sCD27 levels
- High affinity binding & stronger depletion compared to Campath
ARGX-110: Proof of biological activity in patient with Sézary-Syndrome (SS)

- 77 year old woman with CTCL-SS; refractory to multiple lines of chemotherapy
- Elimination of CD70 positive Sezary cells in 2nd CTCL-SS patient
ARGX-110: Proof of biological activity in patient with Angioimmunoblastic T-Cell lymphoma (AITL)

- 61 year-old male AITL patient showing elevated LDH and reduced Hb levels
- Refractory to chemotherapy (CHOP + Etoposide /Cyclosporine /Bendamustine - Transplant )
- After 2 doses of ARGX-110
  - LDH normalized to 365 & Hb increase to 7.9 without transfusion support
  - 16% reduction in tumor size by CT scan
ARGX-110/BCR-ABL1 inhibitor eliminates leukemic stem cells in CML model

Grafting Whole Bone Marrow cells from treated into new mice (10d after start of treatment)

- Leukemic stem cells (LSCs) resistant to BCR-ABL1 inhibitors via CD70 overexpression
- Combo treatment with CD70 blocking mAb eliminates LSCs by synergistic blockade of Wnt signalling pathway

Im: imatinib; V: vehicle; WBM: whole bone marrow
ARGX-111: Superior intervention in c-Met biology

**Best-in-class therapeutic antibody**

- Targets c-Met driven metastasis
- 3 modes of action; SIMPLE Antibody™; POTELLIGENT®, NHance®
- Potential in major c-Met+ cancer indications
- Superior performance to MetMab in preclinical models
- Eliminating circulating tumor cells and blocking metastasis

**Proof of biological activity**

- Metabolic response (FDG-PET) in Met amplified, end-stage gastric cancer patient in Ph1
- Biological activity on bone metastasis and CTCs correlates with preclinical data

**Unmet medical need**

- Metastatic spread represents major unmet medical need
- Metastatic gastric cancer enables focused clinical development plan
- Triple negative breast cancer
ARGX-111: Targeting MET positive tumors and CTC’s

ARGX-111 has several distinct modes of action
- HGF-dependent blocking
- HGF-independent blocking
- Killing MET expressing cells
ARGX-111: Highly effective in preclinical models

**Neoadjuvant animal model**

- **Treatment**
  (4 weeks, twice weekly, 5mg/kg)
- **Surgery**
- **Autopsy**

**Adjuvant animal model**

- **Surgery**
- **Treatment**
  (4 weeks, twice weekly, 5mg/kg)
- **Autopsy**

- Blocks tumor spread and eliminates CTCs in metastatic breast cancer model
ARGX-111: Proof of biological activity in patient with gastric cancer

**Background**

- 50 year old gastric cancer patient with bone metastases; Met amplified
- Multiple lines of previous treatment; including surgery and 2 lines of triplet chemotherapy
- FDG-PET scan observation of biological activity (see right) confirmed on repeat imaging; CTCs reduced by 75%
- Good performance (clinical) status maintained throughout treatment period

**Biological activity**

- Baseline PET scan
- Improvement after 4 doses
- Baseline PET scan
- Improvement after 4 doses
ARGX-111: Phase 1 trial overview

- Advanced cancer population (34 patients)
  - Progressive, end stage disease
  - c-Met+ by IHC AND CTCs by Veridex
  - Monitor tumor metabolism (PET scan)

- ARGX-111 monotherapy

- ‘Off study’ criteria
  - Progressive disease (ir-RECIST)
  - Safety

- Translational biomarkers
  - Efficacy: response and duration of therapy

- Dose escalation
  - 0.3 mg/kg
  - 1 mg/kg
  - 3 mg/kg
  - 10 mg/kg

- Adaptive safety expansion
  - Met amplified cancers

- Details

- 1Q 2014
- 1H 2015
- 2H 2016

- ~50% of patients screened have CTCs
- Safety observations: Infusion related reactions (class effect)
- Biological activity observed in individual patient with gastric cancer with bone metastases

ClinicalTrials.gov Identifier: NCT02055066
ARGX-113: Management of autoimmune crisis

**First-in-class therapeutic antibody fragment**
- Breakthrough management of autoantibody-induced flares
- Targets FcRn involved in IgG recycling
- Uses ABDEG™ technology to rapidly clear pathogenic autoantibodies
- Applicable to niche and major indications

