Creating innovative antibodies for cancer & severe autoimmune diseases

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7-10 June 2016 @ Jefferies 2016 Healthcare Conference, New York

Disclaimer

Agenda

- Introduction

- Creating innovative antibodies

- Differentiated products

- Collaborations

- Financials

Introduction

Creating value from highly differentiated antibodies

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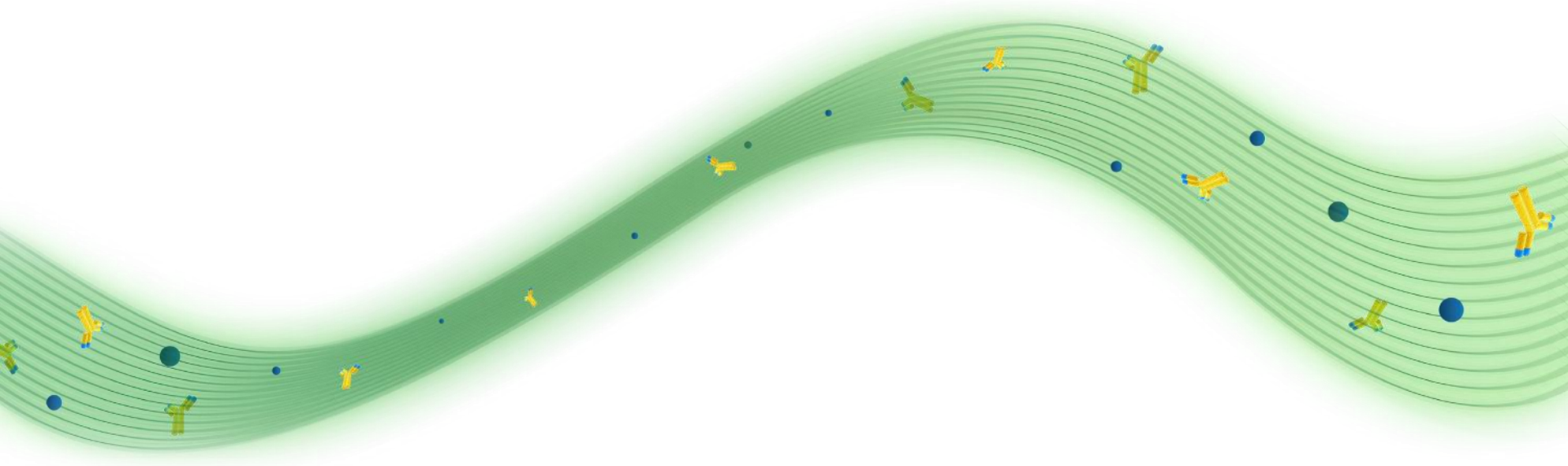
Rich proprietary pipeline

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

Thriving strategic alliances

- Industrial partners
- Innovative Access Program

Competitive technology suite

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

Strong financials

- Strong cash position
  (€ 54Mio March 2016; AbbVie € 35Mio April '16, Private Placement € 30Mio June '16)
- > € 2B potential future income from partnerships

Business model maximizing shareholder value

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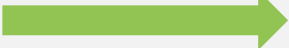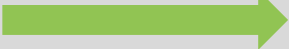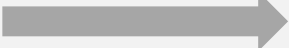
Generating differentiated antibody product candidates...

| Novel | + | arGEN-X technology suite | = | Maximally differentiated mAbs |

... towards Phase II value inflection point

Aug 2015 Product portfolio

- ARGX-110: Ph I ✓
- ARGX-111: Ph I ✓
- ARGX-113: CTA submission ✓
- ARGX-115: Preclinical PoC ✓

End 2017 Product portfolio

- ARGX-110: Ph II ☐
- ARGX-111: Ph II, partnered ☐
- ARGX-113: Ph II autoimmune ☐
- ARGX 115: Ph I oncology ☐
- *Strategic pharma alliances* ✓

Value

Platform deals
- Shire ✓
- BAYER ✓
- IAP*: UCL, de Duve ✓

Preclinical product deals
- Bird Rock Bio ✓
- LEO ✓

abbvie

Preclinical PoC

Clinical PoC

| Discovery | Preclinical development | Early clinical development | Late clinical development |

* IAP: Innovative Access Program

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Proprietary pipeline in cancer and severe autoimmunity

	Drug candidate	Target	Indication	Pre-clinical	Phase 1	Phase 2
	ARGX-113	FcRn	Autoimmunity, Myasthenia Gravis	➡		
	ARGX-110	CD70	Cancer (Blood & Solid), [Autoimmunity]	➡		
	ARGX-111	c-MET	Solid tumors Blood cancer	➡		
	Discovery		Multiple cancer, Autoimmunity	➡		
abbvie	ARGX-115		Cancer Immunotherapy	➡		
BIRD ROCK BIO	ARGX-109 Gerilimzumab		Autoimmunity	➡		
LEO	Undisclosed		Skin inflamation	➡		
Shire	Undisclosed		Undisclosed	➡		
BAYER	Undisclosed		Undisclosed	➡		

Autoimmune diseases

Cancer immunotherapy

Cancer metastasis

Partnered, non-dilutive income

Upcoming news flow 2016

January	February	March	April	May	June

111 opening clinical centers in Asia

111 ASCO: Ph1 safety expansion update

113 JP Morgan: preliminary SAD HV data

Confirmation
→ Favorable safety profile
→ Signs of anti-tumor activity
in MET-amplified patients

LEO Pharma milestone payment

115 AbbVie collaboration

July	August	September	October	November	December

110 First combo trial

110 NPC results

110 ASH: TCL results

110 TCL results

113 MAD HV preliminary data

113 SAD & MAD HV top line data

113 Start Ph2 Dec 2016

R&D day, New York (22 Sept)

Creating innovative antibodies

Unique technology platform: multiple modes of action

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SIMPLE Antibody™

Broad range of leads of therapeutic quality
Novel & complex targets

V-region
Bind to target

Fc-region
Modulate response

POTELLIGENT®
Boost cell killing

NHance®
Extend half-life
Enhance tissue penetration

ABDEG™
Clear disease target &
auto-antibodies

Leapfrogging transgenics:

- V-regions llama & human antibodies virtually identical
- Unprecedent epitope coverage

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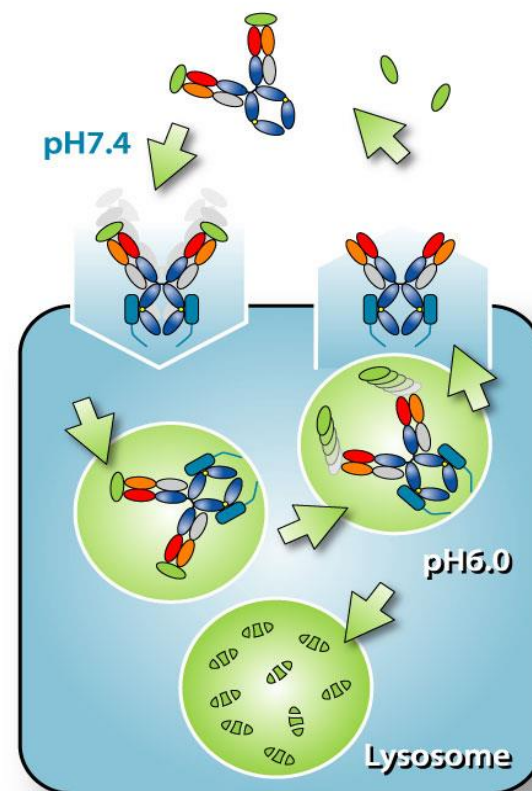
- Clinical potential for indications:
  - with high circulating target concentrations
  - which require fast target clearance
  - e.g. inflammatory cytokines (receptors)

ARGX-113
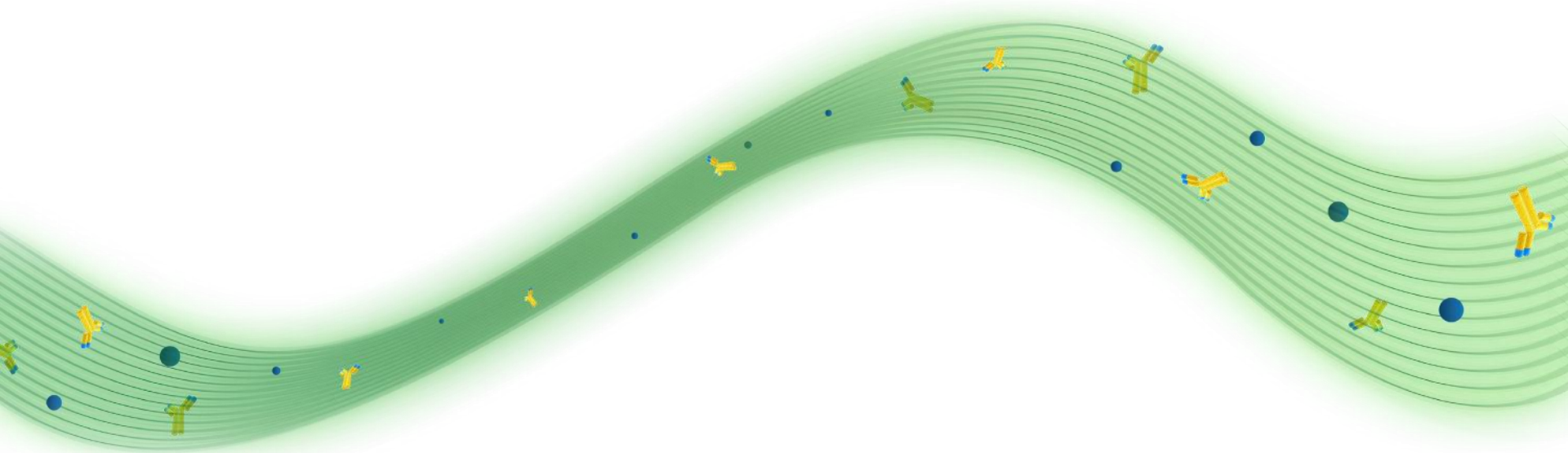
What is autoimmune disease?

