

# DAG VAN DE TIPS

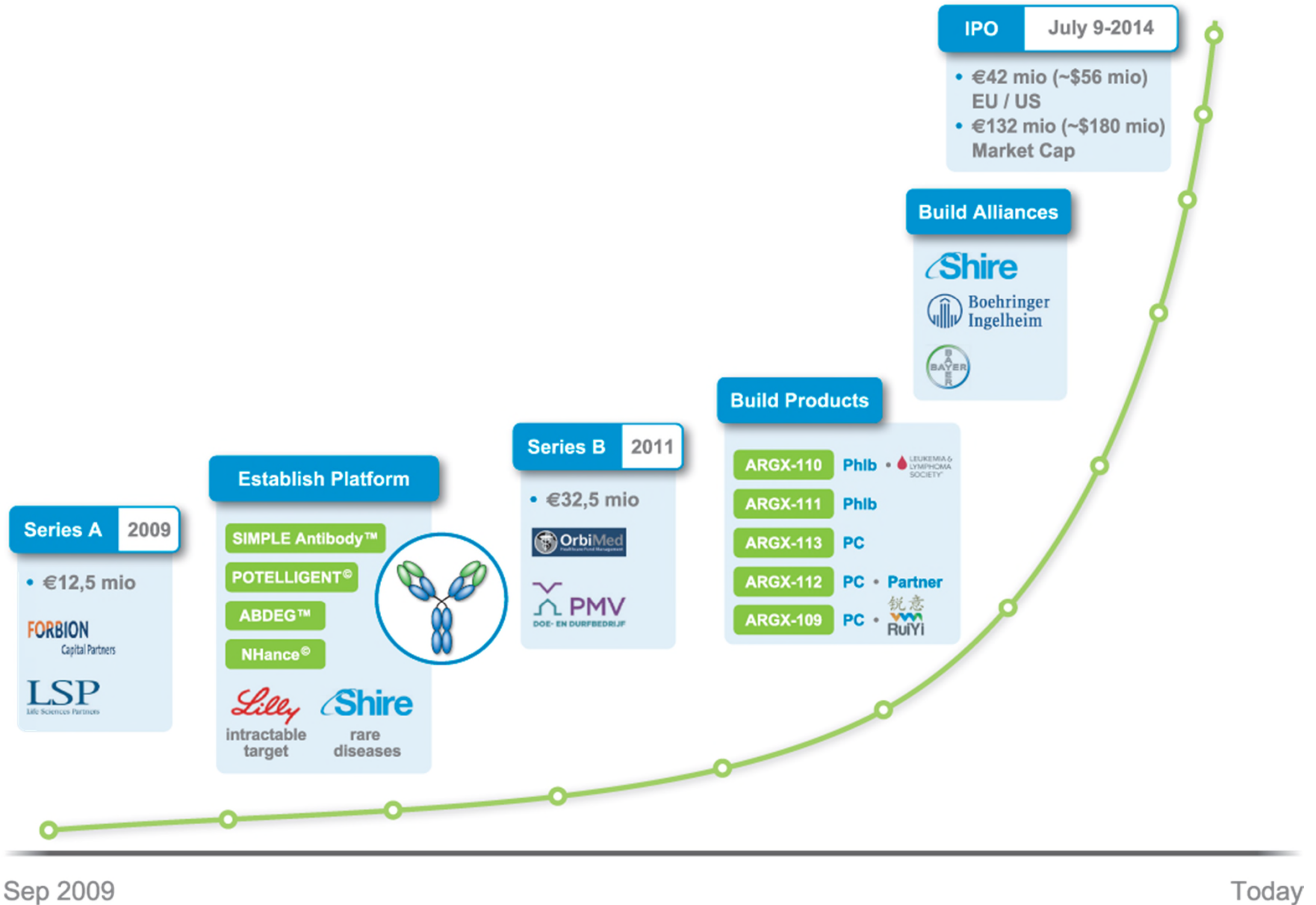
ZATERDAG 4 OKTOBER 2014 - Ghelamco Arena Gent

# DISCLAIMER

## Forward Looking Statements

The contents of this announcement include statements that are, or may be deemed to be, forward-looking statements. These forward-looking statements can be identified by the use of forward-looking terminology, including the terms "believes", "estimates", "anticipates", "expects", "intends", "may", "will", or "should", and include statements arGEN-X concerning the intended results of its strategy. By their nature, forward-looking statements involve risks and uncertainties and readers are cautioned that any such forward-looking statements are not guarantees of future performance. arGEN-X's actual results may differ materially from those predicted by the forward-looking statements. arGEN-X does not undertake the obligation to publicly update or revise forward-looking statements, except as may be required by law.