**Preclinical proof of concept & safety**
- Highly effective in preclinical models of RA, MS, MG, Pemphigus,..
- Safe profile expected (individuals with loss-of-function mutations in FcRn)
- Pharmacology study shows IgM and IgA levels unaffected

**Unmet medical need**
- Several autoimmune drugs address cell compartment but not autoantibody compartment
- Pathogenic autoantibodies play dominant role in many autoimmune diseases
ARGX-113: Manages autoantibody induced flares

Mode of action

Recycling of auto-immune antibodies

1. Uptake by pinocytosis
2. FcRn binds IgG in acidified endosome (pH 6)
3. Recycling of Bound IgG
4. IgG release at neutral pH

Non-FcRn bound proteins are degraded in the lysosome

Design

Fc Fragment - ABDEG™ equipped

ABDEG™ increases IgG clearance

ABDEG™ remains bound at physiological pH

FcRn binding affinity ABDEG™ > endogenous IgG

FcRn blocking IgG recycling

IgG clearance is increased
ARGX-113: Antibody clearance capacity

Therapeutic effect – Cynomolgus monkey model

- Tracer Ab clearance
- ARGX-113: superior antibody clearance capacity vs IVIG

- Endogenous IgG clearance
- Repeated dose ARGX-113 > single dose
ARGX-113: Pharmacodynamics of dose-escalation study

ARGX-113 dose-escalation study in cynomolgus monkey

**Tracer IgG levels:**

<table>
<thead>
<tr>
<th>Days after infusion</th>
<th>Tracer % T₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>150</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td>2</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>7</td>
<td>20 mg/kg</td>
</tr>
<tr>
<td>15</td>
<td>70 mg/kg</td>
</tr>
<tr>
<td>20</td>
<td>200 mg/kg</td>
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**Endogenous IgG levels:**

<table>
<thead>
<tr>
<th>Days after infusion</th>
<th>Tracer % T₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>200</td>
</tr>
<tr>
<td>5</td>
<td>150</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>20</td>
<td>1</td>
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</tbody>
</table>

- Treatments: ARGX-113 at 0.2 mg/kg; 2 mg/kg; 20 mg/kg and 200 mg/kg
- Saturation of PD effect on endogenous IgG levels at ARGX-113 doses ≤ 20 mg/kg
## Clinical rationale for targeting autoantibody clearance

### Myasthenia gravis autoantibody levels and disease score following therapy

<table>
<thead>
<tr>
<th>Treatment*</th>
<th>Plasmapheresis</th>
<th>Immunoadsorption</th>
<th>IVIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in antibody levels (%) after treatment</td>
<td>62.2 ± 6.3</td>
<td>55.1 ± 3.2</td>
<td>28.9 ± 3.8</td>
</tr>
<tr>
<td>Decrease in disease score (%) after treatment</td>
<td>60.8 ± 3.5</td>
<td>42.4 ± 4.2</td>
<td>23.8 ± 3.7</td>
</tr>
<tr>
<td>Clinical efficacy rate after 14 days**</td>
<td>12/15</td>
<td>7/10</td>
<td>6/15</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>12.8 ± 0.28</td>
<td>13.5 ± 0.50</td>
<td>16.0 ± 0.50</td>
</tr>
</tbody>
</table>

* Comparison between 3 cycles of Plasmapheresis/Immunoadsorption every 24h-48h and 5 cycles of IVIG every 24h (Liu et al, 2009)

** Clinical effective if disease score has improved by >50% 14 days after treatment

- Degree autoantibody reduction: correlates with clinical improvement & reduced hospital stay
- Similar observations reported for other autoimmune disorders
ARGX-113: Optionality in niche and major indications

ARGX-113 can address acute autoimmune flares more effectively than IVIG or Plasmapheresis

ARGX-113: indications and market potential

<table>
<thead>
<tr>
<th>Orphan indications</th>
<th>Prevalence per 100,000 (US)</th>
</tr>
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<tbody>
<tr>
<td>Myasthenia gravis</td>
<td>20 - 50</td>
</tr>
<tr>
<td>Skin blistering diseases</td>
<td>18 (Pemphigus)</td>
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<table>
<thead>
<tr>
<th>Major indications</th>
<th>Prevalence per 100,000 (US)</th>
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<tbody>
<tr>
<td>Systemic lupus erythematosus</td>
<td>80-100</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>~90</td>
</tr>
</tbody>
</table>