- 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
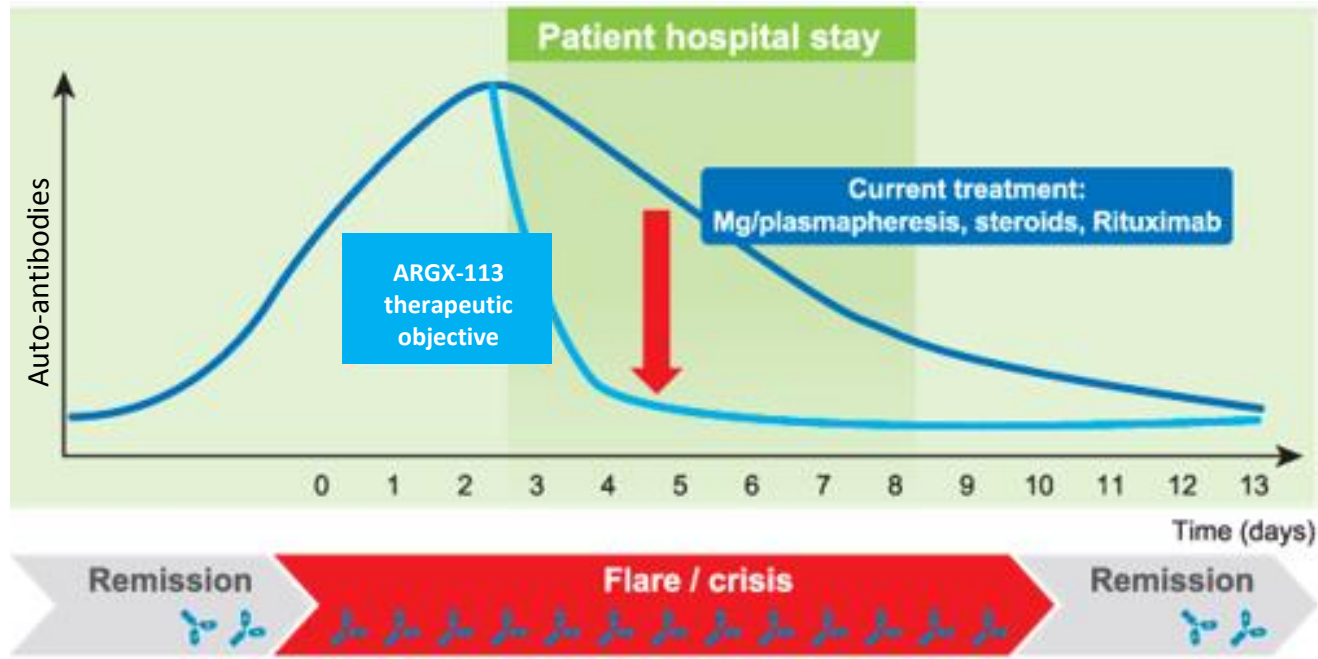
Mode of action

- Targeting auto-immune diseases driven by pathogen autoantibodies (IgG's)

- Fast & deep reduction of pathogenic IgG's

- Prevention & control of disease flares/exacerbation

ARGX-113: How it works - Antibody clearance capability

Proprietary Fc mutations

Block IgG recycling

Resulting in rapid autoantibody clearance

ABDEG™

MST

HN

pH7.4

pH6.0

Lysosome

Antibody Recycling

ARGX-113 Blocking of Recycling

pH6.0

pH7.4
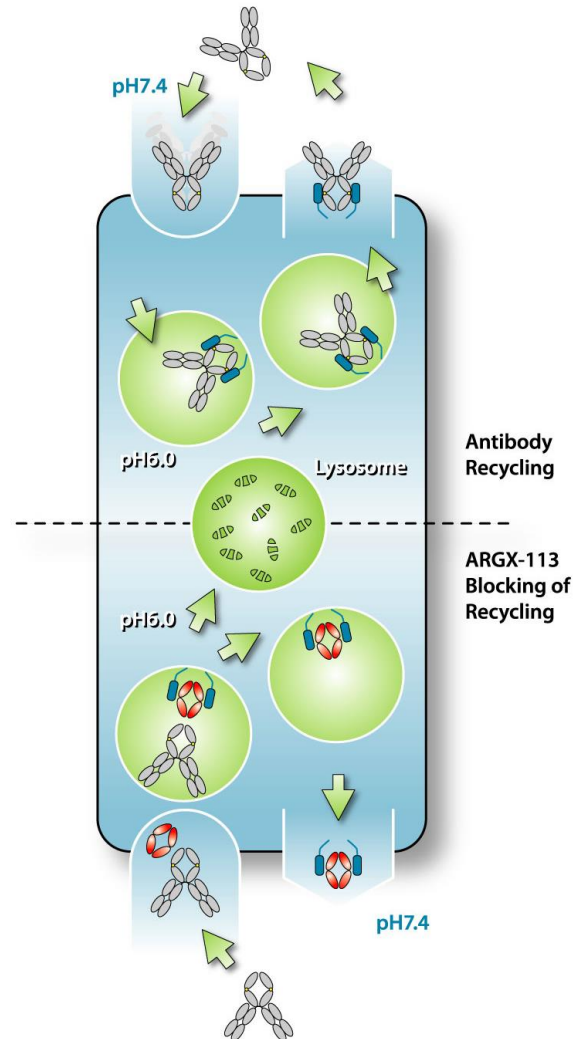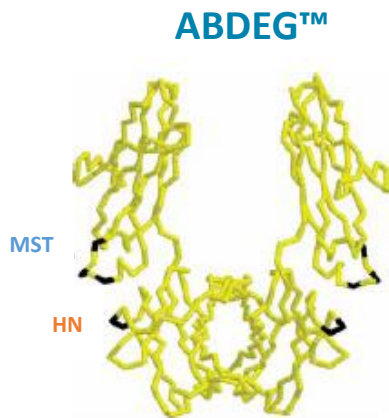
Repeat dose ARGX-113
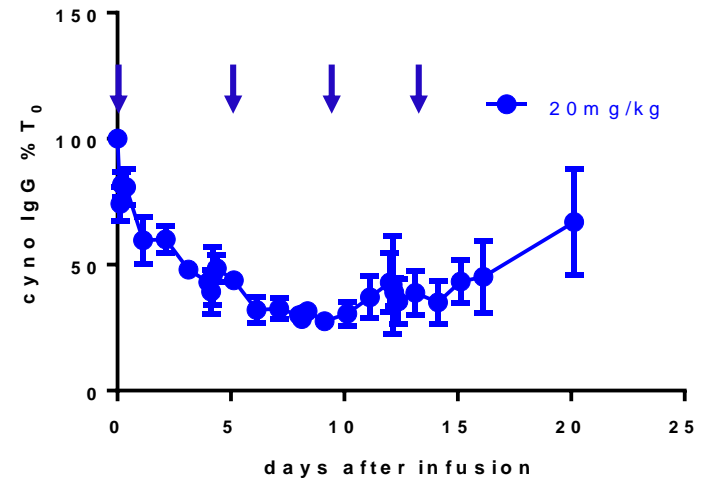
20 mg/kg

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

Vaccaro et al., 2005, Nature Biotechnology

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Clinical rationale for targeting autoantibody clearance

