Creating superior, differentiated antibodies

BIOTECH SHOWCASE
January 12-14, 2015

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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

Boehringer Ingelheim

BAYER

LEUKEMIA & LYMPHOMA SOCIETY

Shire

Strategic alliances with premier partners

- Strategic partnerships fuelled by consistent success
- Cash funding, milestone & royalty payments and product rights
- Strong cash position (~€60m Sept 2014)

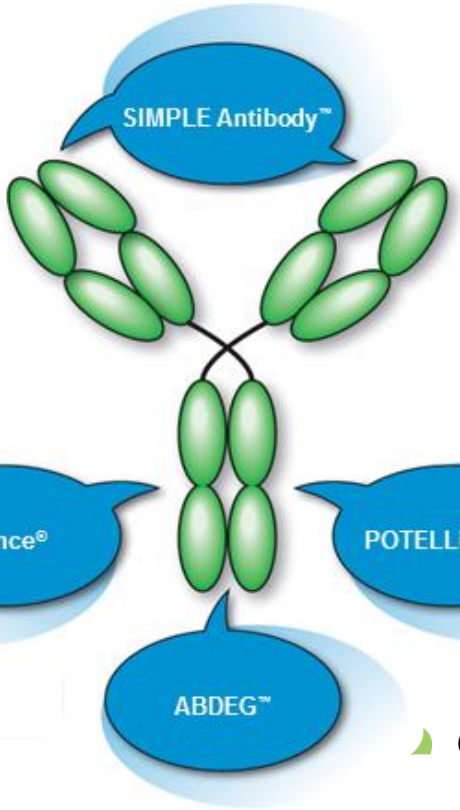
Powerful technology suite

- 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 2028-2033

Suite of complementary antibody technology platforms

Therapeutic antibodies with multiple modes of action against complex targets

Powerful Technology Suite



- Unique llama immune system
- Broad range of leads of therapeutic quality

- Extend half-life

- Boost cell killing

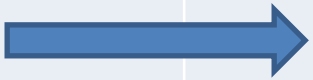
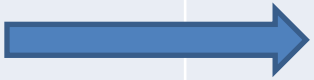
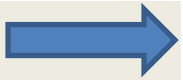
- Clear autoantibody/disease target

- **Highly productive, generating multiple leads**
- **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)**

Recognized promise of arGEN-X technology

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

Rich pipeline approaching major value inflection points

Drug Candidate	Indication	Pre-clinical	Phase 1	Phase 1/2	Ownership	Proposition
ARGX-110	Heme malignancies *TCL; Waldenström's*				Wholly owned	LEUKEMIA & LYMPHOMA SOCIETY® Immune checkpoint inhibition (CD70) Enhanced cell kill
ARGX-110	Solid tumors					
ARGX-110	Autoimmunity					
ARGX-111	Solid tumors Heme malignancies					Complete c-Met blocking Enhanced cell kill
ARGX-113	Autoimmunity *Myasthenia gravis*					Potent FcRn blocking Clears auto-antibodies
ARGX-112	Atopic dermatitis					Potent IL22R blocking
Discovery	Autoimmunity Cancer	*multiple*				Novel, complex targets e.g. GARP
ARGX-109	Autoimmunity Cancer				Partnered	Potent IL-6 blocking Partnered with RuiYi
Shire	Undisclosed					Novel, complex targets
BAYER	Undisclosed					Novel, complex targets
Boehringer Ingelheim	Undisclosed					Novel, complex targets

ARGX-110: pioneers 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 POTELLIGENT®
- Optionality in niche *and* major indications
- 3 development programs: TCL; BCL (WM); CML (*cf*. ASH '14)
- Upside potential in other CD70+ tumors and autoimmunity

- Activity in 3/4 TCL patients in Ph 1
- PFS benefit in RCC, ovarian cancer, mesothelioma,...
- Outstanding safety profile

Clinical activity & safety demonstrated

Partnership with LEUKEMIA & LYMPHOMA SOCIETY

- Funding: 50% of Ph 1/2 study in WM
- Clinical expertise: Dana Farber (Treon), Sloan Kettering (Palombo), Mayo Clinic (Ansell)
- Connection to IWMF

TCL: T-cell lymphoma; BCL: B-cell lymphoma; WM: Waldenström's macroglobulinemia; CML: chronic myeloid leukemia

ARGX-110: development plan

Following biology & signs of clinical activity

Indication	Disease Stage	Therapy	Preclinical	Phase 1	Phase 1/2
B-cell Lymphoma Waldenström's macroglobulinemia	Relapsed, Refractory	Mono	→	→	→ LEUKEMIA & LYMPHOMA SOCIETY®
T-cell Lymphoma CTCL; PTCL	Relapsed, Refractory	Mono	→	→	
CD70⁺ Blood Cancers	Relapsed, Refractory	Mono	→	→	
CD70⁺ Solid Tumors	Relapsed, Refractory	Mono	→	→	
CML	Various	Combo with TKIs	→		