- Xolair® sells for 800 M US$/y
- Benlysta® sells for 35,000 US$/y, IVIg and plasmapheresis are US$ 79,000 and US$ 101,000 per cycle
- Global IVIg market is >US$4B (autoimmune diseases approximately 50%)
ARGX-115: Towards a next generation ipilimumab

**GARP: a novel immune checkpoint**

- GARP upregulated specifically on surface of Tregs only
- GARP presents and activates latent TGF-β1, activating Tregs and suppressing Teff cells
- SIMPLE Antibody™ hitting unique, patented epitope on GARP
- GARP blockade sufficient for MoA – no Treg depletion
- Graft-versus-host model delivered convincing PoC
- Published in Science Translational Medicine

**In vivo efficacy of a-GARP-TGFβ SIMPLE Antibody™ in GVHD model**

NSG mice injected with:
- hPBMC ➔ hPBMC (i.e. CTLs) attack host cells (GVHD)
- +/- hTregs ➔ hTregs delay GVHD
- +/- anti GARP ➔ MHG-8 blocks Treg-mediated protective activity

![Graph showing in vivo efficacy](image)
Products protected by multiple layers of IP

Technology Platforms: SIMPLE Antibody™ platform + one or more Fc engineering platform
- Broad composition of matter and process claims
- Granted claims in US, UK and Israel
- Pending claims in US, EU, other major territories

Product and methods of use patents: ARGX-110, ARGX-111, ARGX-113, ARGX-109 specific
- Both specific and broad composition of matter claims and method of use claims
- Granted US claims for ARGX-110, ARGX-111, ARGX-113
- Pending claims in EU, other major territories

Patents currently expected to expire in 2028-2033 window
- ARGX-110 and ARGX-111 core patents eligible for up to five years of Patent Term Extension

Under our industrial partnerships, only non-exclusive licenses have been granted to our technology platforms
Building partnerships for the long term

**Strategic Alliances**

- Non-exclusive product discovery and development, leveraging entire technology suite
- Upfront funding, R&D support, development milestones, royalties, product reversion rights

**Collaboration Agreements**

- Non-exclusive discovery collaborations, applying SIMPLE Antibody™ to complex targets
- Technology access fees, R&D support, milestones, royalties

**Innovative Access Program**

- Non-exclusive access to antibody technologies for academic and biotech centers of excellence
- Creative deal structures including option to acquire asset, golden share,...

- €19.3 million in cumulative revenue to date
- >€1.4B* potential cumulative revenues from existing partnerships

*Assuming specific development and sales milestones are met for all potential discovery targets
Well capitalized to execute strategic plan

Operating income and expenses (MEUR) 1Q15

- Operating income 19.3
- R&D expenses 45.7
- G&A expenses 12.3
- Capital raised 87.8
- Cash and cash-equivalents 52.2

Shareholder structure

- Historical shareholders, including VC's
- Free float
- New shareholders Shire and JP Morgan

(*) not including deferred revenue and accruals
## 2015 strategic goals

<table>
<thead>
<tr>
<th>Priority</th>
<th>Status</th>
<th>Milestones</th>
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</table>
| ARGX-110 <br> *Safety & Efficacy data in T-cell lymphoma Preclinical data in CML and AML* | ✓ | • Obtain IND approval  
• Presentation TCL Ph1/ results heme cohort – ICML  
• Workshop ARGX-110 / Leukemia data – ASH |
| ARGX-111 <br> *Safety & Efficacy data in Met amplified solid tumors* | ✓ ✓ ✓ 2H 2016 | • Determine dose  
• Open safety expansion part of Phase 1b study  
• Presentation of dose escalation results – ASCO  
• Report Phase 1b study |
| ARGX-113 <br> *Enter clinic* | ✓ ✓ 2H 15 End 2015 | • GLP Tox data  
• Presentation at PEGS, Boston  
• CTA filing & approval  
• Start first HV study |
| ARGX-115 <br> *Preclinical development* | ✓ | • Report preclinical progress on GARP |
| Partnerships | ✓ ... | • Alliance with LEO Pharma  
• Enter 2nd new partnership |
| US presence | Ongoing Ongoing Ongoing | • Collaborations  
• Clinical trials  
• Investor relations (Conferences, ND roadshows) |
Creating innovative antibodies for cancer & auto-immune diseases

Tim Van Hauwermeiren, Chief Executive Officer - arGEN-X
Jefferies Healthcare Conference, New York
2 June 2015