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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
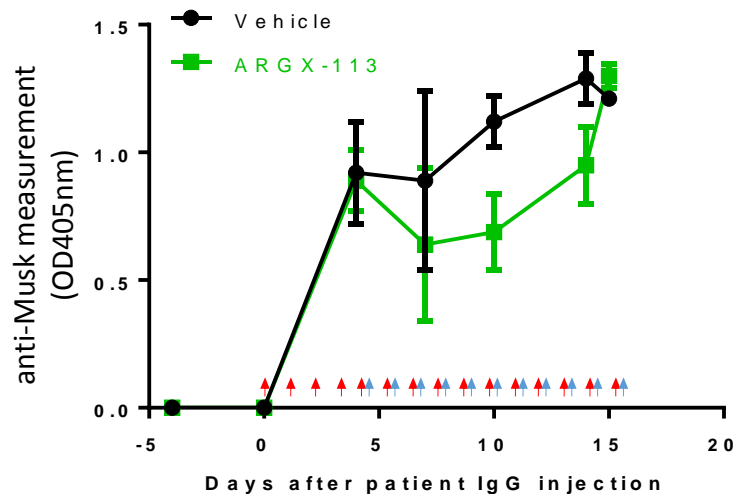
Inverted Mesh
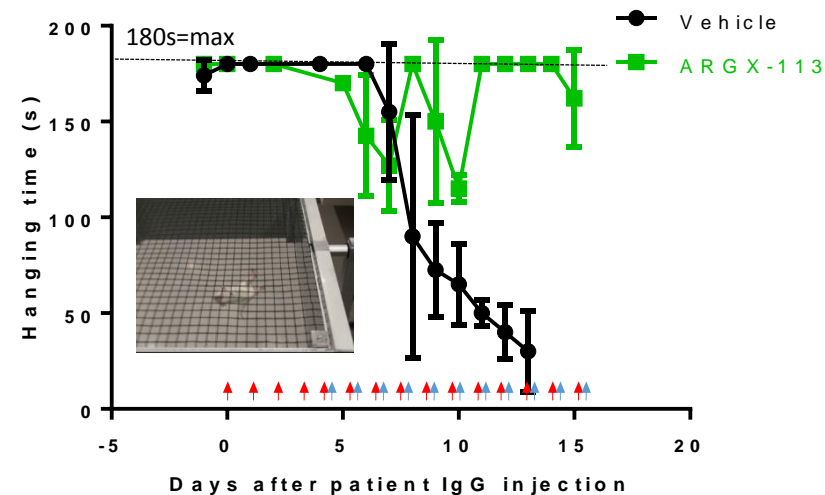
↑ **Patient IgG injection (37 mg)**
↑ **ARGX-113 treatment (1 mg)**

- 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

Single ascending dose (SAD)	Multiple ascending dose (MAD)	Data analysis

(mg/kg)

50

End SAD in-life phase

25

25

10

10

End MAD in-life phase

2

- **Complete safety profile**
- **Complete PK/PD profile**
- **Ph2 dose selected**

0.2

4:2 → active:placebo

6:2 → active:placebo
Up to 6 doses

4 months **4 months** **2 months**
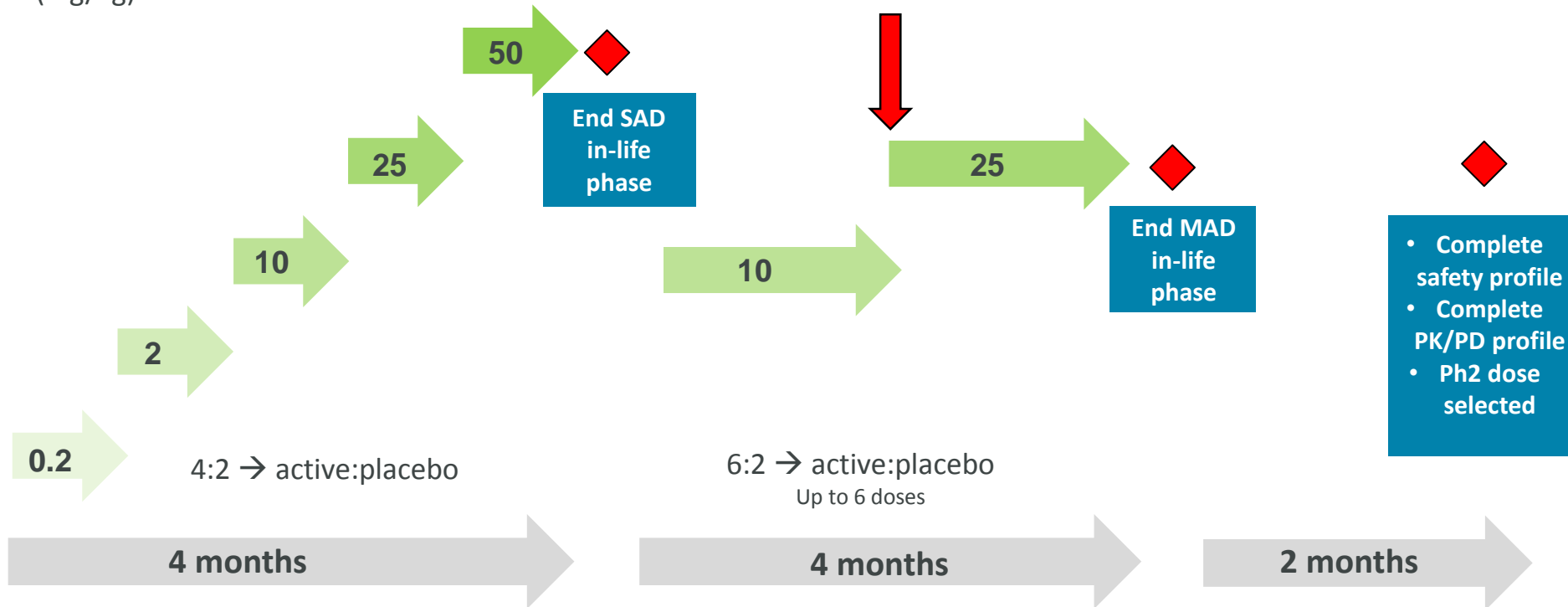
- SAD completed according to plan (38 healthy volunteers in total)
- Favourable safety and tolerability profile observed (no serious adverse events reported)

ARGX-113: PD marker readout for SAD
Double-blinded, placebo-controlled study in healthy volunteers

Rapid, deep and specific IgG reduction
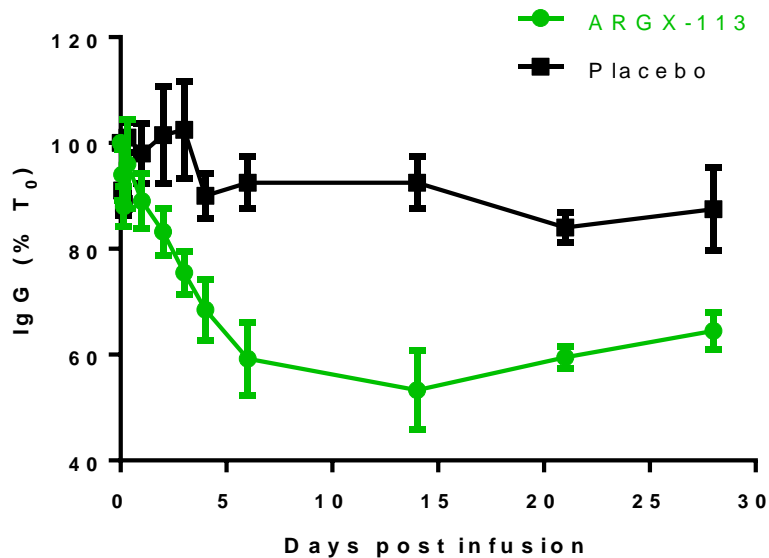
	ARGX-113 vs. IVIg[*]
Speed of IgG reduction	>>>
Level of IgG reduction	>>
Duration of PD effect	>