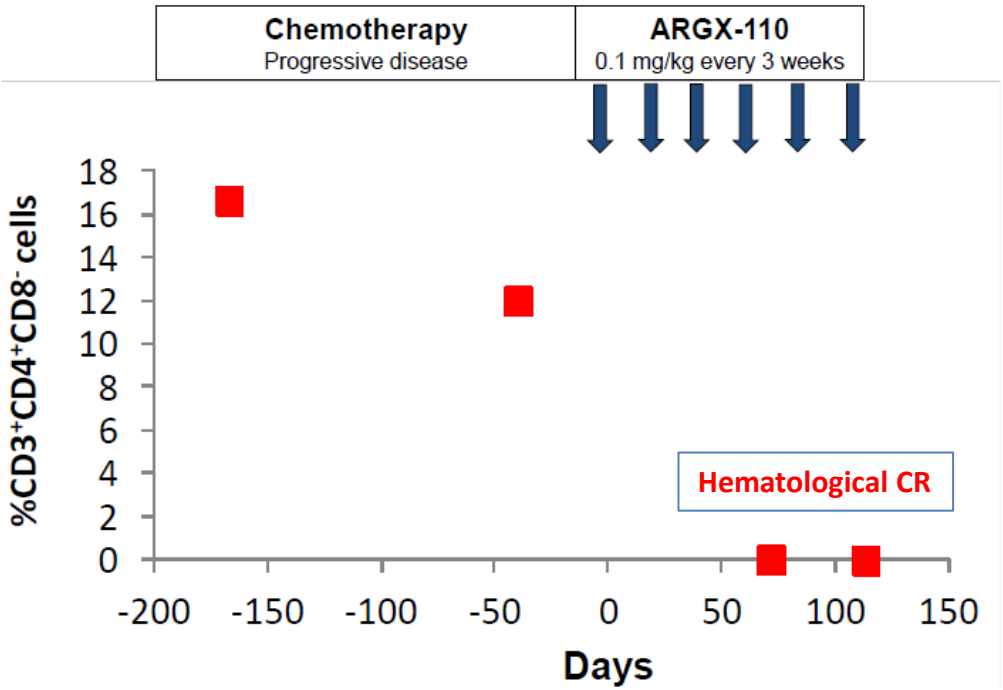
Key Findings To Date

- **~ 50% of all comers are CD70⁺**
- **No dose-limiting toxicity or autoimmune related AEs: supports combination therapy**
- **Biological activity observed in TCL; PFS benefit in RCC, ovarian cancer, mesothelioma**
- **Strong preclinical rationale for WM, CML**

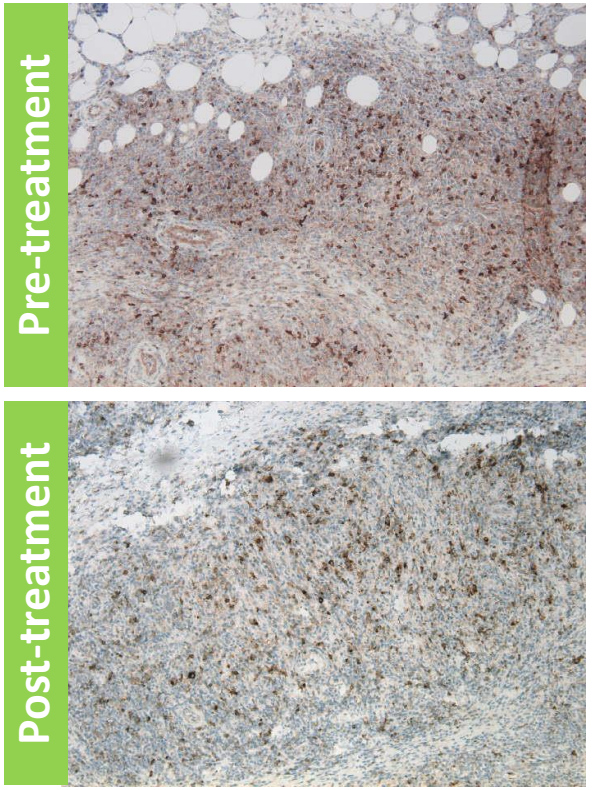
ARGX-110: proof of biological activity

Complete hematological response; stable skin & nodal lesions in patient with Sézary –Syndrome (SS)

Blood compartment cleared from malignant cells ( )



