Creating innovative antibodies for cancer & severe autoimmune diseases

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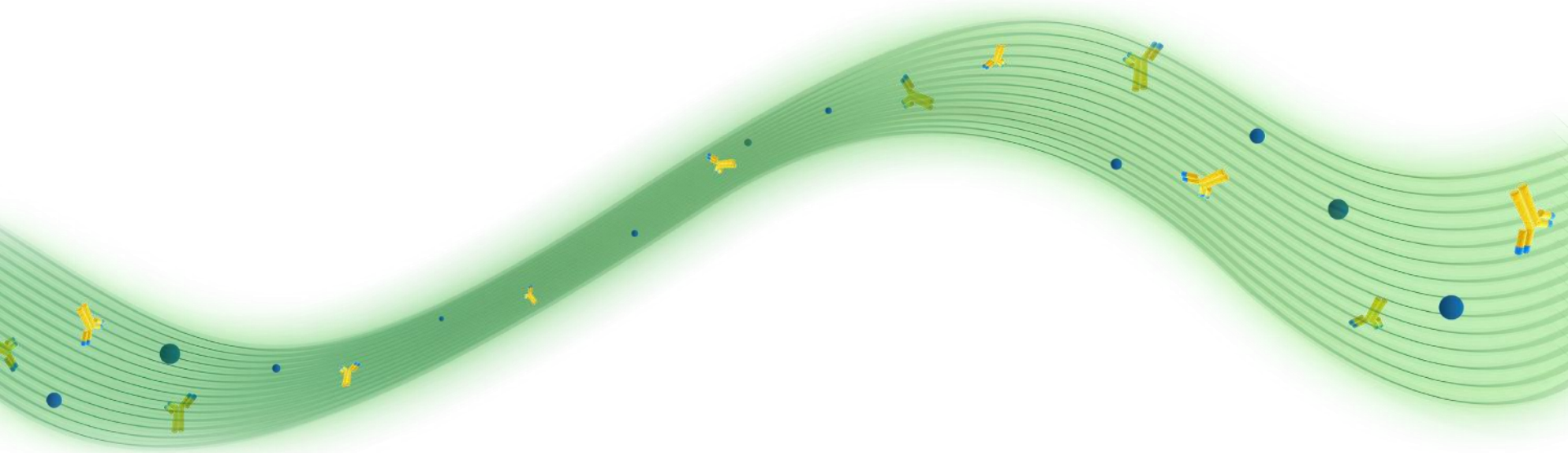
Agenda

- Introduction
- Creating innovative antibodies
- Differentiated products
- Collaborations
- Financials

Introduction



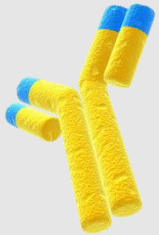
Creating value from highly differentiated antibodies

Rich pipeline with multiple proprietary programs

- Oncology & severe autoimmune diseases
- 4 products in clinical phase

Strategic alliances with premier pharma partners

- Industrial partners
- Innovative Access Program



Competitive technology suite

- Antibodies with differentiated modes of action
- Based on llama immune system and unique Fc engineering

Financial strength

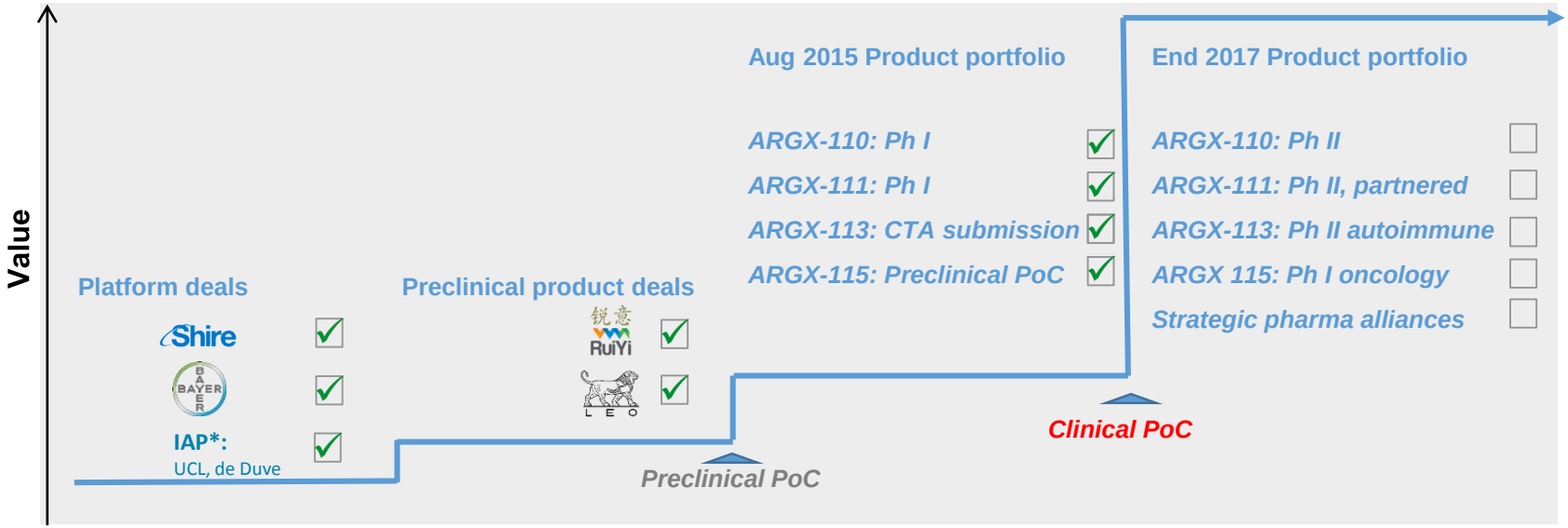
- Strong cash position (€ 54.3Mio Feb 2016)
- € 1.4B potential future income from partnerships

Business model maximizing shareholder value

Generating differentiated antibody product candidates…

Novel + arGEN-X technology suite =  Maximally differentiated mAbs

… towards Phase II value inflection point



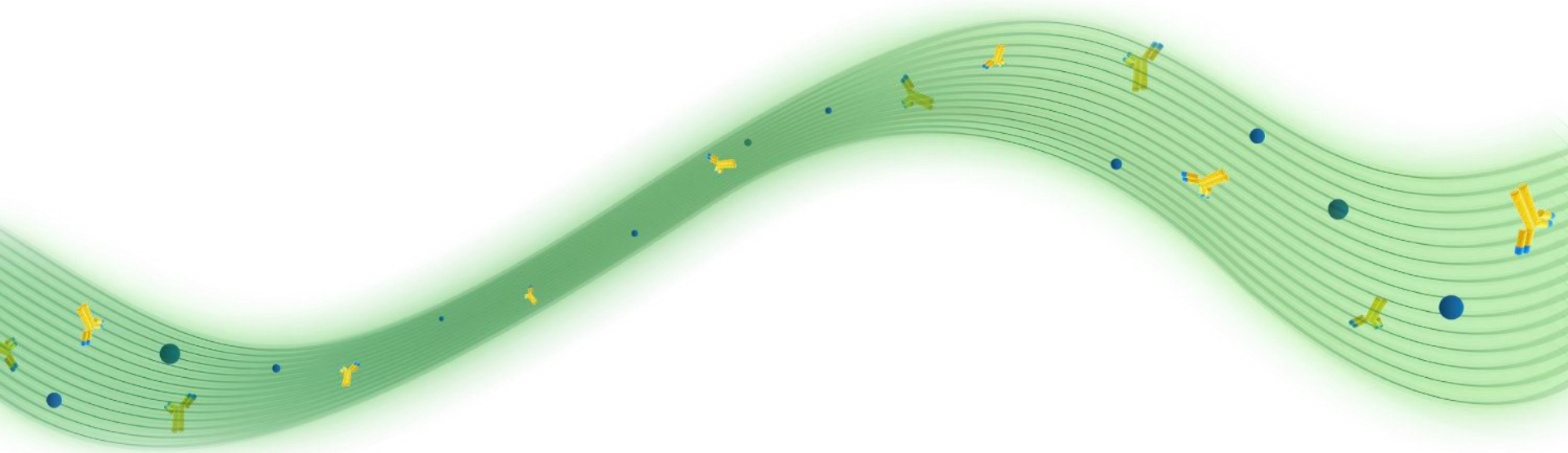
* IAP: Innovative Access Program

Rich pipeline approaching major value inflection points

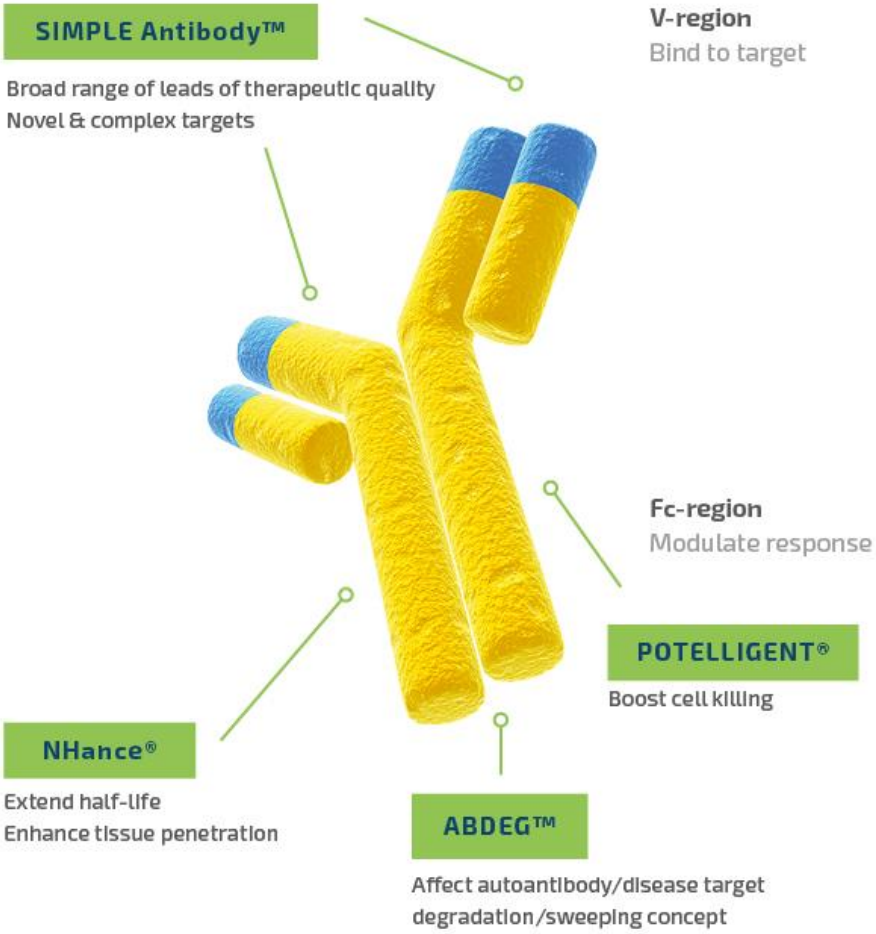
- **Cancer immunotherapy**
- **Cancer metastasis**
- **Autoimmune diseases**
- **Non-dilutive income**

Drug Candidate	Indication	Preclinical	Phase 1	Phase 2	Owner-ship
ARGX-110 (CD70)	Blood cancers *TCL*	→	→		Wholly owned
ARGX-110 (CD70)	Solid tumors	→	→		
ARGX-115 (GARP)	Cancer immunotherapy	→			
ARGX-111 (c-MET)	Solid tumors Blood cancers	→	→		
ARGX-113 (FcRn)	Autoimmunity *Myasthenia gravis*	→	→		
ARGX-110 (CD70)	Autoimmunity	→			
Discovery	Autoimmunity Cancer	*multiple*			
锐意 RuiYi	Autoimmunity Cancer	→	→		Partnered
Shire	Undisclosed	→			
LEO	Chronic inflammation	→			
BAYER	Undisclosed	→			