* 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

Rapid speed of onset

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

More convenient administration

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

Superior efficacy

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

Better tolerated, shorter procedure with limited follow-up
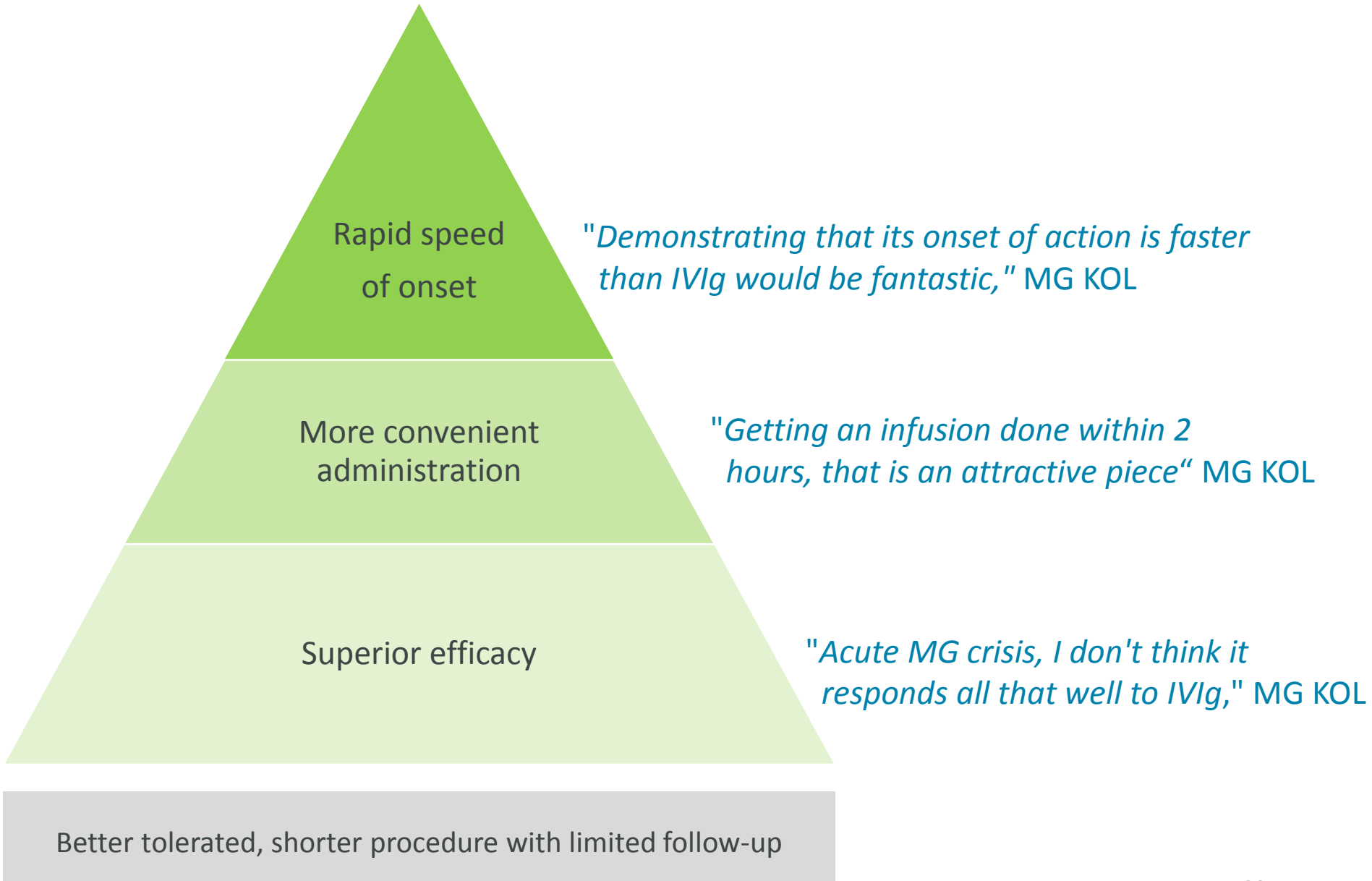
ARGX-113 vs. IVIg/PLEX: Key differentiators for ABD

Rapid speed of onset

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

More convenient administration

"PLEX is a nightmare to apply," ABD KOL

Superior efficacy

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

Better tolerated, shorter procedure with limited follow-up

ARGX-113: What next?

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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
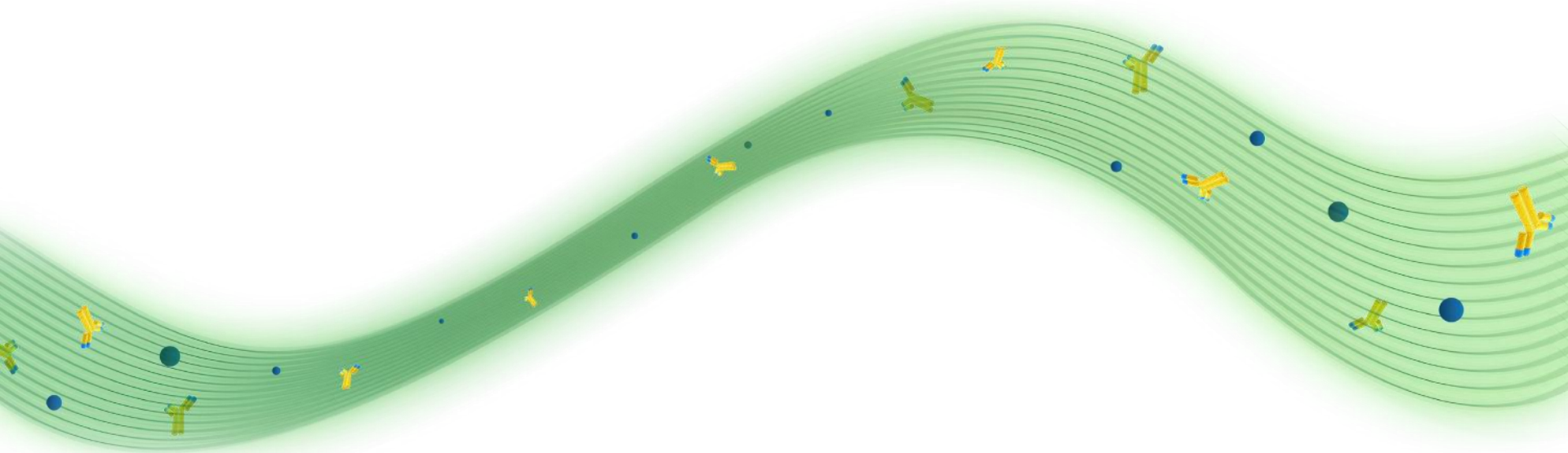
ARGX-110: 3 distinct modes of action

1. Block tumor growth signal

2. Kill tumor

3. Restore immune surveillance
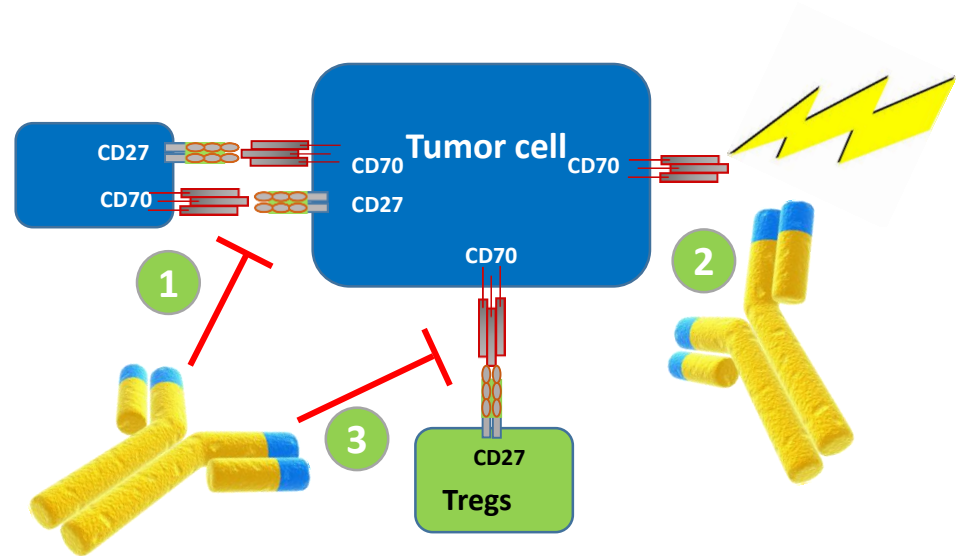
Silence et al., 2014, mAbs

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
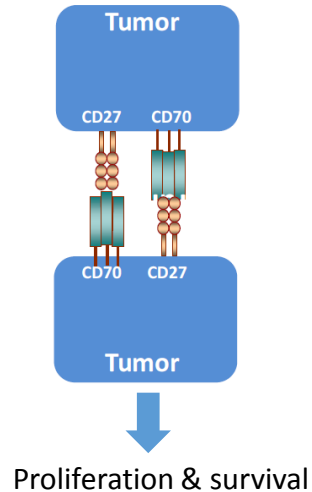
IHC of CD70 expression in TCL biopsies
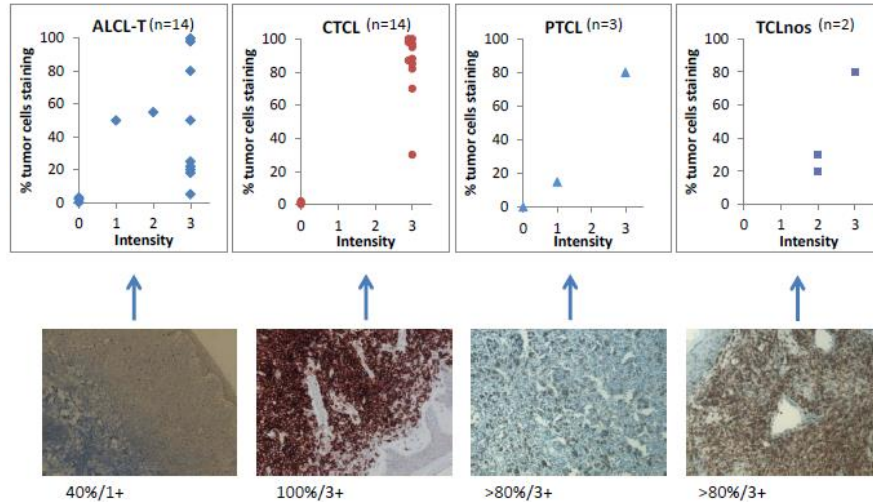
sCD27 levels in TCL patient sera