Skin lesions flare – then stabilize

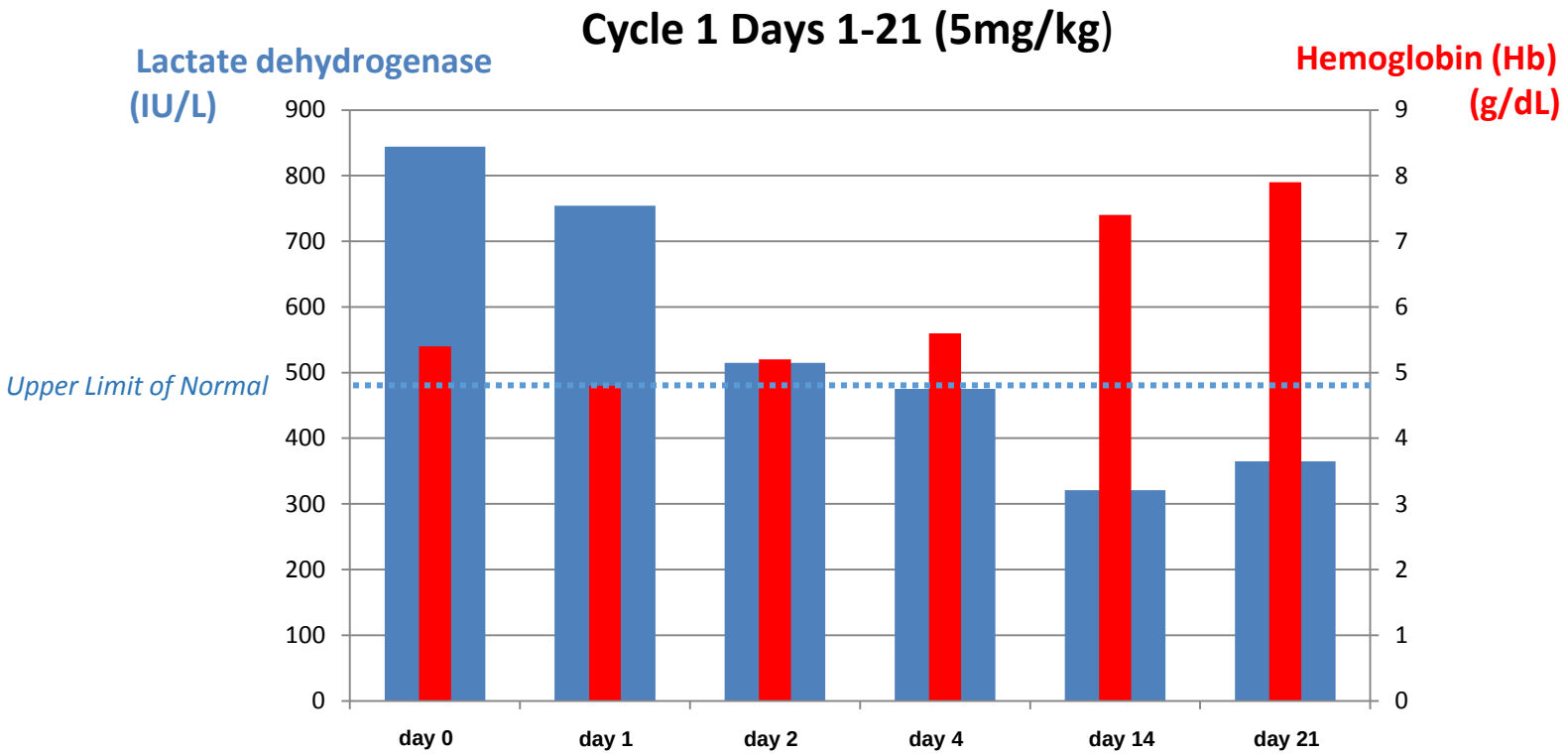


CD70 IHC staining unchanged in skin biopsies pre- and post-treatment

- **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

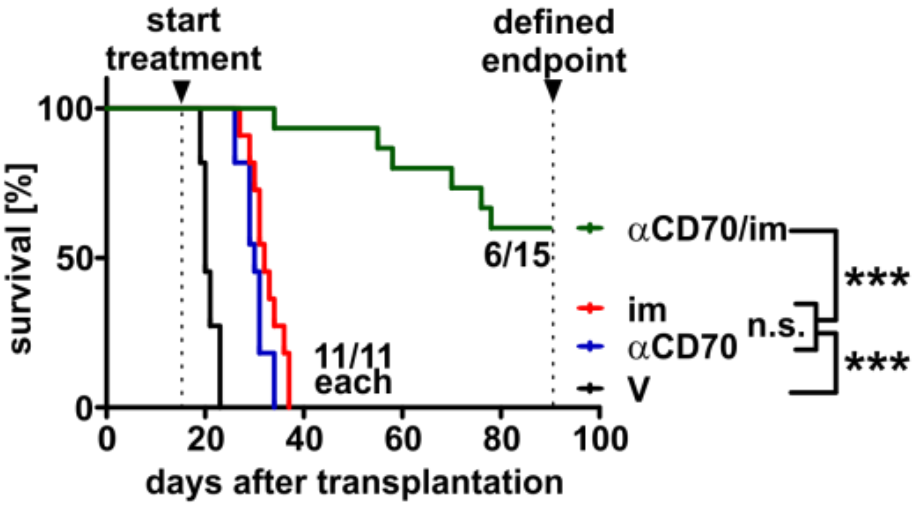
Angioimmunoblastic T-Cell lymphoma (AITL) with autoimmune hemolytic anemia