Creating innovative antibodies



Unique technology platform: multiple modes of action



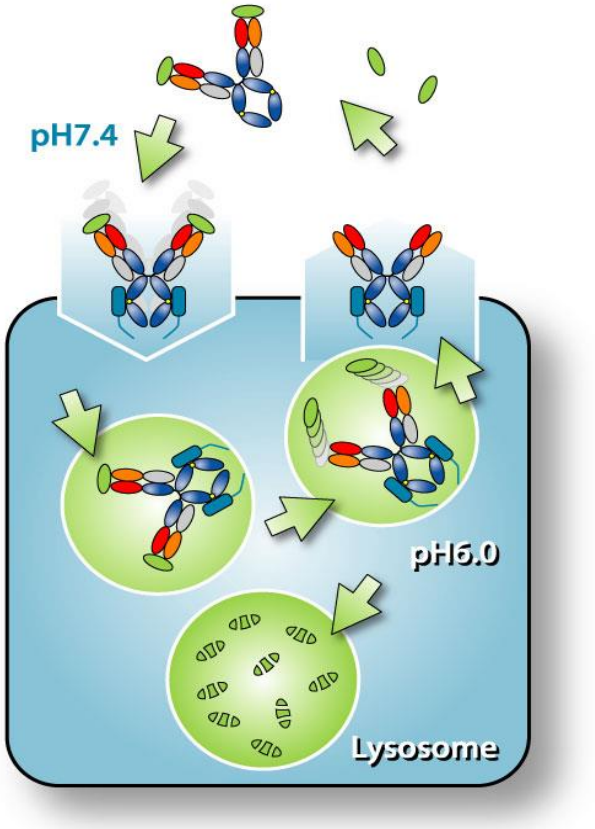
Protein, cell or
DNA immunization

- 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)

Continuous technology innovation: antibody mediated target clearance

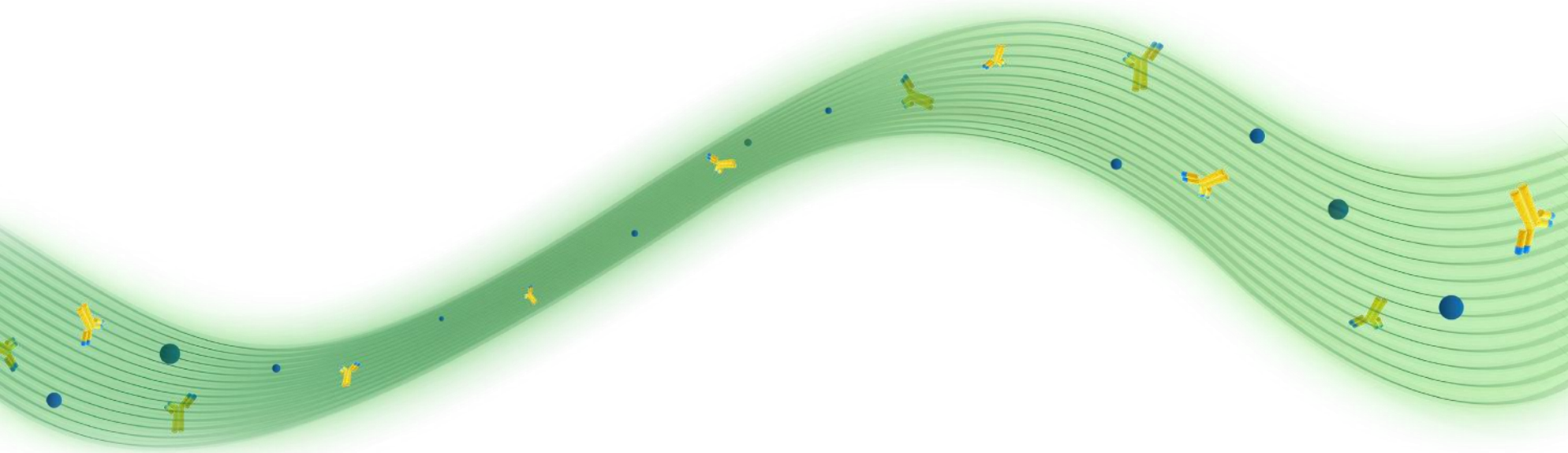
NHance®/ABDEG™
FcRn modulation

SIMPLE ANTIBODY™
pH-dependent target binding

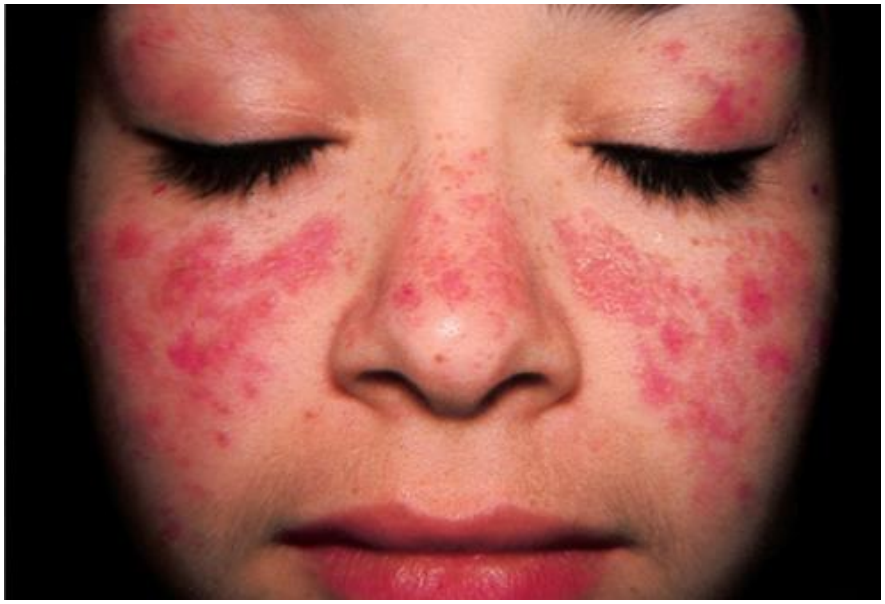


- Clinical potential for indications:
  - with high circulating target concentrations
  - which require fast target clearance
  - e.g. inflammatory cytokines (receptors)

ARGX-113



What is autoimmune disease?



- Immune system attacks own organs
- Tissue destruction by autoantibodies
- Common diseases include: multiple sclerosis, lupus, rheumatoid arthritis, psoriasis, myasthenia gravis

Why target autoimmune diseases?

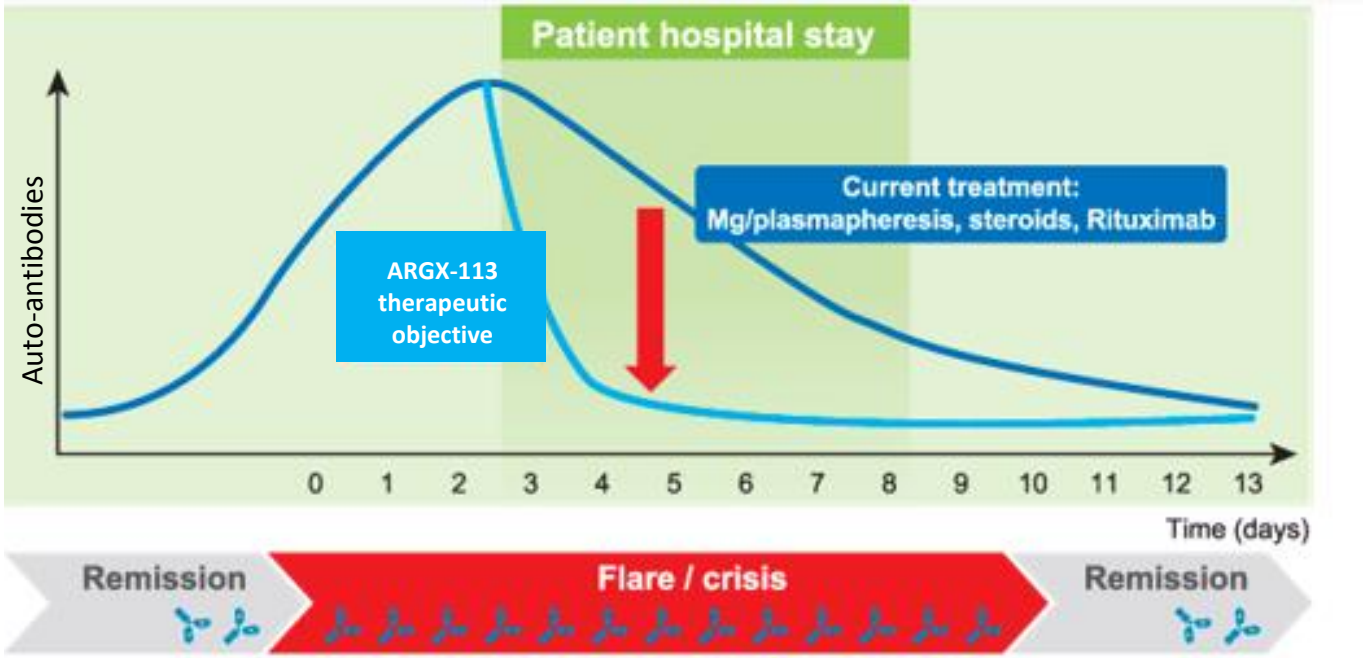
- 10% of population suffers from autoimmune diseases
- Antibody therapy used for rheumatoid arthritis, multiple sclerosis & psoriasis
- ARGX-113 targets severe autoimmune diseases

Current treatment

- High dose corticosteroids and broad immunosuppressive agents: severe side effects
- IVIg or Plasmapheresis: incomplete effect, slow onset of action

ARGX-113: Potential breakthrough in autoimmune disease

ARGX-113 addresses acute autoimmune flares more effectively



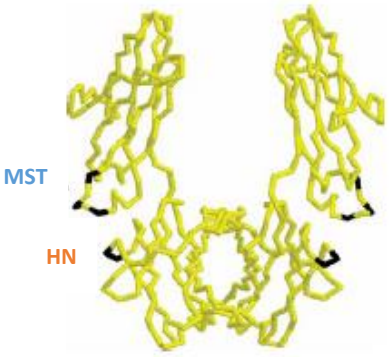
Clinical rationale for targeting autoantibody clearance

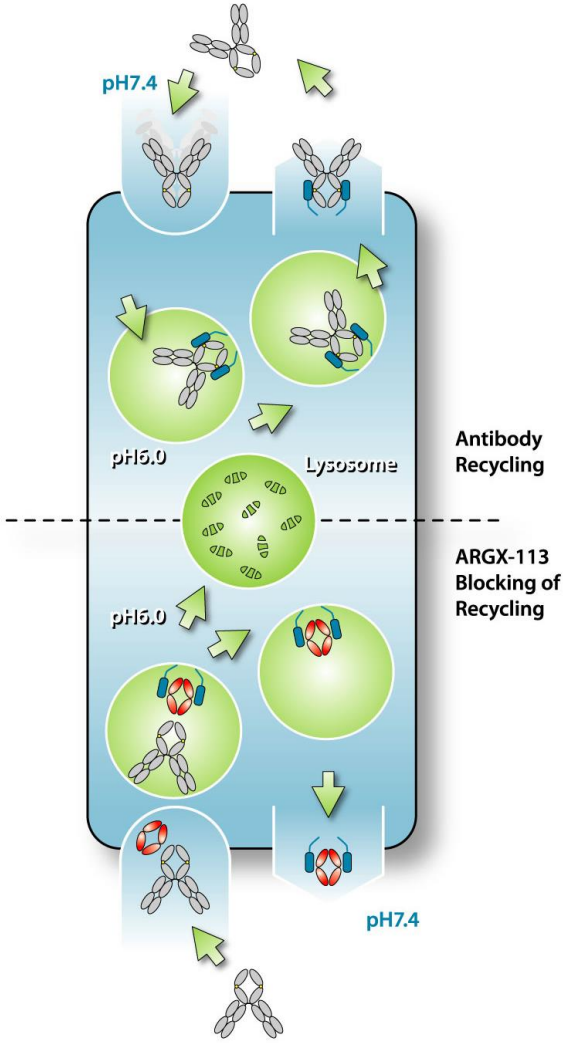
Treatment	Plasmapheresis in human *	ARGX-113 in primate **
Decrease in antibody levels (%)	62.8	75
Decrease in disease score (%)	60.8	N/A
Speed of onset	slow	fast