Proliferation & survival

40%/1+

100%/3+

>80%/3+

>80%/3+

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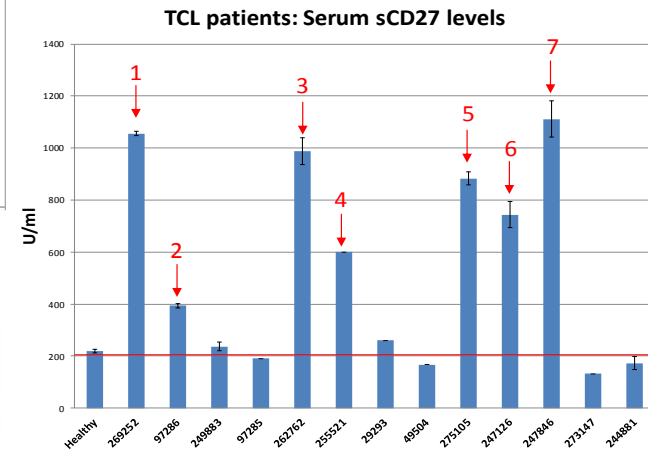
- CD70 strongly overexpressed across different TCL types
- Elevated sCD27 levels suggest strong pathway activity in TCL

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

Blood compartment cleared from malignant cells (■)
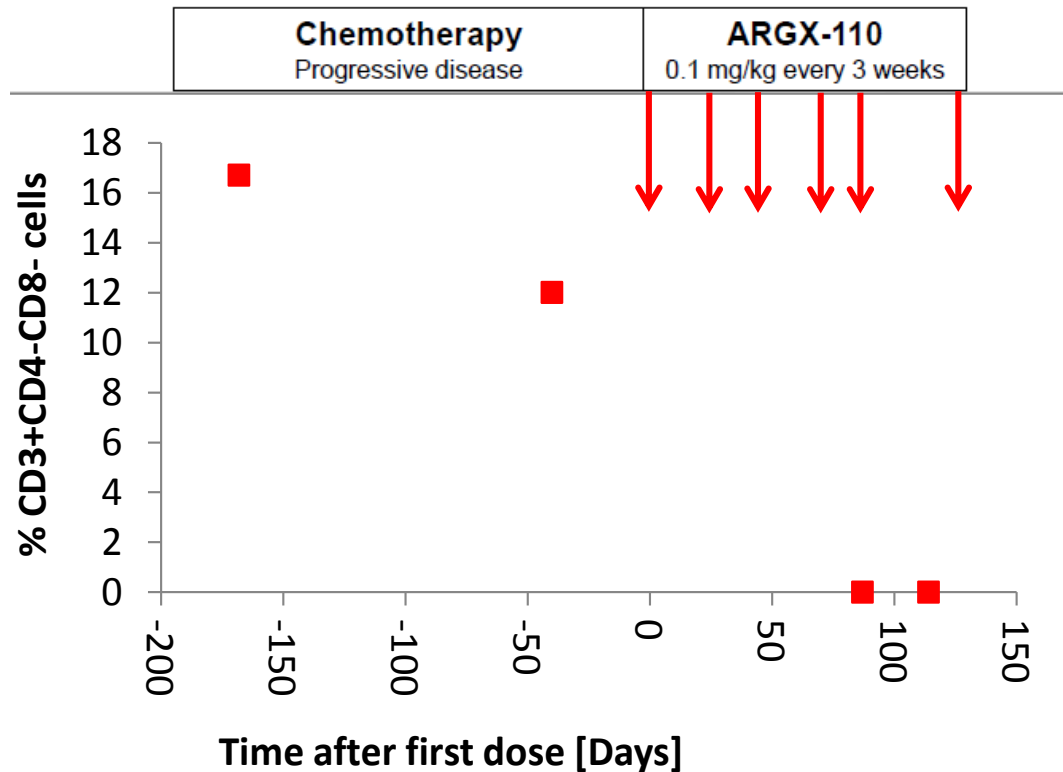
Stabilized skin lesions

| | Chemotherapy Progressive disease | ARGX-110 0.1 mg/kg every 3 weeks |

% CD3+CD4-CD8- cells (y-axis: 0 to 18)
Time after first dose [Days] (x-axis: -200 to 150)

a. Pre treatment

b. Post cycle 2

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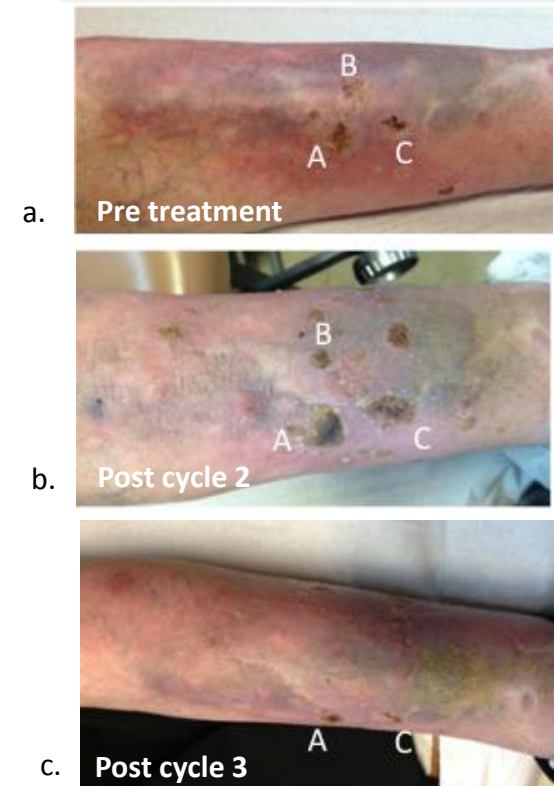
- 78 year old woman with CTCL-SS; refractory to multiple lines of chemotherapy
- ARGX-110 treatment (0.1 mg/kg every 3 weeks)
  - Complete response in blood compartment
  - Stabilized disease in skin lesions (see image a. & c.) & lymph nodes
- Elimination of CD70 positive Sézary cells from blood in 2nd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

- Patient anecdotes -

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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 19 cycles on study (15 months)

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

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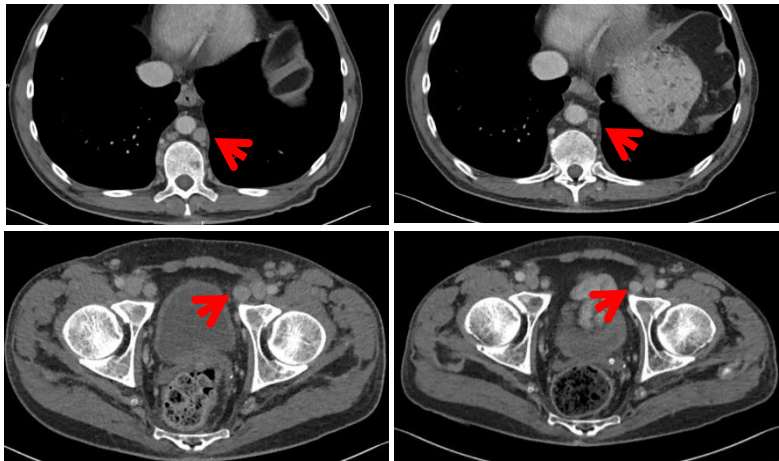
Ref. Lesions	Shrinkage
L1	24%
L2	4%
L3	4%
L4	39%
Non-Ref. Lesions	
L5	65%
L6	50%
L7	59%
L8	43%

Transfusion independent

LDH — IU/ml vs Days after first dose ARGX-110 (ARGX-110 doses marked)
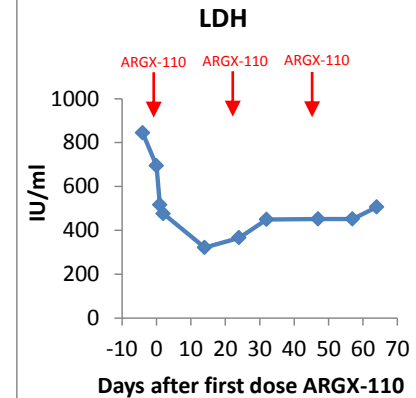
- 61 year-old male AITL patient with severe Hemolytic Anemia
- Refractory to chemotherapy: CHOP + Etoposide/Cyclosporine /Bendamustine - Transplant