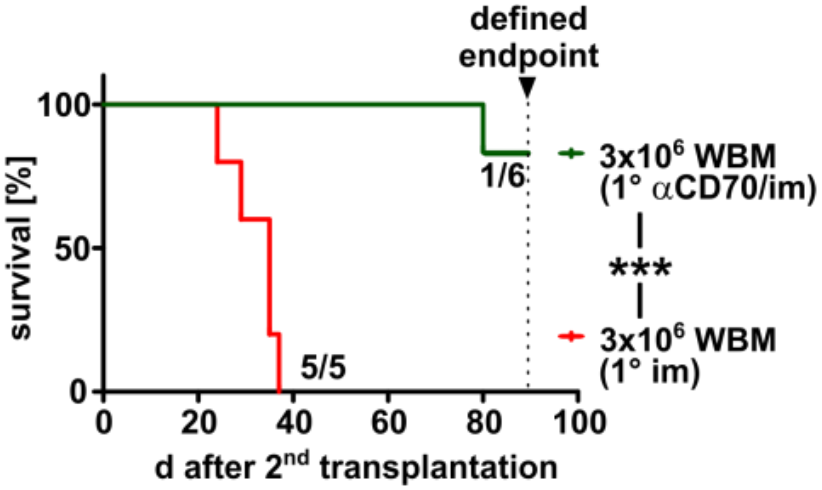


- **61 year-old male AITL patient showing elevated LDH and reduced Hb levels**
- **Refractory to chemotherapy (CHOP + Etoposide /Cyclosporine /Bendamustine - Transplant)**
- **After 2 doses of ARGX-110**
  - **Hb increase to 7.9 without transfusion support**
  - **LDH normalized to 365**
  - **10% reduction in tumor size by CT scan**

ARGX-110/BCR-ABL1 inhibitor synergistic in CML model

Curative potential by potent elimination of leukemic stem cells (LSCs)





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

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

- **LSCs become resistant to BCR-ABL1 inhibitors via CD70 overexpression**
- **Combo treatment with CD70 blocking mAb eliminates LSCs by synergistic blockade of Wnt signalling pathway**

ARGX-111: superior intervention in c-Met biology

Best-in-class antibody targeting c-Met positive tumors and circulating tumor cells

Best-in-class therapeutic antibody

- Targets c-Met driven metastatis using SIMPLE Antibody™;POTELLIGENT®, NHance®
- 3 modes of action
- Potential in major c-Met+ cancer indications
- Superior performance to MetMab in preclinical models
- Highly effective in eliminating circulating tumor cells and blocking metastatic spread in preclinical models
- Targeting specifically Met amplified patients

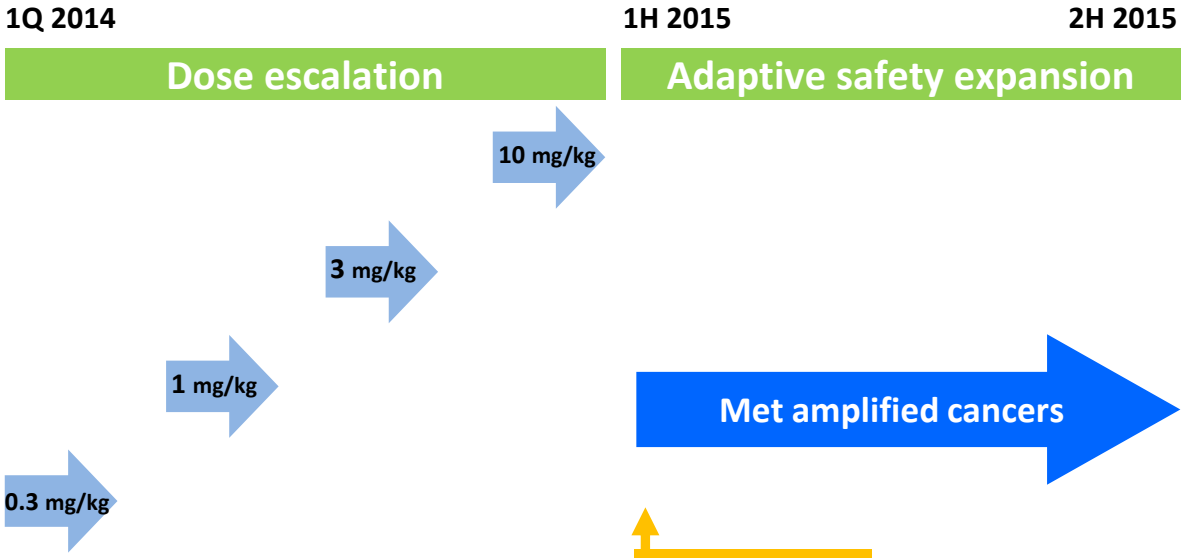
Unmet medical need

- Metastatic spread represents major unmet medical need
- Metastatic gastric cancer enables focused clinical development plan

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

ARGX-111: phase 1 trial overview



Details

- **Advanced cancer population (total of 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**