ARGX-113: How it works - Antibody clearance capability

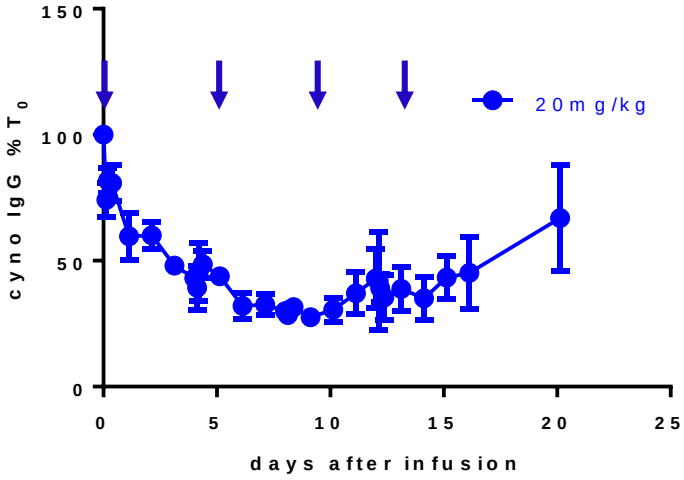
Proprietary Fc mutations | **Block IgG recycling** | **Resulting in rapid autoantibody clearance**

ABDEG™





Repeat dose ARGX-113



- Saturation of PD effect at doses ≥ 20 mg/kg
- Repeat dosing > single dose

Vaccaro et al., 2005, Nature Biotechnology

Clinical rationale for targeting autoantibody clearance

argenx

Myasthenia gravis autoantibody levels and disease score following therapy

Treatment*	Plasmapheresis	Immunoadsorption	IVIg
Decrease in antibody levels (%) after treatment	62.2 ± 6.3	55.1 ± 3.2	28.9 ± 3.8
Decrease in disease score (%) after treatment	60.8 ± 3.5	42.4 ± 4.2	23.8 ± 3.7
Clinical efficacy rate after 14 days**	12/15	7/10	6/15
Duration of hospital stay (days)	12.80 ± 0.28	13.50 ± 0.50	16.00 ± 0.50

* Comparison between 3 cycles of Plasmapheresis/Immunoadsorption every 24h-48h and 5 cycles of IVIG every 24h
** Clinically effective if disease score has improved by >50% 14 days after treatment

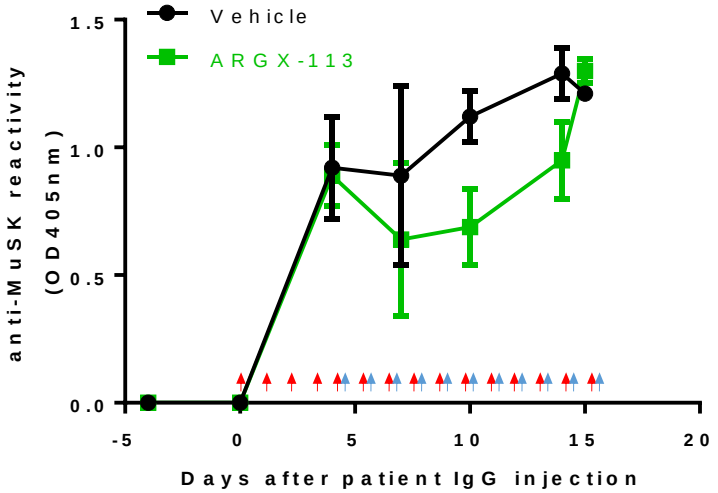
Liu et al., 2009

- Degree of autoantibody reduction: correlates with clinical improvement & reduced hospital stay
- Similar observations reported for other autoimmune disorders

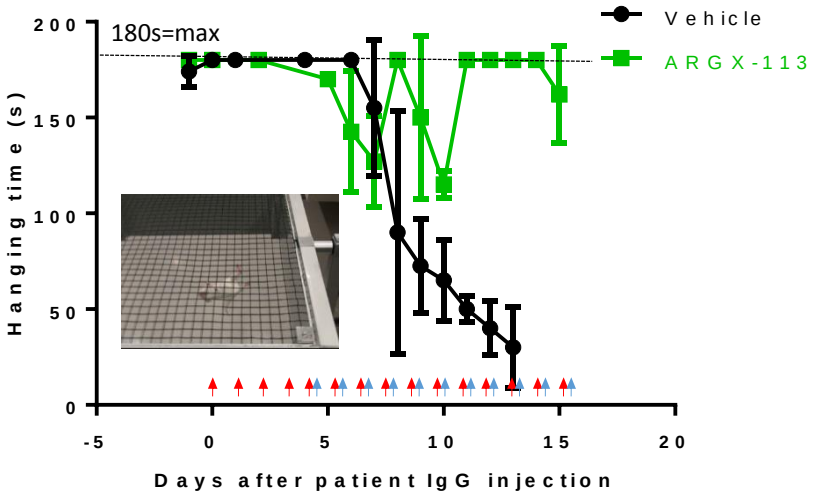
ARGX-113: In vivo PoC

MuSK-MG transfer model – therapeutic setting

Anti-MuSK Ab-levels



Inverted Mesh



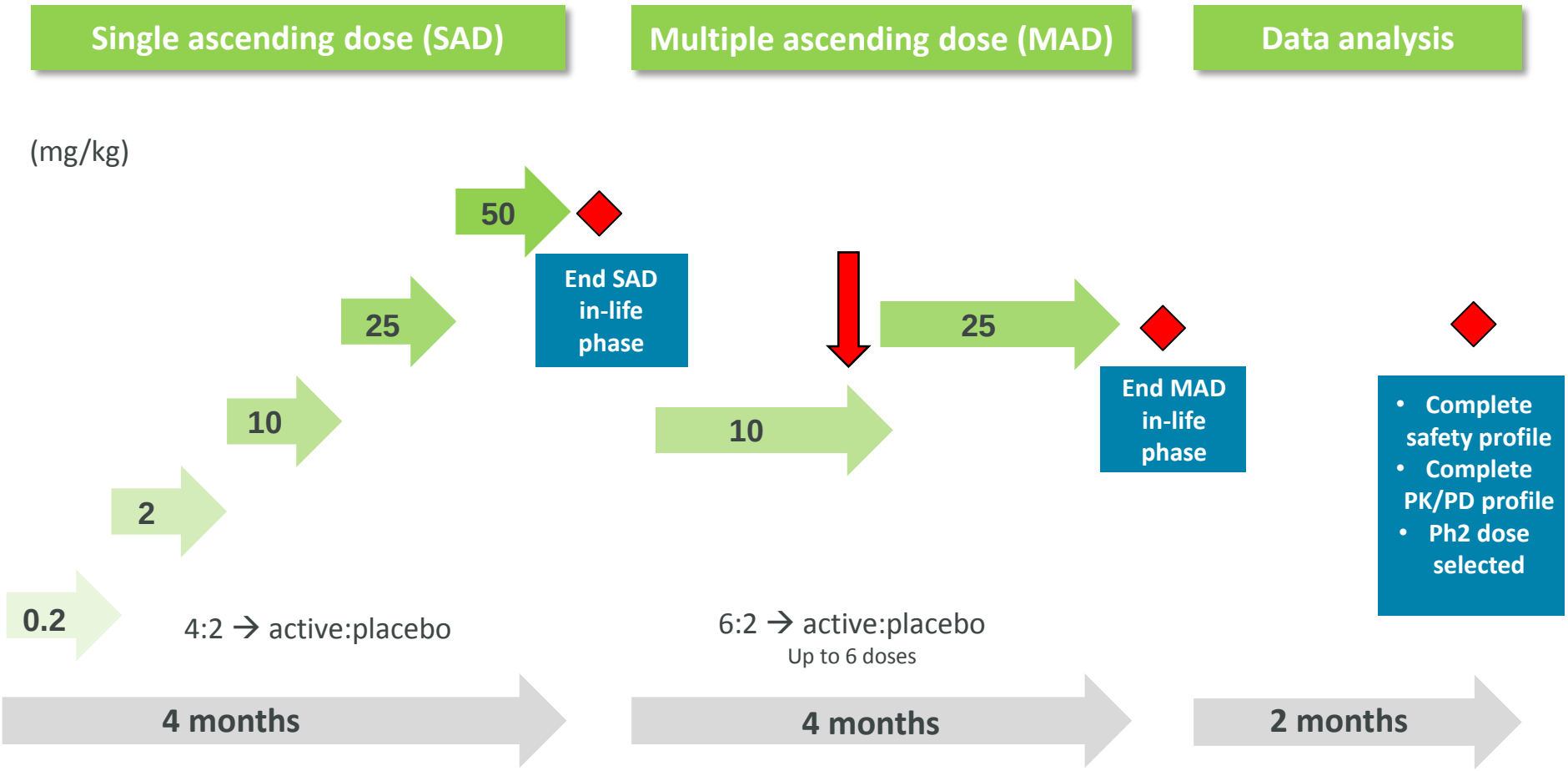
Patient IgG injection (37 mg)

ARGX-113 treatment (1 mg)

- Daily injection of MuSK-MG patient IgG causes Myasthenia gravis in NOD/SCID mice
- ARGX-113 (1mg) administration:
  - reduces autoantibody levels (anti-MuSK Ab-levels)
  - stabilizes disease: measured by inverted mesh (see graph) and grip strength (not shown)

ARGX-113: Phase 1 study design & interim safety read out

Double-blinded, placebo-controlled study in healthy volunteers

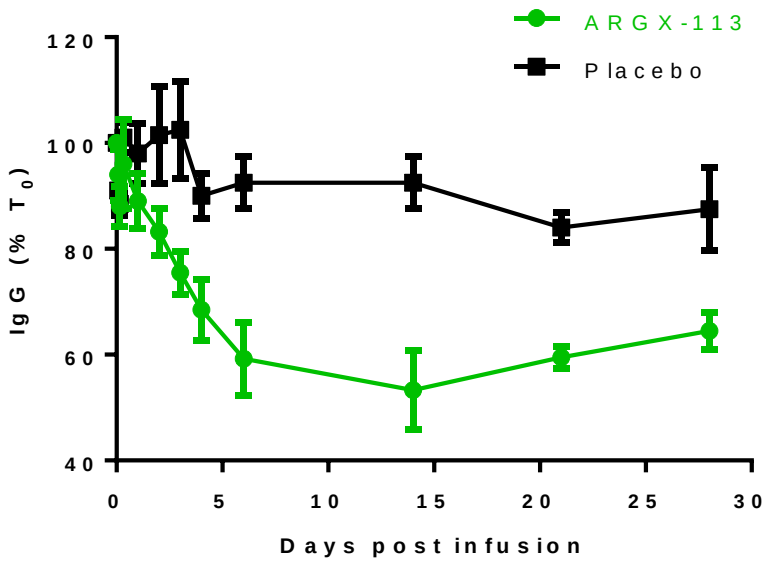


- SAD completed according to plan (38 healthy volunteers in total)
- Favourable safety and tolerability profile observed (no serious adverse events reported)