- 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 -

Hb — g/dl vs Days after first dose ARGX-110 (ARGX-110 doses marked)
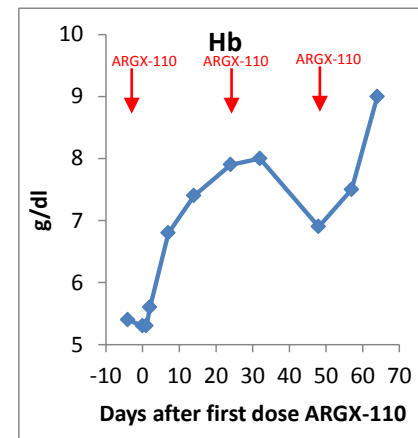
ARGX-110/BCR-ABL1 inhibitor eliminates leukemic stem cells in CML model

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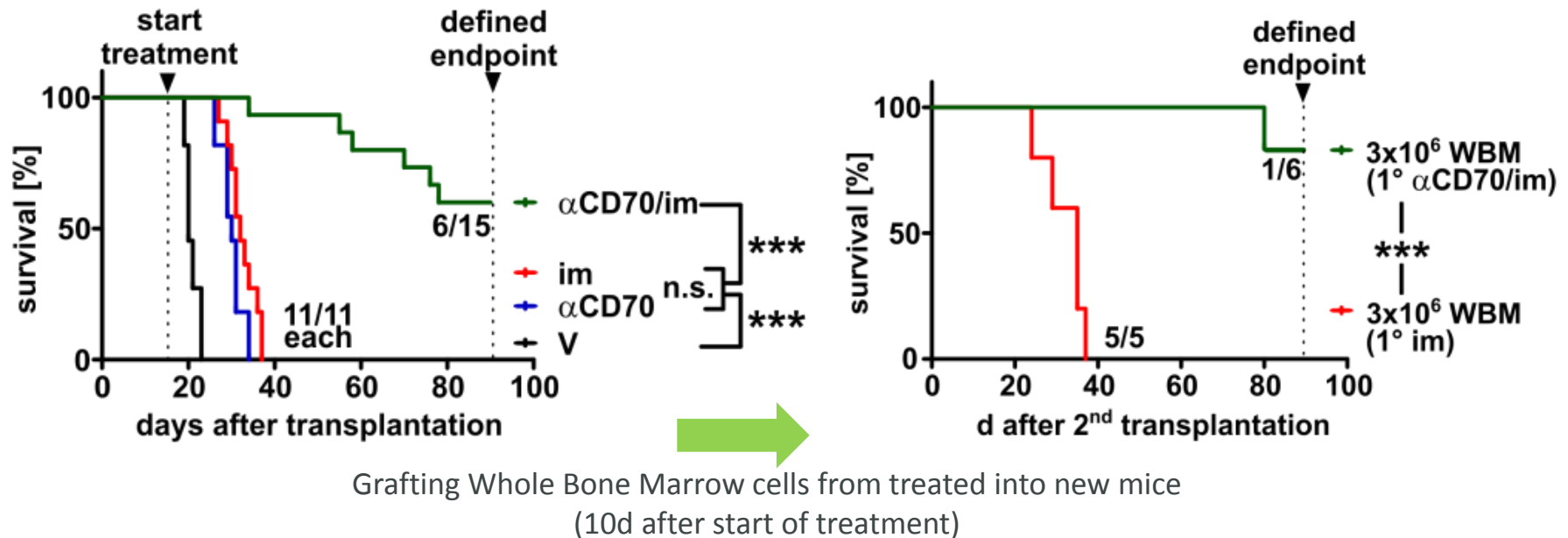
- Leukemic stem cells (LSCs) resistant to BCR-ABL1 inhibitors via CD70 overexpression
- Combo treatment with CD70 blocking mAb eliminates LSCs by synergistic blockade of Wnt signalling pathway

Im: imatinib; V: vehicle; WBM: whole bone marrow

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

ARGX-110: What next?

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Ongoing clinical studies

- **Hematological tumors**
  - T-Cell Lymphoma (TCL): Phase 1b → 6 sites (BE, FR, IT)
  - Recruiting up to 10 CTCL (min 5 Sz) - 10 PTCL (min 5 AITL) patients
  - 10 patients enrolled; on track to complete enrollment by end July

Site	Investigator	Status	Patients (pre)screening	On treatment/ treated
UZ Ghent (BE)	Dr. Offner	Open	2X	1X
Jules Bordet Institute (BE)	Dr. Maerevoet	Open	2X	1X
Gustav Roussy (FR)	Dr. Ribrag	Open	11X	4X
St. Louis (FR)	Dr. Bagot	Open	8X	3X
Lille (FR)	Dr. Morschhauser	Open	3X	1X
Bologna (IT)	Dr. Zinzani	Open	1X	

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

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ARGX-111

ARGX-111: Addressing the end game of cancer
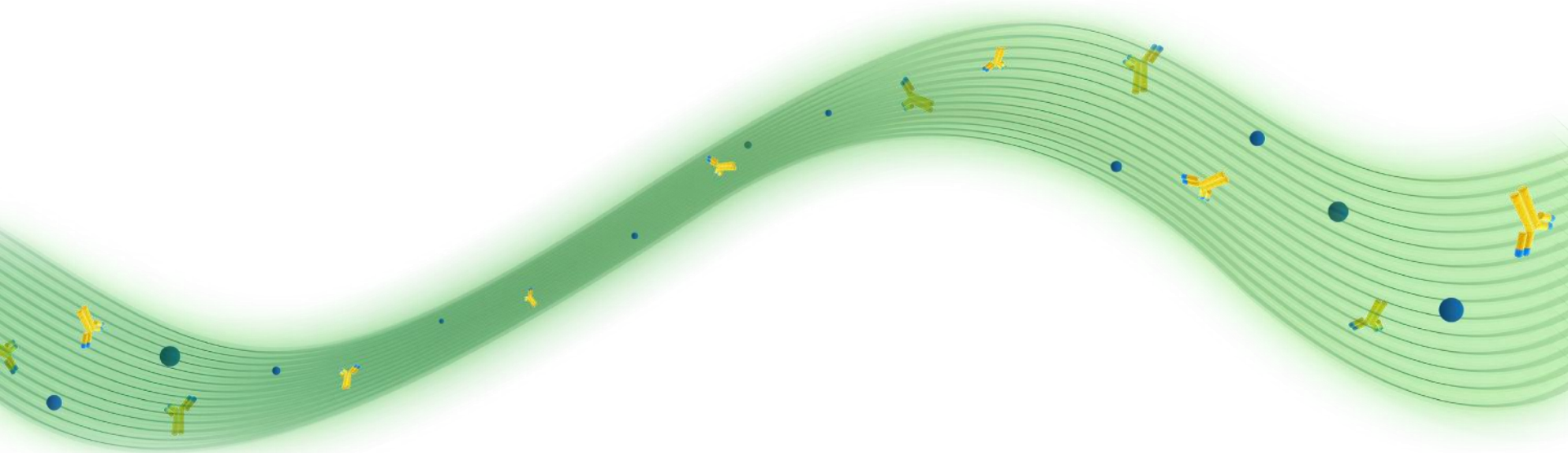
Targeting MET, receptor responsible for tumor growth and metastasis
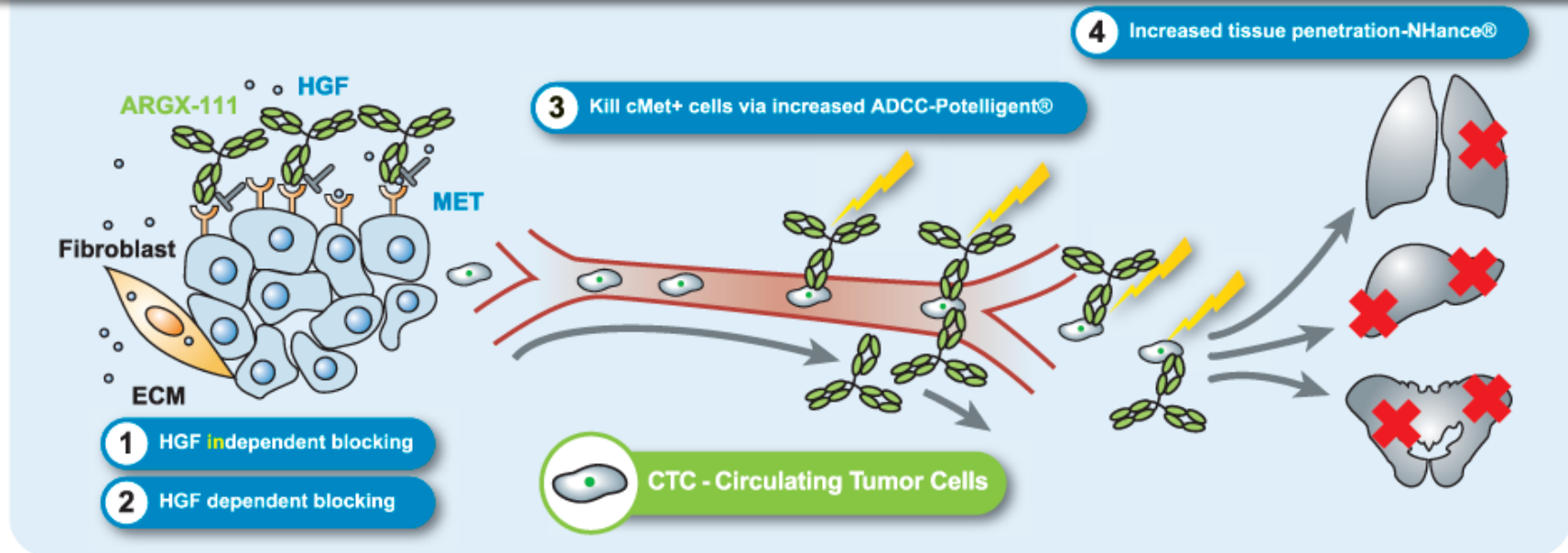
Hultberg et al., 2014, Cancer Research – Gherardi et al., 2013, Nature Reviews Cancer