- **~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: highly effective in preclinical models

Blocks tumor spread and eliminates CTCs in metastatic breast cancer model

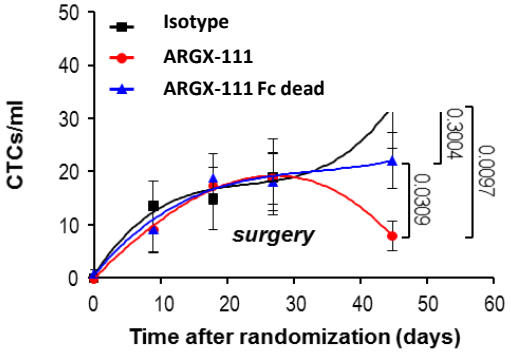
neoadjuvant animal model

Treatment
(4 weeks, twice weekly, 5mg/kg)

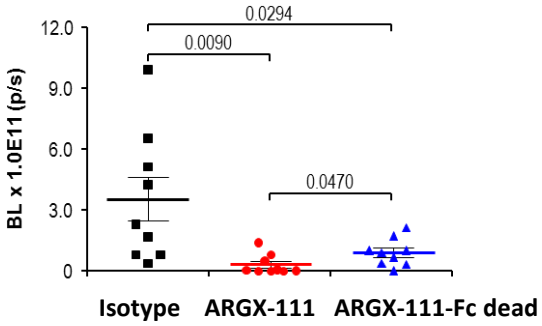
Surgery

Autopsy

CTC counts



Lung metastases



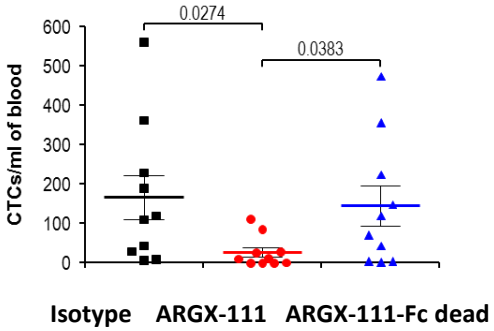
adjuvant animal model

Surgery

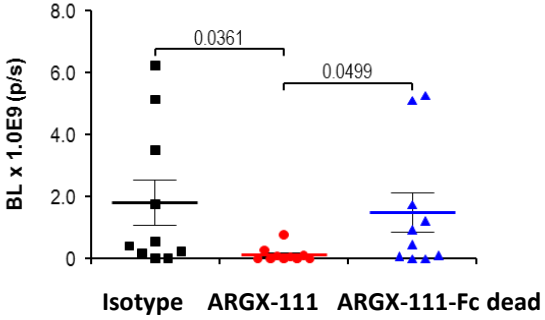
Treatment
(4 weeks, twice weekly, 5mg/kg)

Autopsy

CTC counts



Lung metastases



Metastases detected by bioluminescence in lungs of animals treated with ARGX-111 after orthotopic implantation of breast cancer cells
In house, collaboration with Prof Michieli (Institute for Cancer Research, Turin, Italy)