ARGX-113: PD marker readout for SAD

Double-blinded, placebo-controlled study in healthy volunteers

Rapid, deep and specific IgG reduction

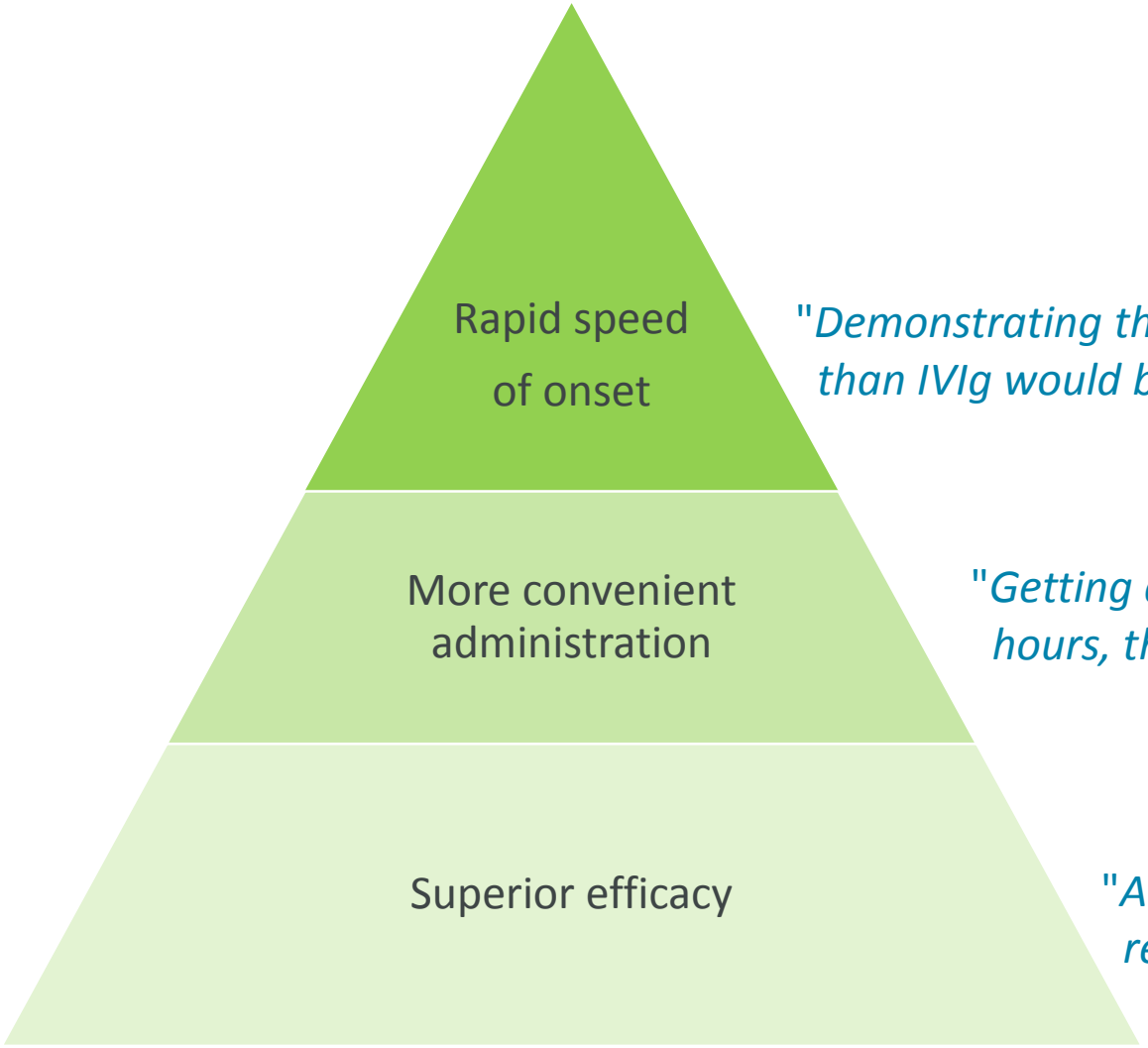


	ARGX-113 vs. IVIg*
Speed of IgG reduction	>>>
Level of IgG reduction	>>
Duration of PD effect	>

* Extrapolated based on literature data

- Single 2h infusion: rapid reduction of IgG, not affecting IgM/IgA and albumin levels
- Maximal PD effect (~50% IgG reduction) as of 6 days after infusion
- Low IgG levels maintained for >1 week

ARGX-113 vs. IVIg/PLEX: Key differentiators for MG



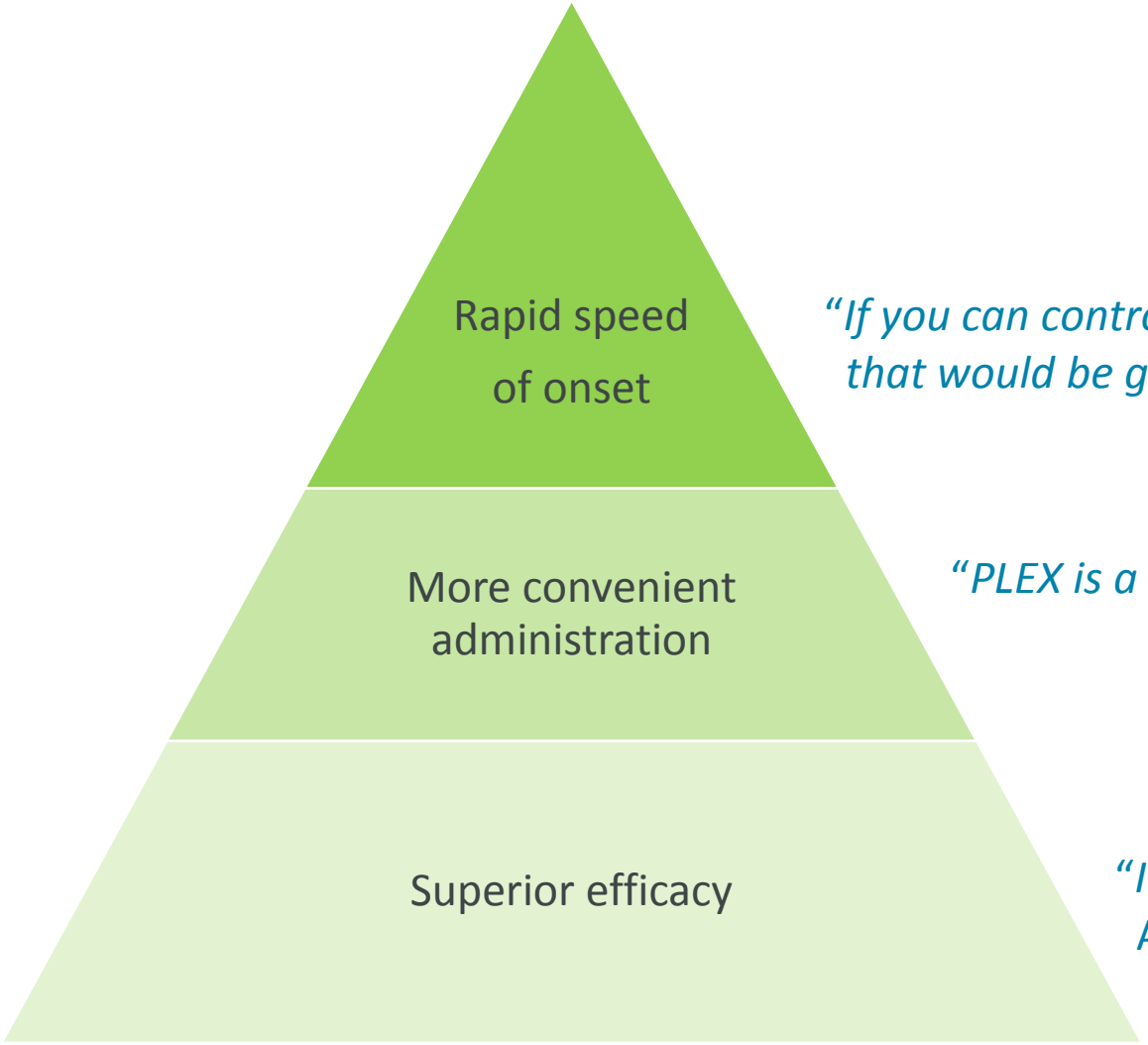
"*Demonstrating that its onset of action is faster than IVIg would be fantastic,*" MG KOL

"*Getting an infusion done within 2 hours, that is an attractive piece*“ MG KOL

"*Acute MG crisis, I don't think it responds all that well to IVIg*," MG KOL

Better tolerated, shorter procedure with limited follow-up

ARGX-113 vs. IVIg/PLEX: Key differentiators for ABD



"If you can control the disease within a week or two, that would be great," ABD KOL

"PLEX is a nightmare to apply," ABD KOL

"IVIg just doesn't work that great," ABD KOL

Better tolerated, shorter procedure with limited follow-up

ARGX-113: What next?

Next steps

Clinical Status

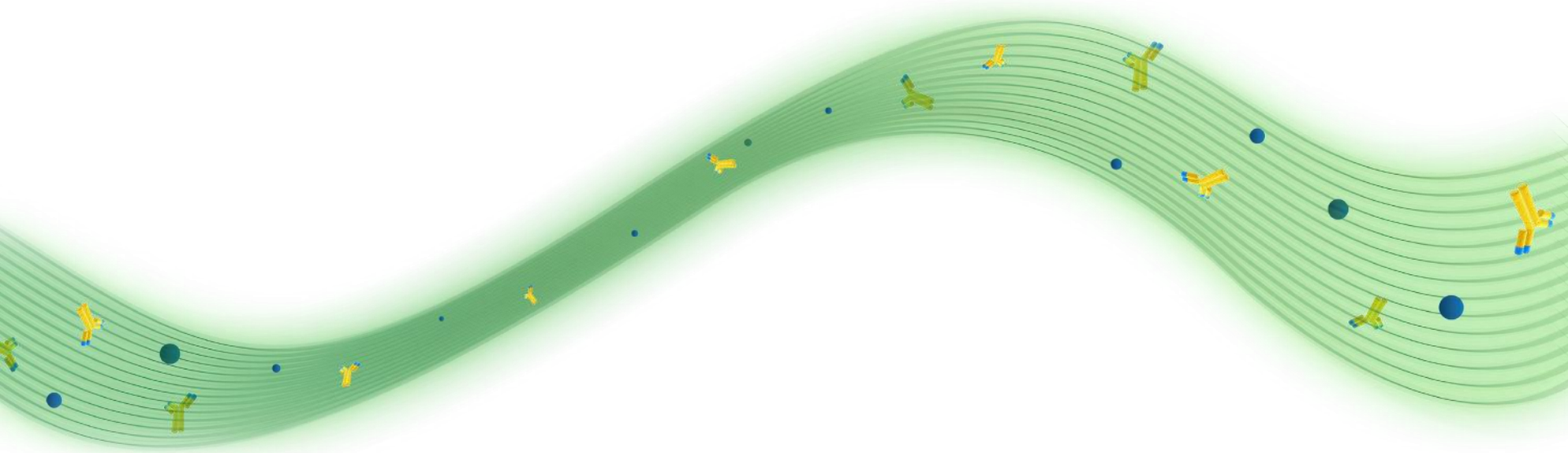
- Multiple Ascending Dose study (MAD)
- Start of Phase 2 in first indication

Market potential

Benchmark therapeutic treatments

- IVIg: annually > $ 4B (autoimmune diseases approx. 50%)
- IVIg: $ 79K/cycle
- Benlysta®: $ 35K/year
- Plasmapheresis: $ 101K/cycle
- Xolair® annual sales exceed $ 800M

ARGX-110

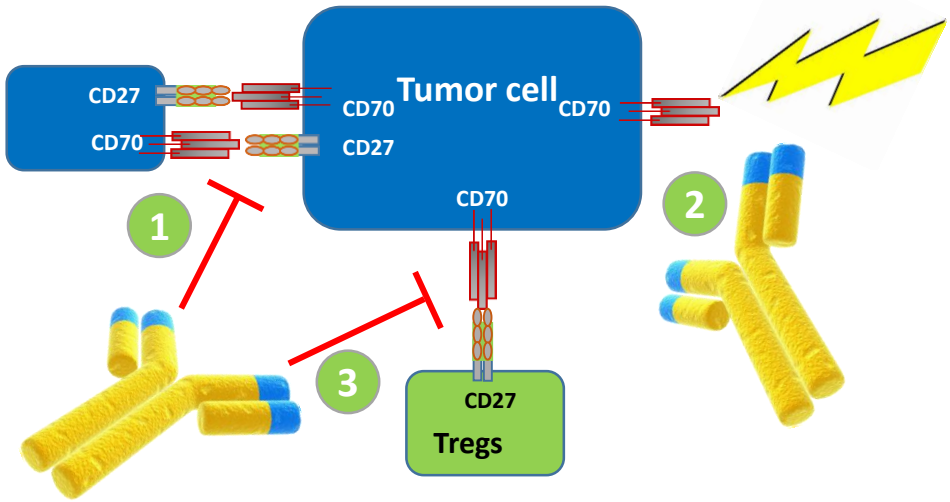


ARGX-110: 3 distinct modes of action

1. Block tumor growth signal

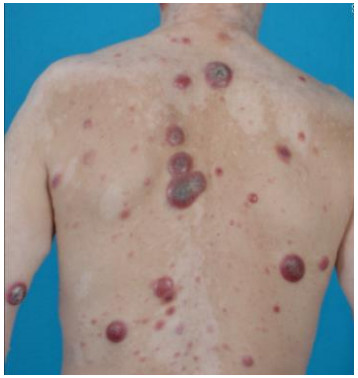
2. Kill tumor

3. Restore immune surveillance



Silence et al., 2014, mAbs

Why T Cell Lymphoma?