- 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

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1Q 2014   **1H 2015**   **2H 2016**

| Dose escalation | Adaptive safety expansion | Details |

Phase 1   **Phase 1b**

(mg/kg)

10

3

1

0.3

MET-amplified cancers

Ph1 safety expansion update (ASCO)
NCT02055066

- Favorable safety profile
- Biological activity (SD, PR)
  - Gastric* (2), Renal* (2), Cholangio, Lung*
- Preclinical PoC:
  - ARGX-111 impacts MDSC's in tumor environment

* MET-amplified

- **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

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
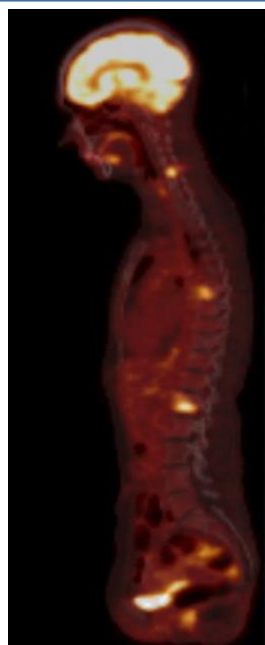
Biological activity

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®
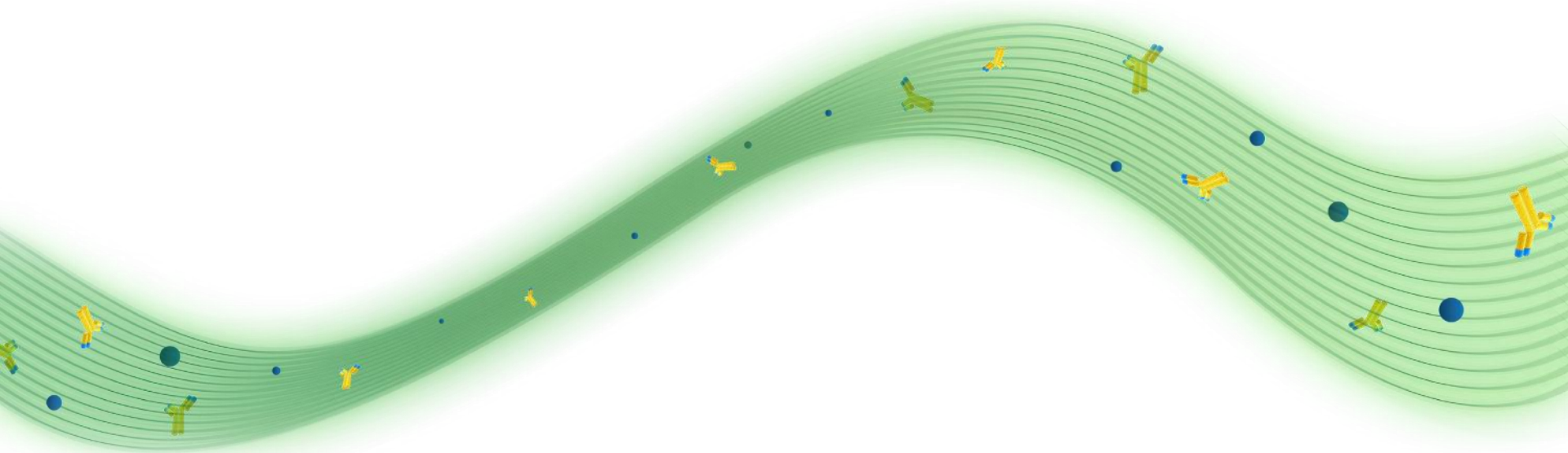
GARP: a novel immune checkpoint
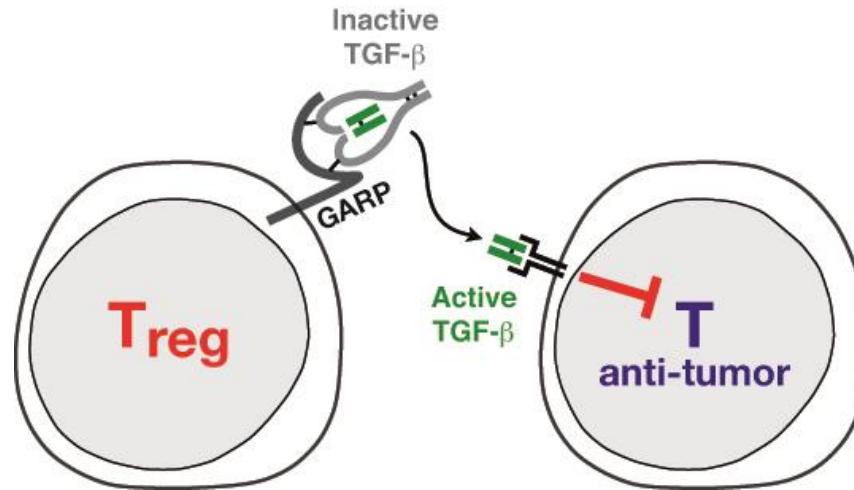
- GARP upregulated specifically on surface of Tregs only