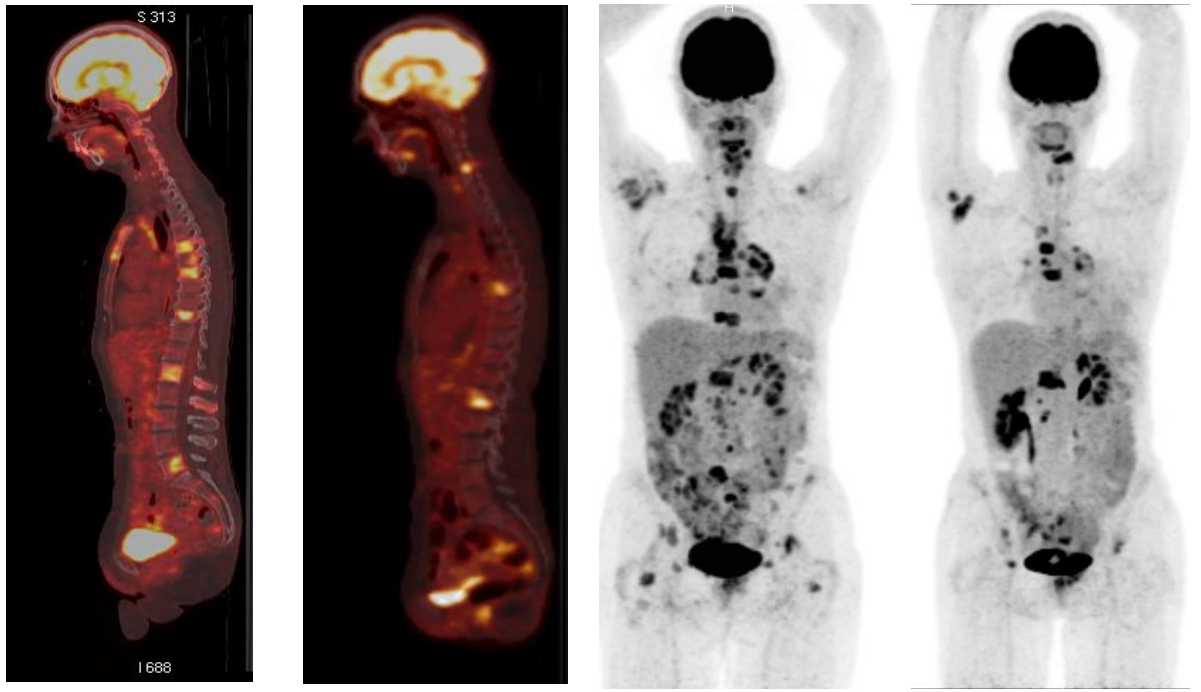
ARGX-111: proof of biological activity

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



Mixed response for patient for bone metastasis on PET scan

In house data

ARGX-111: development plan

Deliverables and next steps Phase 1

- Expanded safety data - expected 2H 2015
- Preliminary efficacy data - expected 2H 2015

Clinical development plan

- 2nd line therapy gastric cancer
- Targeting specifically Met amplified patients (FISH method)
- Available for partnering

In house data

ARGX-113 management of autoimmune crisis

First-in-class antibody fragment targeting FcRn

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

Pre-clinical Proof of Concept & Safety

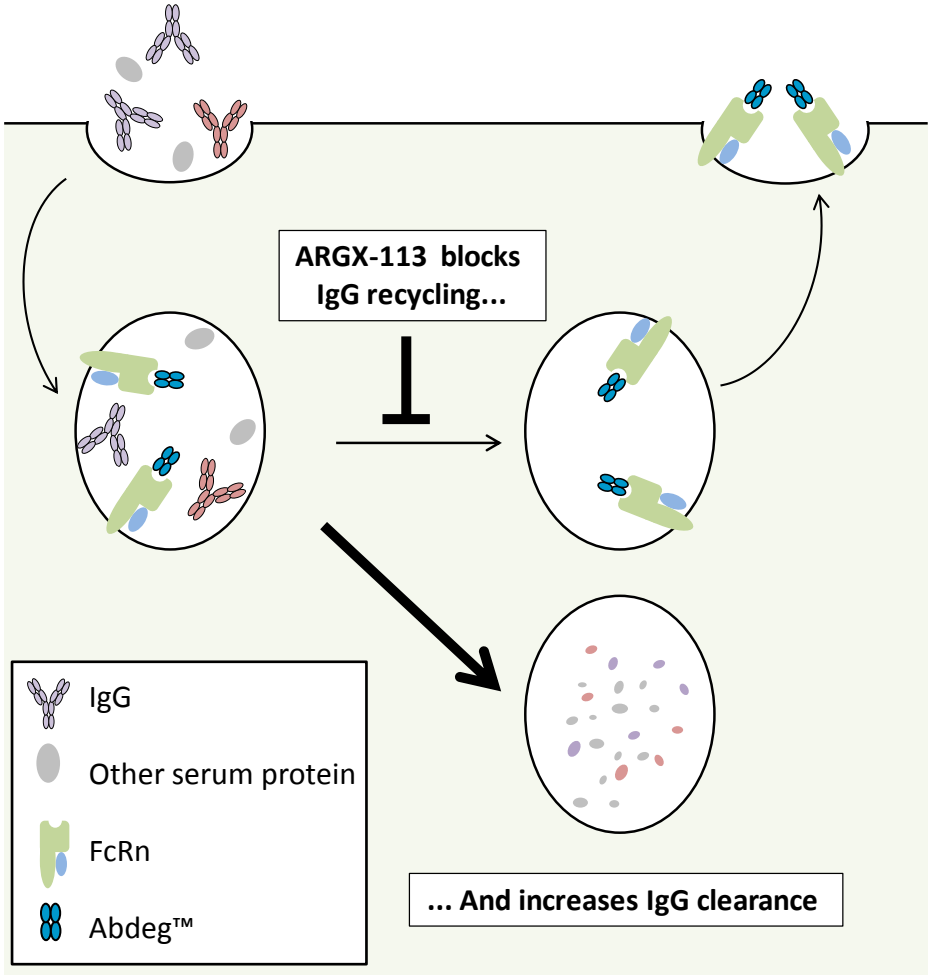
- Highly effective in preclinical models of RA, MS, MG,...
- Safe profile expected (individuals with loss-of-function mutations in FcRn)
- Phamacology study shows IgM and IgA levels unaffected

Unmet medical need

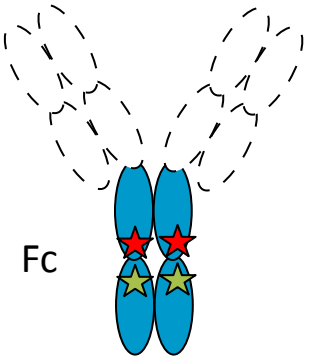
- Several autoimmune drugs address cell compartment but not autoantibody compartment
- Pathogenic autoantibodies play dominant role in many autoimmune diseases