T Cell Lymphoma: rare and heterogeneous disease

- Eldery (> 60y)
- Rare (1/100,000) but underdiagnosed
- Treatment: first by dermatologist, then by oncologist
- Present in skin, blood and lymph compartments; susceptible to infections

"We haven't made much progress in TCL survival in the last decades. With PFS getting worse after each relapse, we are desperate for the next Rituxan for TCL. This would be a real game changer."

Dr. O'Connor, Columbia University Medical Center

Very high unmet medical need

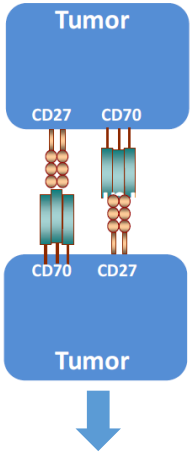
- Unfit for chemo or stem cell transplantation
- Current thearpies: only moderately effective, not curative
  - Retinoids; HDAC inhibitors
  - Antifolates; chemo

ARGX-110 potential

- Ph I results demonstrate biological activity in skin, blood, lymph compartment
- Favorable safety profile enables mono and combo therapy

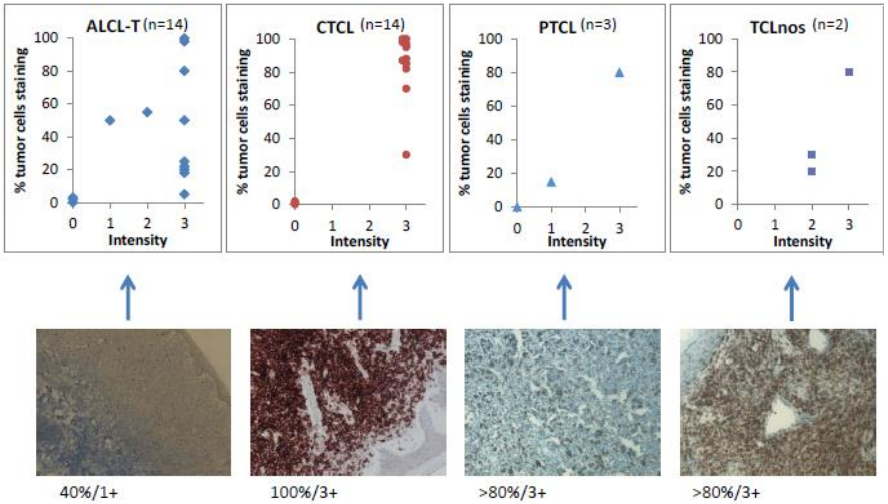
ARGX-110: CD70/CD27 pathway highly relevant in TCL

CD70/CD27 on tumor cells

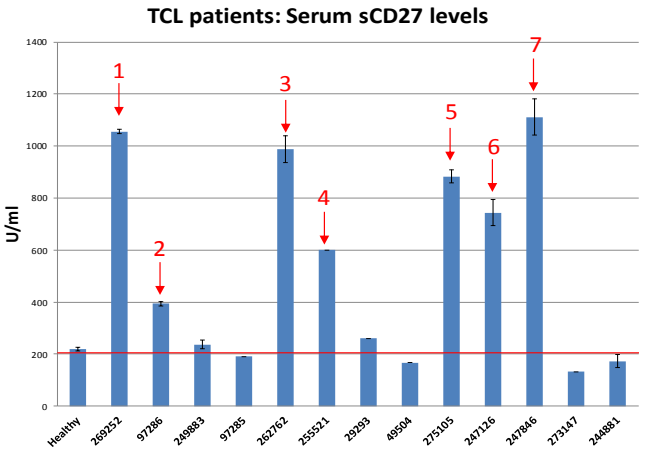


Proliferation & survival

IHC of CD70 expression in TCL biopsies



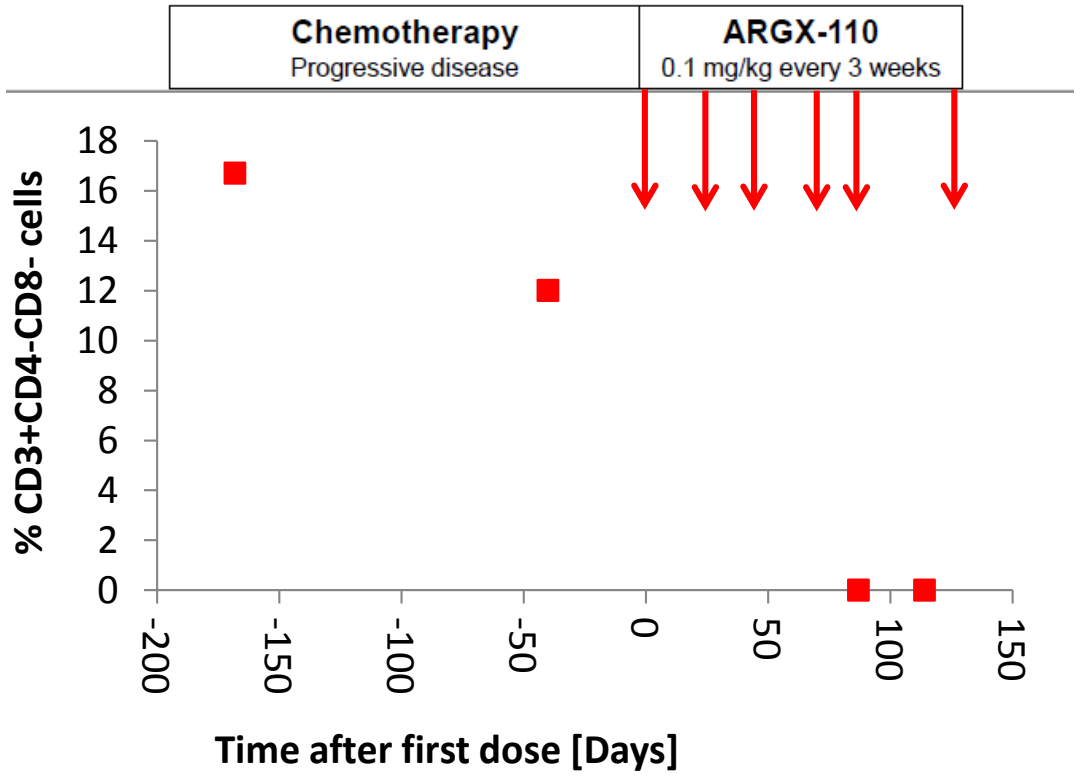
sCD27 levels in TCL patient sera



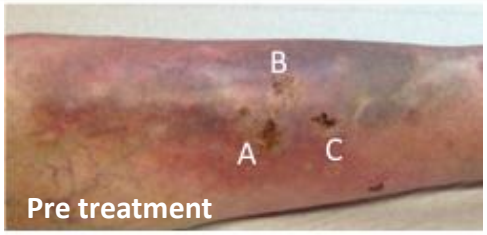
- CD70 strongly overexpressed across different TCL types
- Elevated sCD27 levels suggest strong pathway activity in TCL

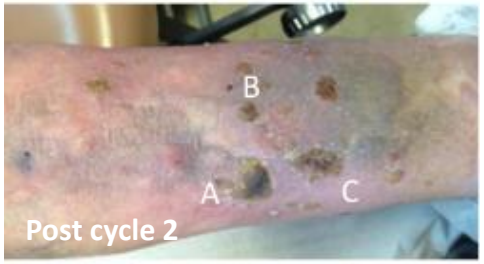
ARGX-110: Proof of biological activity in 2 patients with Cutaneous T-Cell Lymphoma (Sézary-Syndrome)

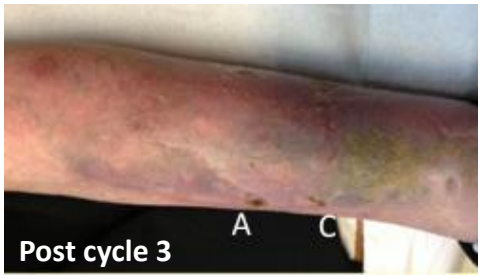
Blood compartment cleared from malignant cells (■)



Stabilized skin lesions

a. 

b. 

c. 

- 78 year old woman with CTCL-SS; refractory to multiple lines of chemotherapy *- Patient anecdotes -*
- ARGX-110 treatment (0.1 mg/kg every 3 weeks)
  - Complete response in blood compartment
  - Stabilized disease in skin lesions (see image a. & c.) & lymph nodes
- Elimination of CD70 positive Sézary cells from blood in 2nd CTCL-SS patient

ARGX-110: Proof of biological activity in patient with Cutaneous Follicular Helper T Cell Lymphoma

Stable disease in skin lesions

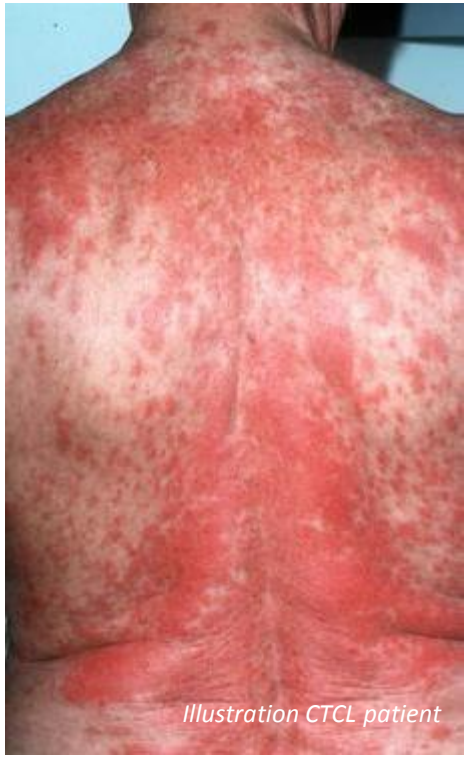


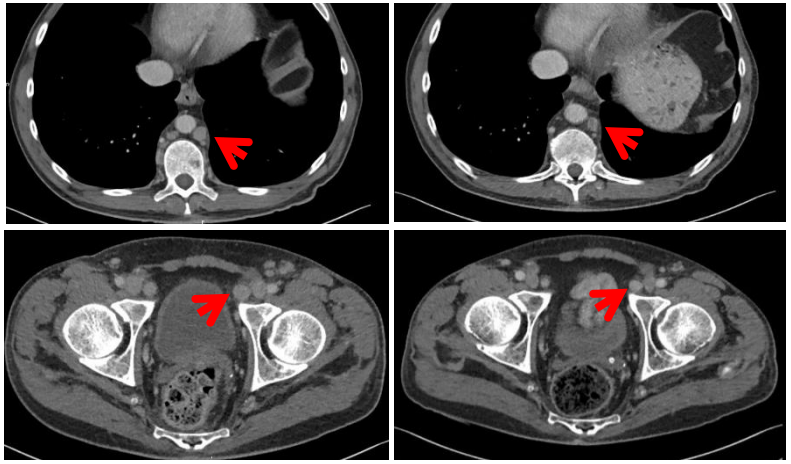
Illustration CTCL patient

- 55 year old male with cutaneous T_{FH} lymphoma
- Disease in skin
- Treated with Interferon and PUVA