- 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

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

AbbVie Option Deal for ARGX-115: Key Elements

- **Financial terms**
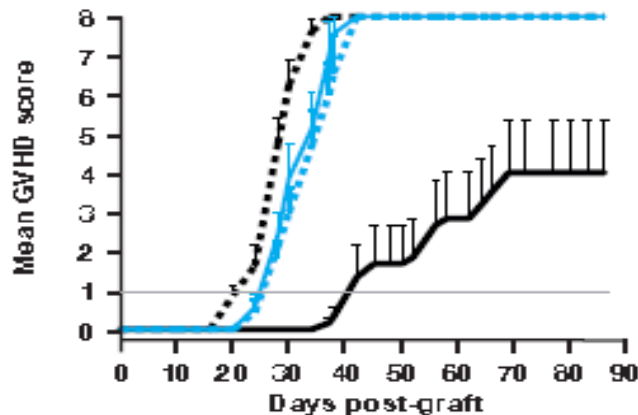
  - $40MM upfront

  - Preclinical milestones 2x $10MM

  - Up to $625MM development, regulatory and commercial milestones

  - Tiered, up to double-digit royalty payments on net sales

- **Deal Structure**

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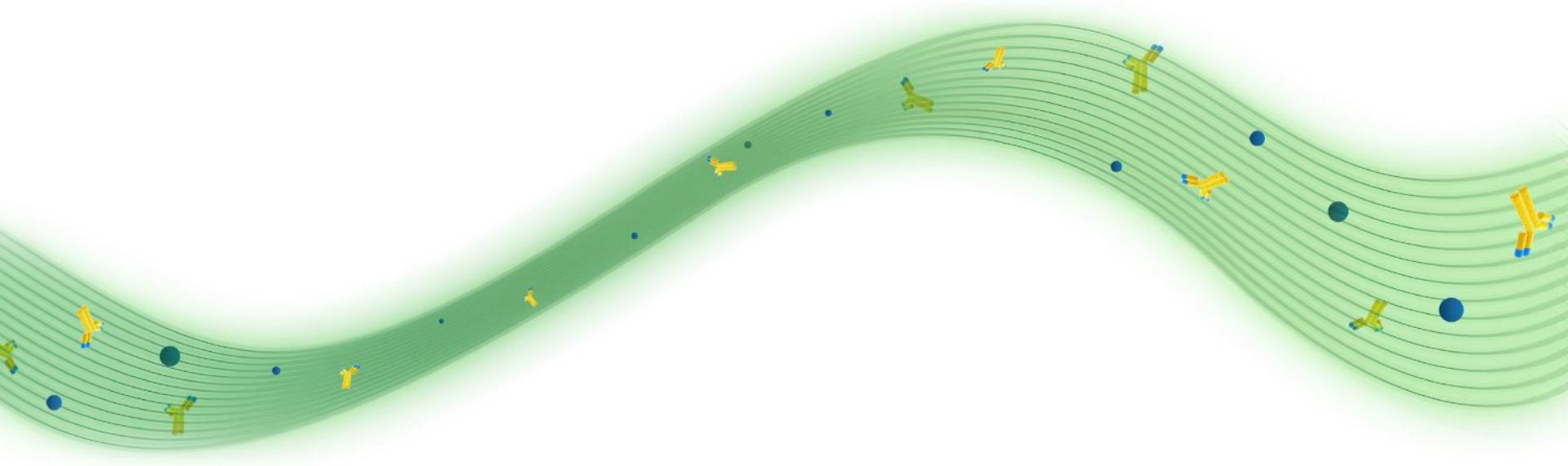
  - Responsible for delivering IND data package
  - May combine ARGX-115 with its own pipeline mAbs
  - Co-promotion right to GARP-targeted products (EU/Swiss Economic Area)

  abbvie

  - Option to exclusive development and commercialization license
  - Will fund further GARP-related research for initial period of 2years, subject to argenx reaching pre-determined preclinical stage milestone
  - Right to license additional therapeutic programs resulting from this research in return for additional milestone and royalty payments

Partnerships

Building partnerships for the long term

- **Alliances with premier pharma partners** abbvie   LEO   Shire   BAYER

  - Exclusive product partnership

  - Non-exclusive discovery collaborations leveraging entire technology suite

  - Upfront payments, R&D funding, development milestones, royalties, product reversion rights

- **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,…
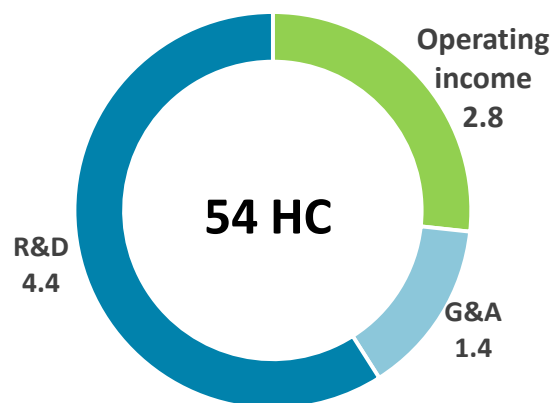
- € 31Mio in cumulative revenue (1Q16) (AbbVie € 35Mio April 2016)
- >€ 2B* potential cumulative revenues from existing partnerships

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

Financials
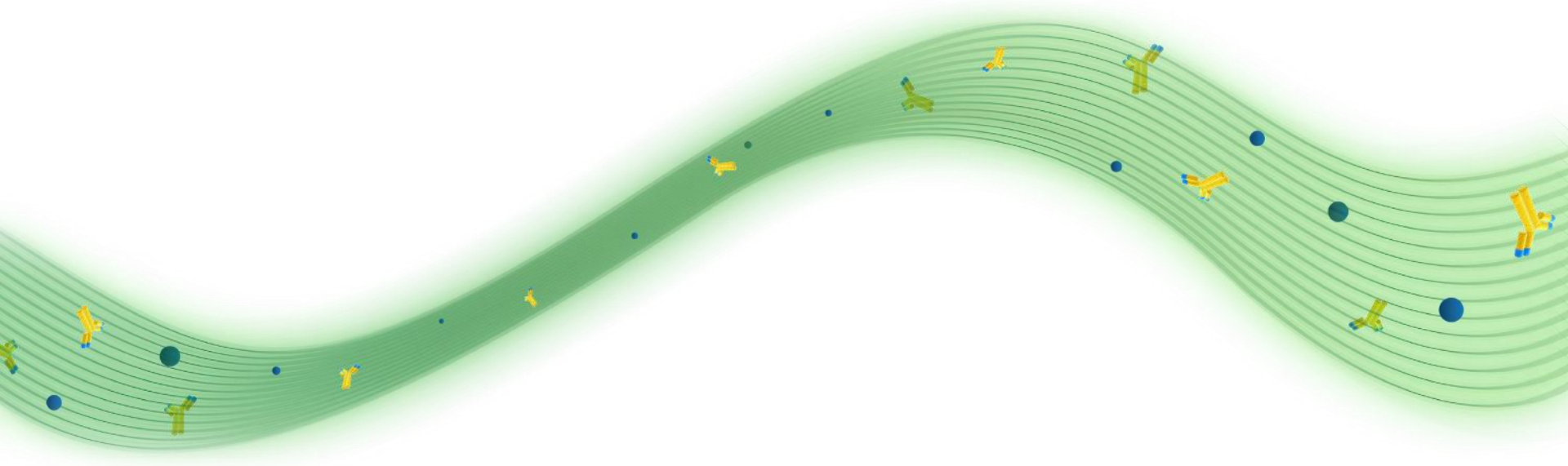
Well capitalized to execute strategic plan

argenx

Operating income & expenses
1Q16 (MEUR)

54 HC

Operating income 2.8
G&A 1.4
R&D 4.4

Operating income, expenses & capital raised since inception (*)
1Q16 (MEUR)

(*) not including deferred revenue and accruals

Operating income	31.1
R&D expenses	66.9
G&A expenses	18.2
Capital raised	103.8
Cash and cash-equivalants	53.8
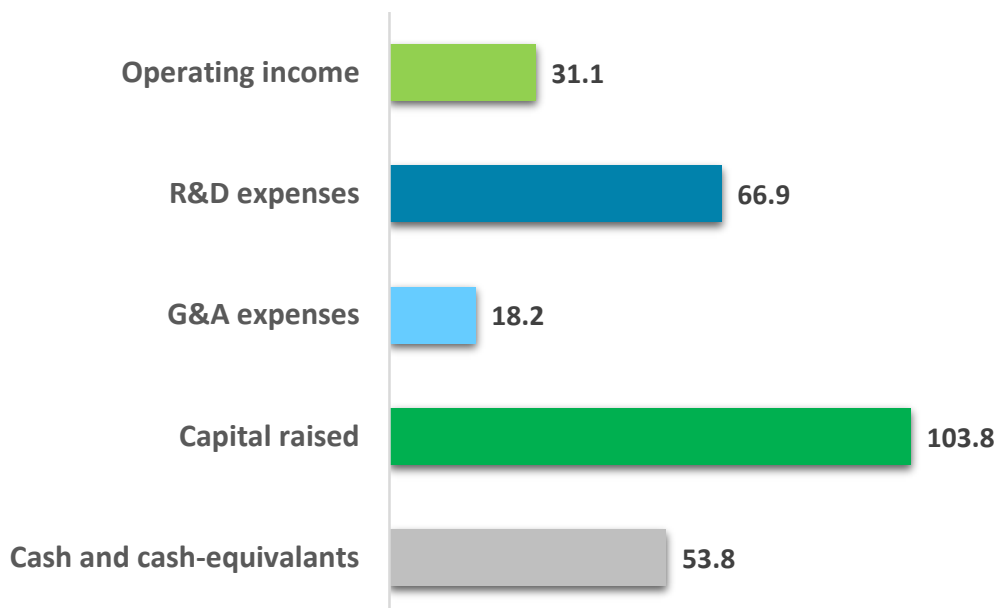
Capital raised & cash
June 16 (MEUR)

Private placement
+ 30

AbbVie
+ 35.1   + 30
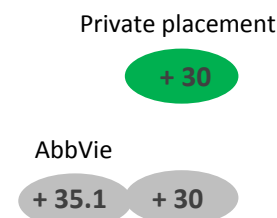
Shareholder structure (fully diluted)
June 16

9%

40%
Forbion, LSP, Orbimed...

51%
Aquilo, Federated investors, JP Morgan, MPM, Perceptive, RTW, Van Herk...

- Historical VC
- Free float
- Stock options

Upcoming news flow 2016

January	February	March	April	May	June

111 opening clinical centers in Asia

111 ASCO: Ph1 safety expansion update

113 JP Morgan: preliminary SAD HV data

Confirmation
→ Favorable safety profile
→ Signs of anti-tumor activity
in MET-amplified patients

115 AbbVie collaboration

LEO Pharma milestone payment

July	August	September	October	November	December

110 First combo trial

110 NPC results

110 ASH: TCL results

110 TCL results

113 MAD HV preliminary data

113 SAD & MAD HV top line data

113 Start Ph2 Dec 2016

R&D day, New York (22 Sept)