ARGX-113 manages autoantibody induced flares

Mode of action

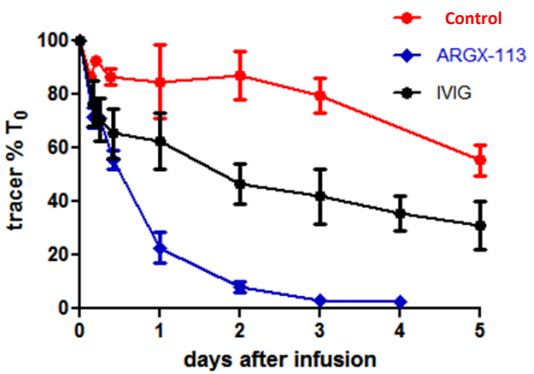


Design



Fc Fragment - ABDEG™ equipped

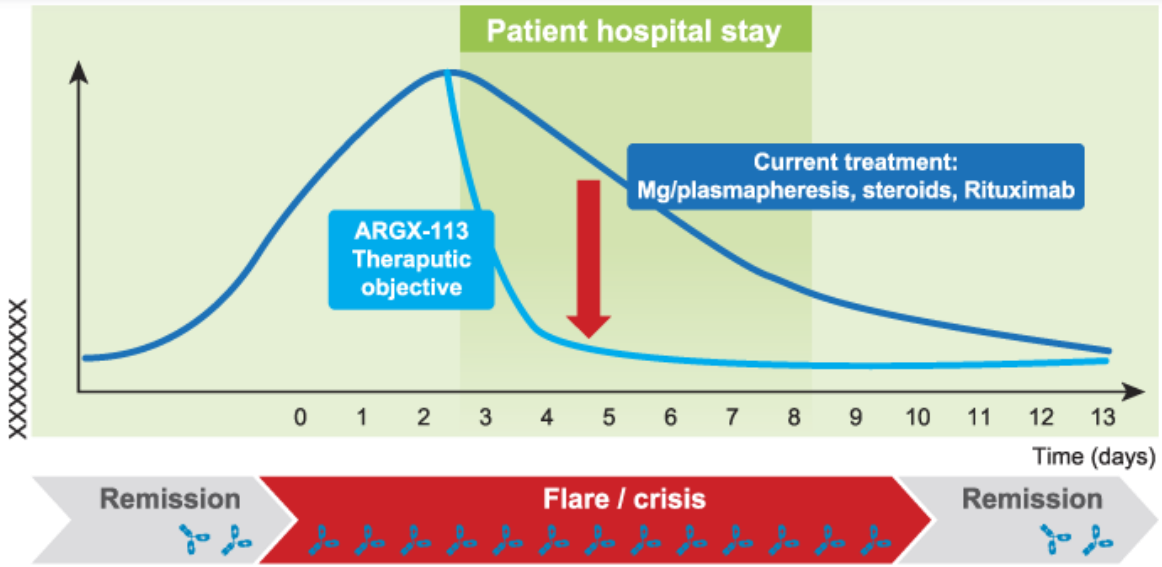
Therapeutic effect



Comparison of tracer antibody clearance capacity of ARGX-113 vs IVIG (cynomolgus monkey model)

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

Orphan indications	Prevalence *per 100,000 (US)*
Myasthenia gravis	20 - 50
Skin blistering diseases	18 (Pemphigus)

Major indications	Prevalence *per 100,000 (US)*
Systemic lupus erythematosus	80-100
Multiple sclerosis	~90

- 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%)