- ARGX-110 treatment (5 mg/kg)
  - Stabilized disease up to cycle 3
  - After 3 cycles: skin lesions decreased in number and size
  - Patient already 13 cycles on study (9 months)

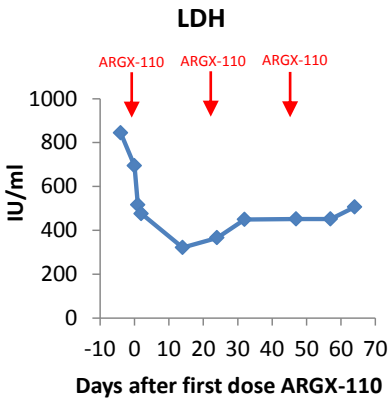
ARGX-110: Proof of biological activity in patient with Angioimmunoblastic T-Cell lymphoma (AITL)

Tumor shrinkage in lymph nodes



Ref. Lesions	Shrinkage
L1	24%
L2	4%
L3	4%
L4	39%
Non-Ref. Lesions	
L5	65%
L6	50%
L7	59%
L8	43%

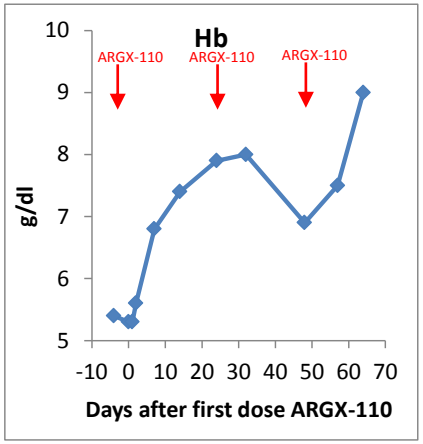
Transfusion independent



- 61 year-old male AITL patient with severe Hemolytic Anemia
- Refractory to chemotherapy: CHOP + Etoposide/Cyclosporine /Bendamustine - Transplant

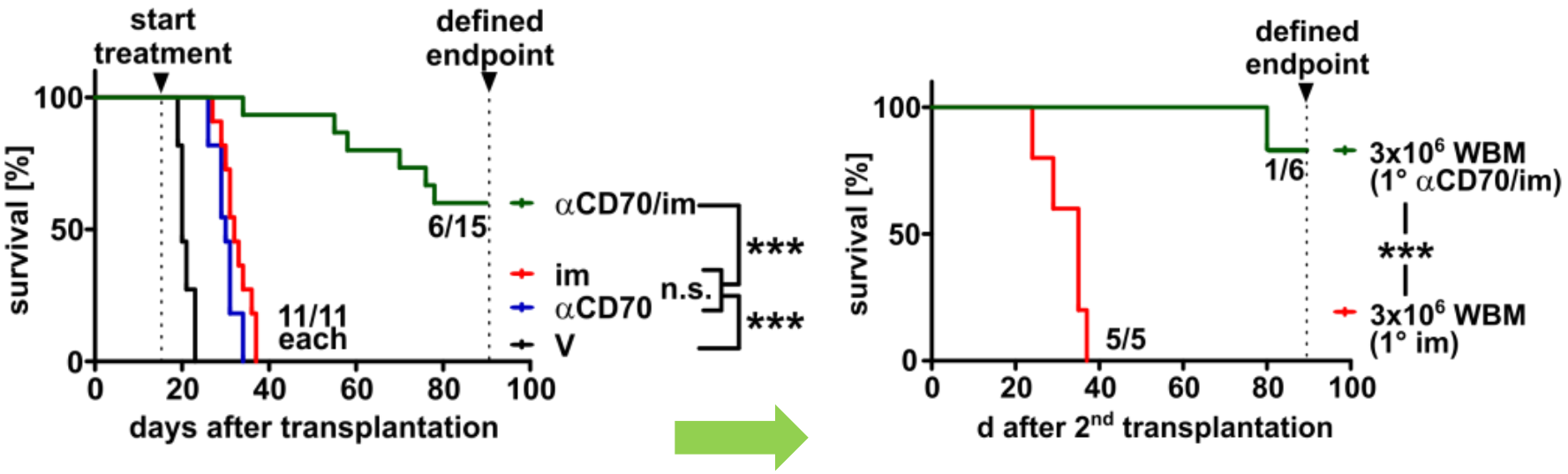
- After 2 doses of ARGX-110 (5 mg/kg)
  - Clinical response in lymph nodes
    - Reference lesions shrink between 4-40 %
    - Clear tendency for all other lesions to shrink
  - Clinical response in blood
    - Transfusion independent
    - Coomb positive → Coomb negative after 1 cycle

- Patient anecdote -



ARGX-110/BCR-ABL1 inhibitor eliminates leukemic stem cells in CML model

Curative potential of combo treatment ARGX-110/BCR-ABL1 inhibitor



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

Riether and Schürch et al., 2015, Science Translational Medicine

ARGX-110: What next?

argenx

Next steps

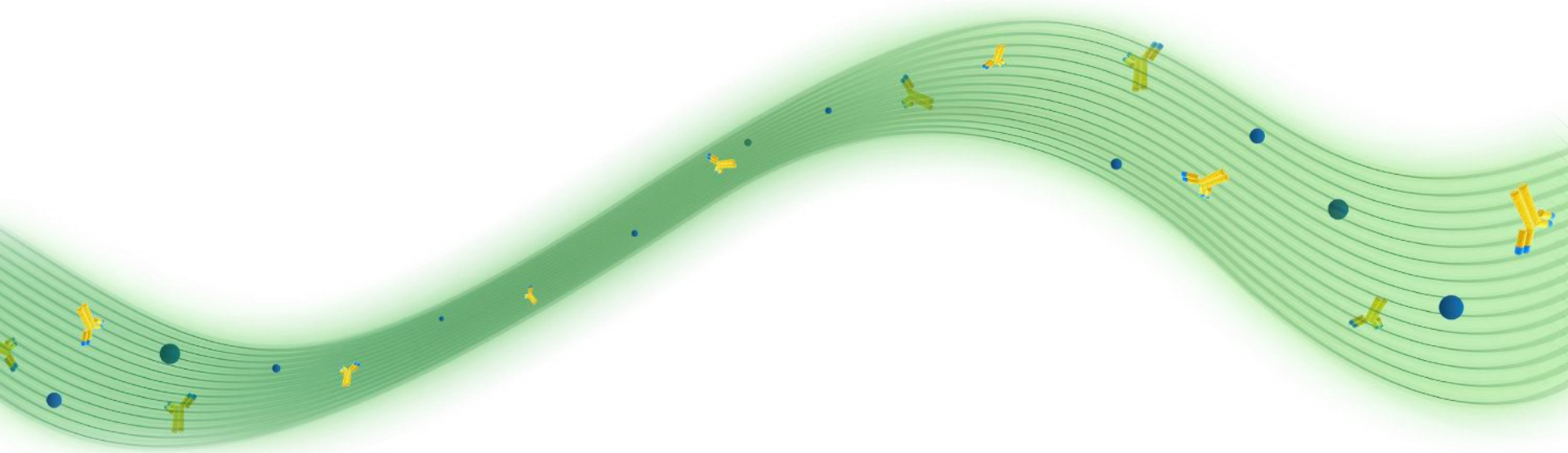
Ongoing clinical studies

- **Hematological tumors**
  - T-Cell Lymphoma (TCL): Phase 1b → 6 sites (BE, FR, IT)
  - Recruiting 10 CTCL (min 5 Sz) - 10 PTCL (min 5 AITL) patients
  - 12 patients identified, 4 patients on treatment

Site	Investigator	Status	Patients (pre)screening	On treatment/ treated
UZ Ghent (BE)	Dr. Offner	Open		1X CTCL
Jules Bordet Institute (BE)	Dr. Maerevoet	Open		1X CTCL
Gustav Roussy (FR)	Dr. Ribrag	Open	6X CTCL & PTCL	
St. Louis (FR)	Dr. Bagot	Open	1 X CTCL	2X CTCL
Lille (FR)	Dr. Morschhauser	Open	1X CTCL	
Bologna (IT)	Dr. Zinzani	Open in March		

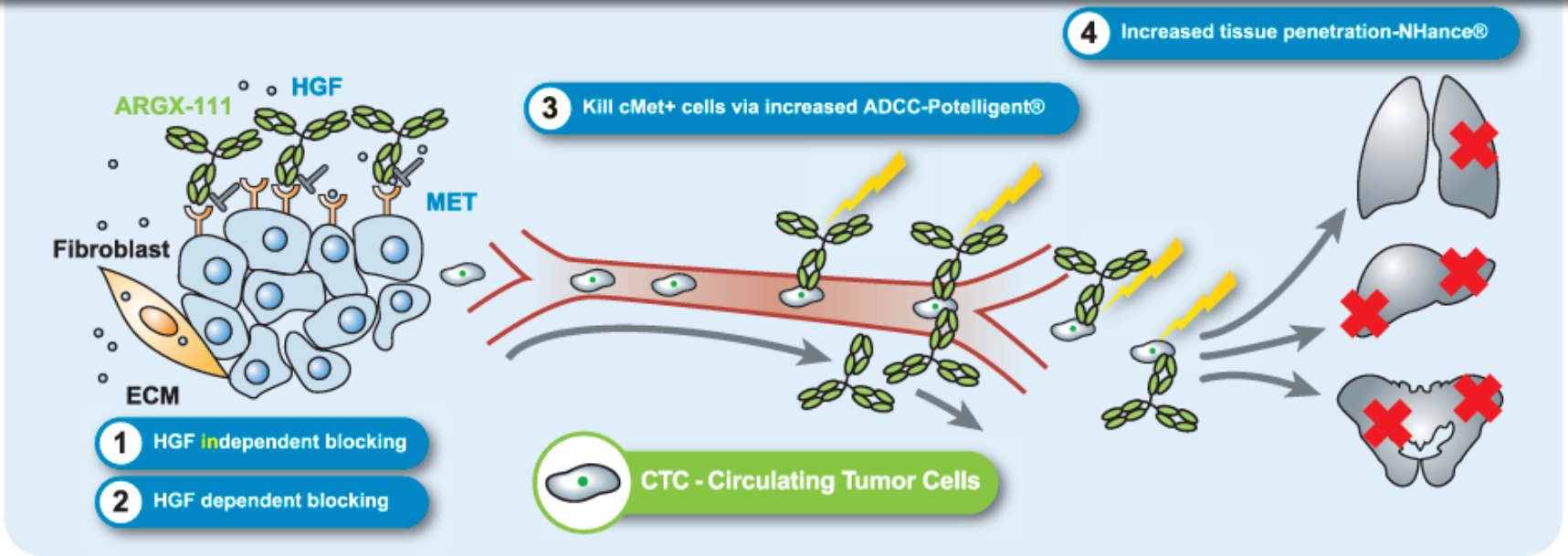
- **Solid tumors**
  - Nasopharyngeal carcinoma (NPC): Phase 1b (UZ Gent)

ARGX-111



ARGX-111: Addressing the end game of cancer

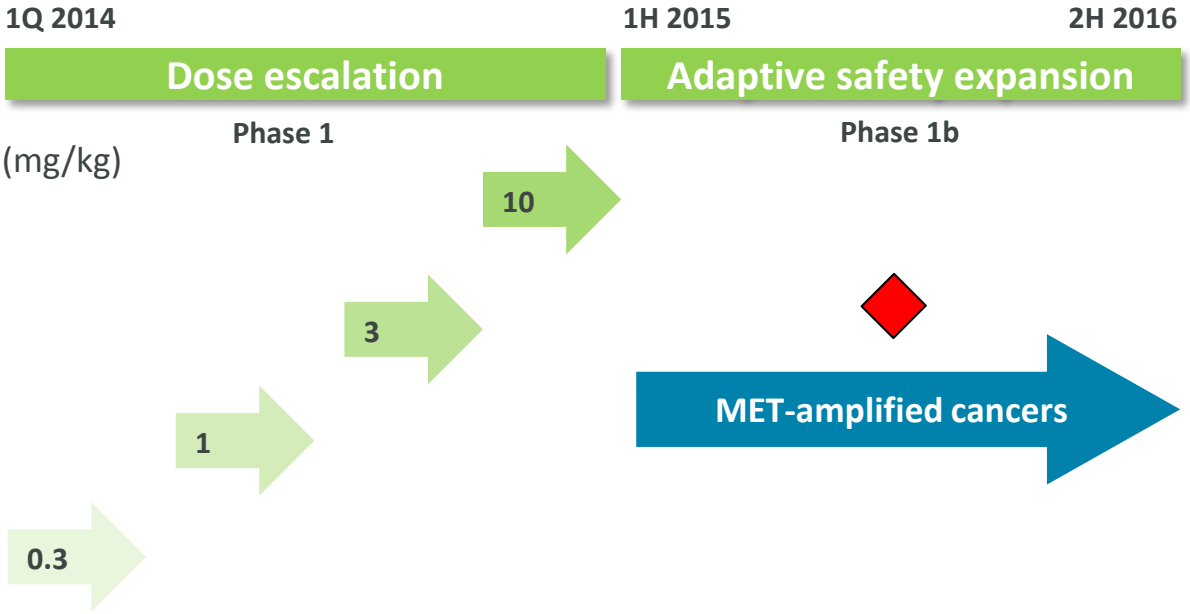
Targeting MET, receptor responsible for tumor growth and metastasis



Hultberg et al., 2014, Cancer Research – Gherardi et al., 2013, Nature Reviews Cancer

- ARGX-111 has several distinct modes of action
  - HGF-dependent blocking
  - HGF-independent blocking
  - Killing MET-expressing cells
  - Specific targeting of tumor tissue

ARGX-111: Phase 1 trial design



Details

- **Advanced cancer population (34 patients)**
  - Progressive, end stage disease
  - 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**

- ~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

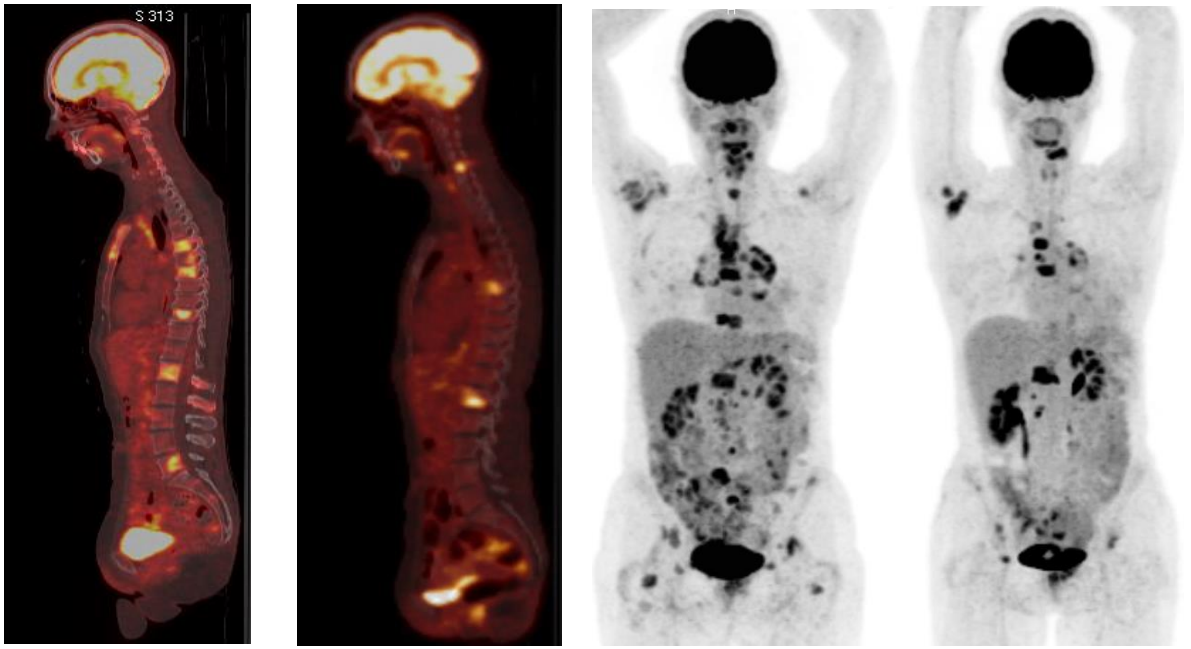
ARGX-111: Proof of biological activity in MET-amplified cancer patients

Gastric cancer patient

- 50 year old gastric cancer patient with bone metastases; MET-amplified
- Multiple lines of previous treatment
- PET/CT scan: biological activity
- CTCs reduced by 75%
- Good clinical performance

Biological activity

Baseline PET scan | Improvement after 4 doses | Baseline PET scan | Improvement after 4 doses



Renal cancer patient

- 57 year old renal cancer patient; MET-amplified
- 11 cycles on study; progressive disease stabilized after 2 cycles
- PET/CT scan: biological activity
- 30% reduction of lesion in lymph node

Renal cancer patient

- 58 year old year old renal cancer patient; MET-amplified
- 4 cycles on study

ARGX-111: What next?

Next steps

Clinical Status

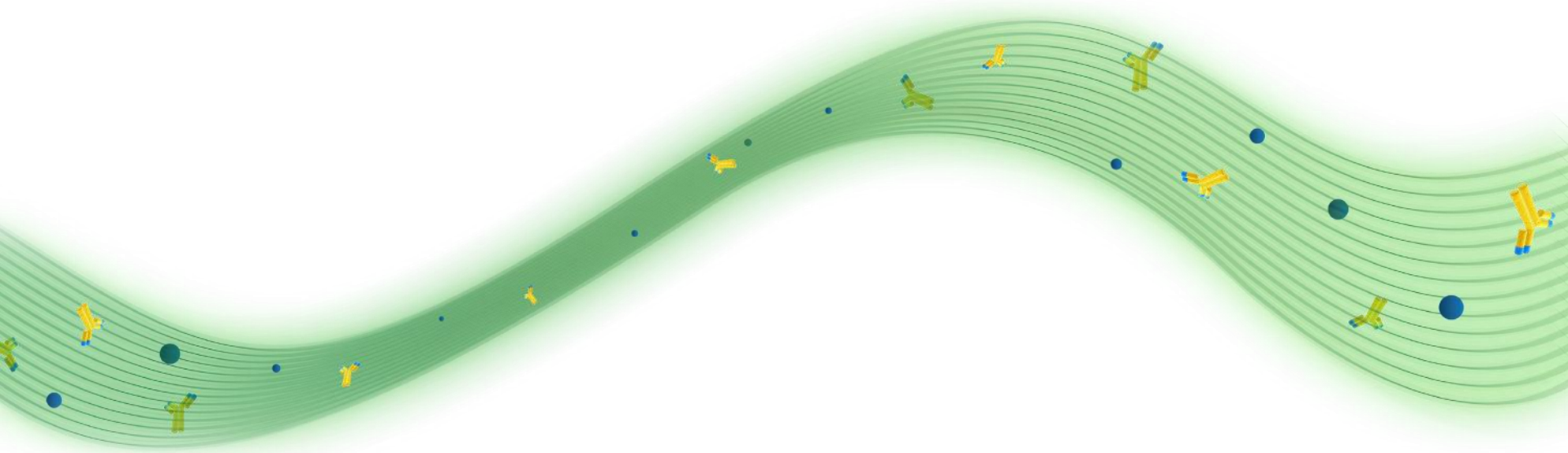
- Phase 1b in MET-amplified patients ongoing
- 5 clinics open EU (BE, FR)
- 3 clinics open in Asia
- Recruiting up to 15 MET-amplified patients

Market potential

Benchmark cancer treatments

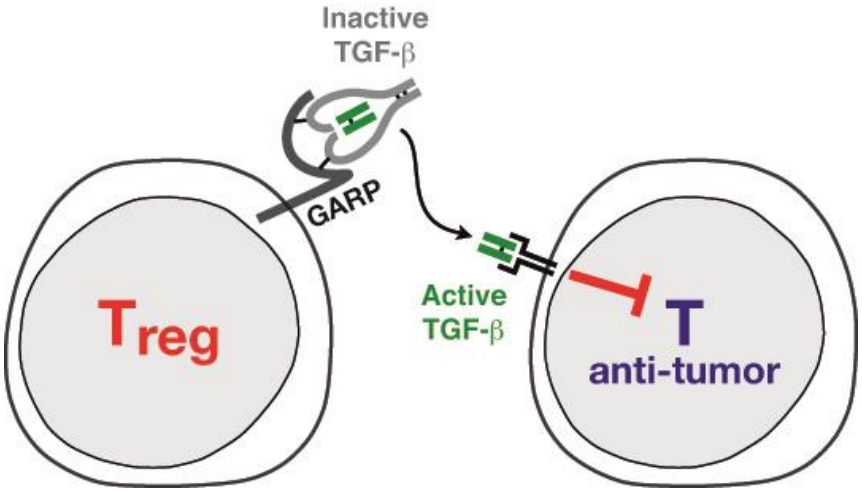
- Herceptin®: $ 54K/y
- Avastin®: $ 42.8K– 55K/y
- Erbitux®: $ 80K/y
- Crizotinib: $ 1B/y sales based on 3% of ALK-positive NSCLC patients

ARGX-115



ARGX-115: Towards a next generation Yervoy®

GARP: a novel immune checkpoint

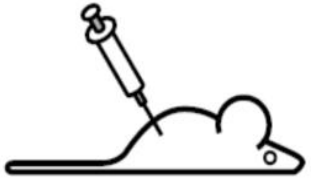


- GARP upregulated specifically on surface of Tregs only
- GARP presents and activates latent TGF-ß1, activating Tregs and suppressing Teff cells
- SIMPLE Antibody™ hitting unique, patented epitope on GARP
- GARP blockade sufficient for MoA – no Treg depletion
- Graft-versus-host-disease model delivered convincing PoC

Cuende et al., 2015, Science Translational Medicine

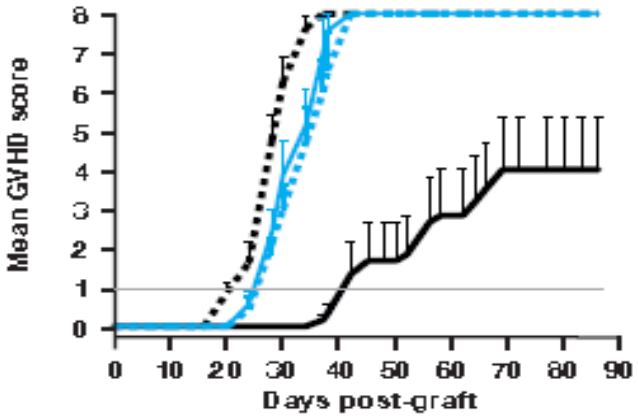
ARGX-115: Towards a next generation Yervoy®