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**

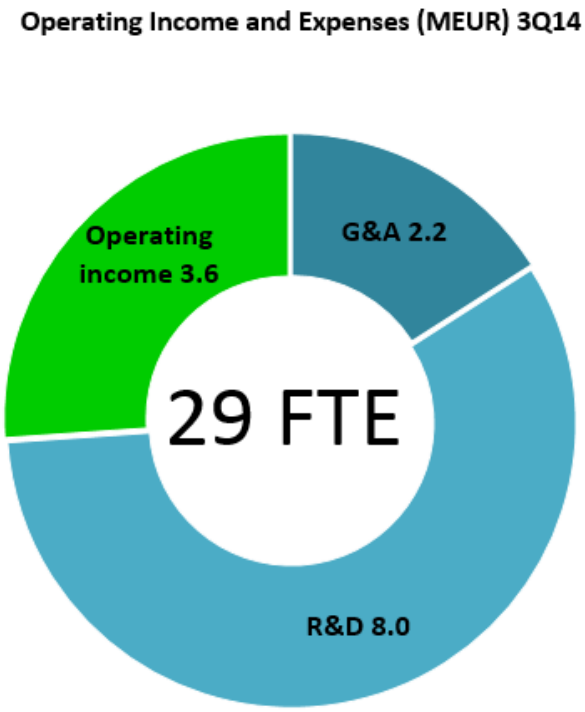
Building partnerships for the long term

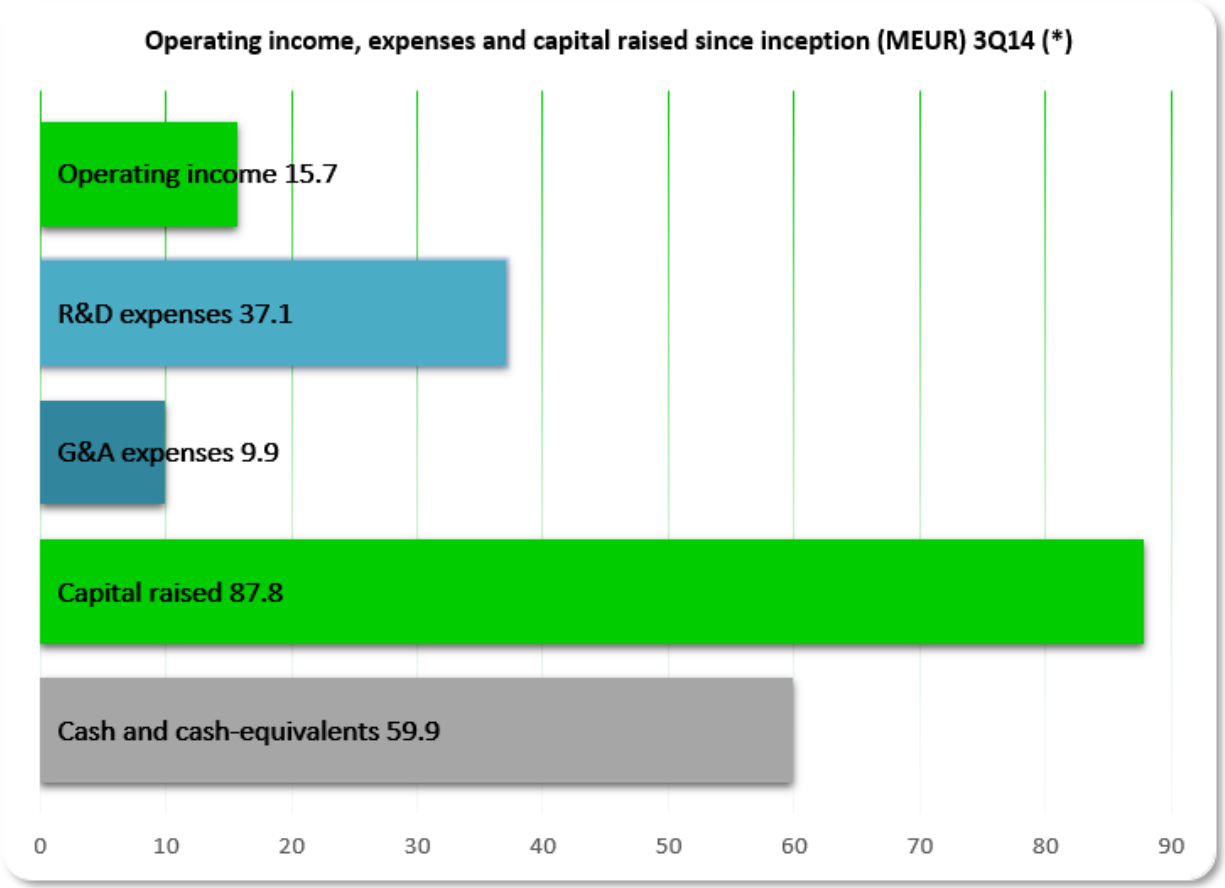
- **Strategic Alliances** Shire
  - Non-exclusive product discovery and development, leveraging entire technology suite
  - Upfront funding, R&D support, development milestones, royalties, product reversion rights
- **Collaboration Agreements** Shire BAYER Boehringer Ingelheim
  - Non-exclusive discovery 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,...

- **€19.1 million in cumulative revenue to date**
- **>€1.3B* 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





(*) not including deferred revenue and accruals

2015 strategic goals

Priority	Status	Milestones
ARGX-110 ***Safety & Efficacy data in B/T- cell NHL***	2H15 ... ☑ 2H15 2H15	• Report Ph1 data (n=56) • Report Ph1/2 T-cell lymphoma initial data (n=15) • Obtain IND approval • Report Ph1/2 WM initial data (n=15) • Initiate 3rd indication specific study
ARGX-111 ***Safety & Efficacy data in Met amplified solid tumors***	☑ ...	• Determine dose • Report Ph1 interim data
ARGX-113 ***Enter clinic***	1H15 2H15	• GLP Tox data • Start first HV study
Preclinical pipeline ***Nominate candidate***	...	• Report progress GARP
Partnerships	☑	• Report progress existing partnerships • Enter 1st new partnership • Enter 2nd new partnership
US presence	... ...	• First US investors post-IPO • Regular presence US investor conferences • Non-deal roadshows

Creating superior, differentiated antibodies

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