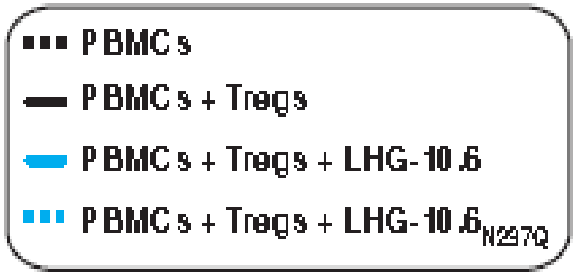
In vivo efficacy of anti-GARP-TGFβ SIMPLE Antibody™ in GVHD Model



NSG mice injected with:

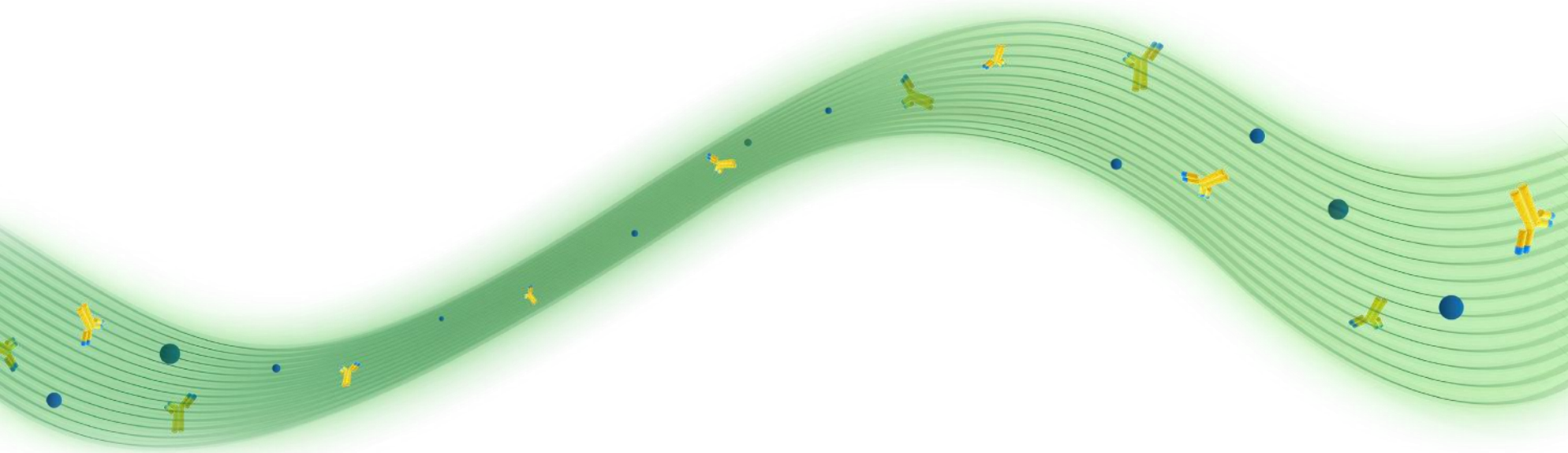
hPBMC → hPBMC (i.e. CTLs) attack host cells (GVHD)
+/- hTregs → hTregs delay GVHD
+/- anti GARP → LHG-10.6 blocks Treg-mediated protective activity





Cuende et al., 2015, Science Translational Medicine

Partnerships



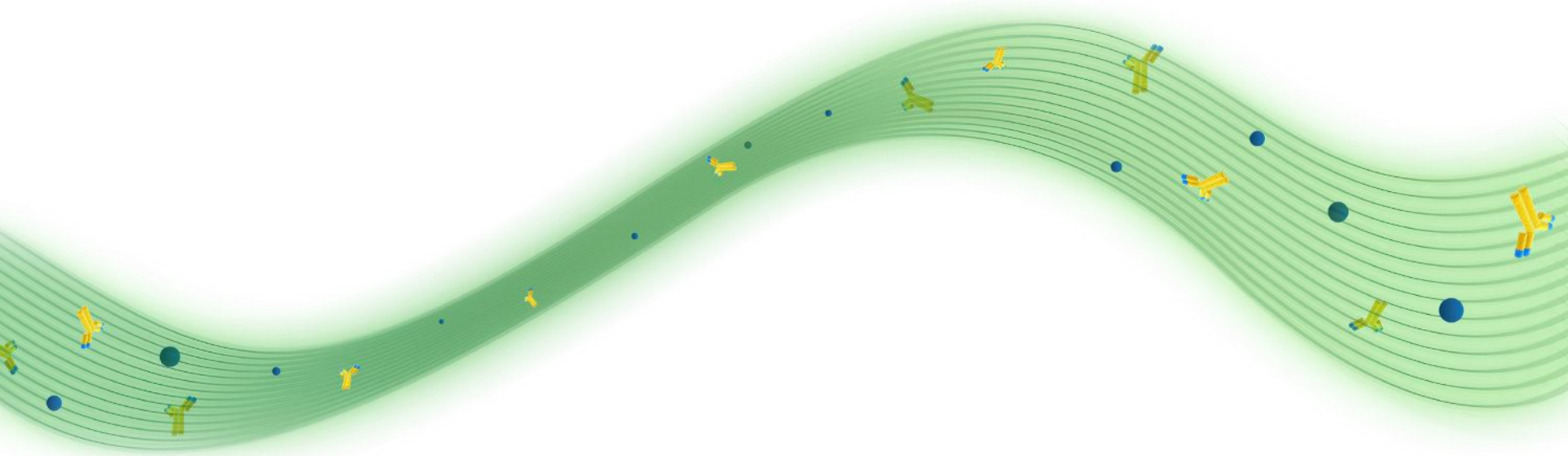
Building partnerships for the long term

- **Strategic Alliances** Shire
  - Non-exclusive product discovery and development, leveraging entire technology suite
  - Upfront funding, R&D support, development milestones, royalties, product reversion rights
- **Collaboration Agreements** Shire LEO BAYER
  - Non-exclusive discovery collaborations, applying SIMPLE Antibody™ to complex targets
  - Technology access fees, R&D support, milestones, royalties
- **Innovative Access Program** UCL Université catholique de Louvain UNNAMED BIOTECH
  - Non-exclusive access to antibody technologies for academic and biotech centers of excellence
  - Creative deal structures including option to acquire asset, golden share,...

- € 28.3Mio in cumulative revenue (31 Dec 2015)
- >€ 1.4B* potential cumulative revenues from existing partnerships

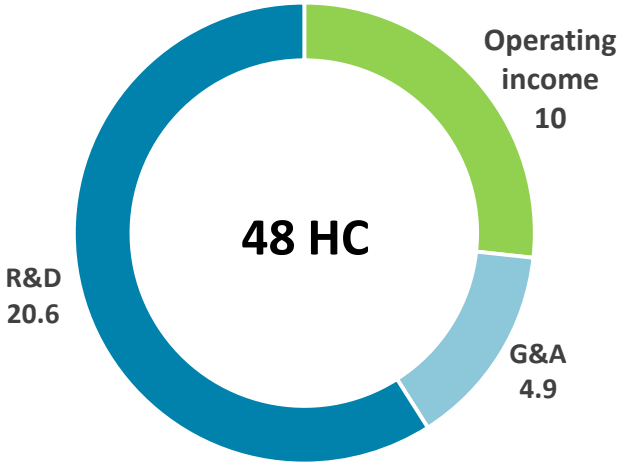
** Assuming specific development and sales milestones are met for all potential discovery targets*

Financials



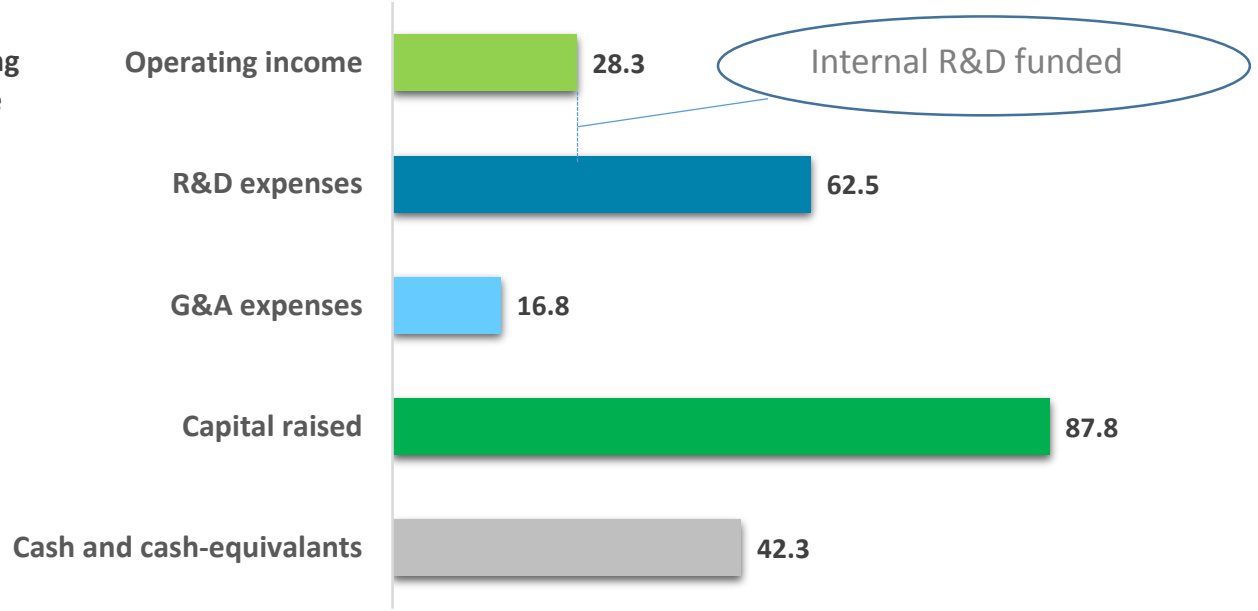
Well capitalized to execute strategic plan

Operating income and expenses (MEUR) 4Q15



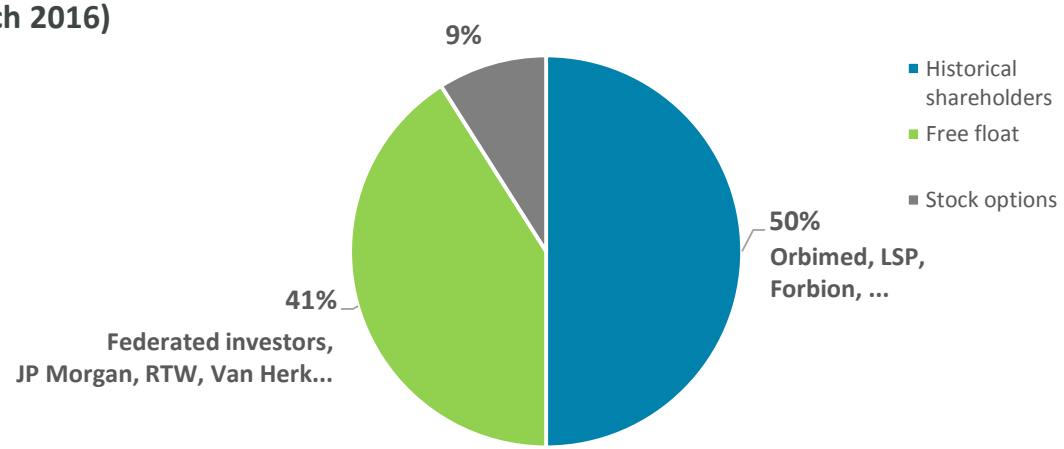
Operating income, expenses and capital raised since inception (MEUR) 4Q15 (*)

(*) not including deferred revenue and accruals



Shareholder structure (March 2016)

Fully diluted



Upcoming news flow 2016