# Antibody expert lift-off



# Focus on the fast growing, dynamic antibody market

## Successful drug class

- ▶ Across therapeutic areas
- ▶ Big in cancer and autoimmune diseases
- ▶ Large and orphan indications
- ▶ 9.2% cumulative annual growth rate\*
- ▶ 18-29% approval rates
- ▶ Greater resistance to generic competition
- ▶ Promising new immunotherapy drugs

## Leading antibodies

Trade name	Name	2012 sales (US\$B)
Humira®	Adalimumab	9.5
Remicade®	Infliximab	7.5
Rituxan®	Rituximab	7.1
Herceptin®	Trastuzumab	6.3
Avastin®	Bevacizumab	6.1
Lucentis®	Ranibizumab	4.0
Erbitux®	Centuximab	1.9
Tysabri®	Natalizumab	1.6
Xolair®	Omalizumab	1.3
Soliris®	Eculizumab	1.1

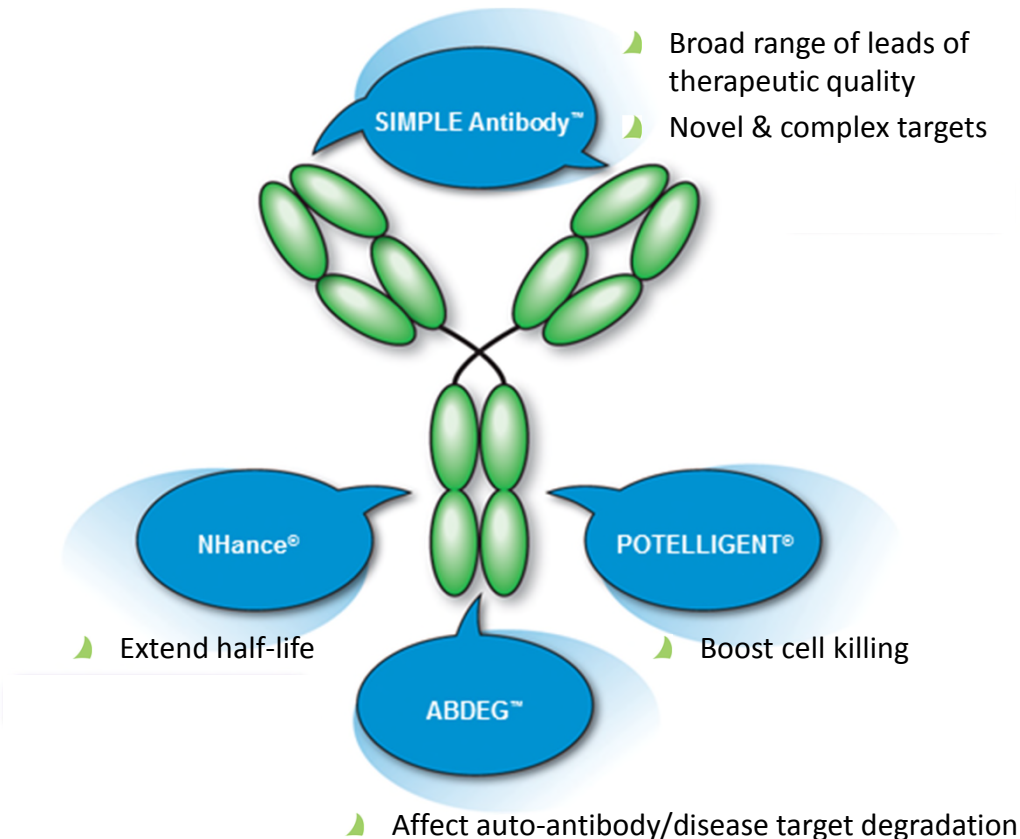
- 43 approved (US/EU) therapeutic antibodies currently on the market
- More than \$60B in global annual sales

\* Forecast till 2015  
La Merie Publishing, Top 30 Biologics 2012, May 7, 2013; Ivin (2013); CitiResearch; [www.imgt.org/mAb-DB/index#Approval\\_antibodies](http://www.imgt.org/mAb-DB/index#Approval_antibodies)

# Suite of complementary antibody technology platforms

*Therapeutic antibodies with multiple modes of action against complex targets*

The strength of arGEN-X' technology suite...



...is recognized by its partners

"One cannot engineer such diversity"  
**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**



"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**



- SIMPLE Antibody™: Unlock novel and complex targets
- NHance®, ABDEG™, POTELLIGENT®: Enhance SIMPLE Antibody™ leads

# Clinical stage pipeline of differentiated products


Drug Candidate	Indication	Pre-clinical	Phase 1	Phase 2	Ownership	Proposition
<b>ARGX-110</b>	Heme malignancies			LEUKEMIA & LYMPHOMA SOCIETY*	<b>Wholly owned</b>	Immune checkpoint (CD70) inhibitor Enhanced cell kill  Complete c-Met blocking Enhanced cell kill  Potent FcRn blocking  Complete IL22R blocking  Novel, complex targets e.g. GARP
<b>ARGX-110</b>	Solid tumors					
<b>ARGX-110</b>	Autoimmunity					
<b>ARGX-111</b>	Solid tumors Heme malignancies					
<b>ARGX-113</b>	Autoimmunity					
<b>ARGX-112</b>	Atopic dermatitis					
<b>Discovery</b>	Autoimmunity Cancer	<i>multiple</i>				
<b>ARGX-109</b>	Autoimmunity Cancer				<b>Partnered</b>	Potent IL-6 blocking Partnered with RuiYi
<b>Shire</b>	Undisclosed					Novel, complex targets
	Undisclosed					Novel, complex targets
<b>Boehringer Ingelheim</b>	Undisclosed					Novel, complex targets

# Near-term value inflection points

2014

2015

ARGX-110

- Start Phase 1 safety expansion
- Partnership with  LEUKEMIA & LYMPHOMA SOCIETY
- H2: Waldenström's study open

- H1: Phase 1 safety expansion recruited
- H2: Phase 1 read out: safety & biologic activity
- H2: Start 2<sup>nd</sup> Phase 2 in heme-onc
- H2: Start Phase 1 solid tumor combination therapy

ARGX-111

- Start Phase 1 dose escalation
- H2: Dose selected

- H1: Start Phase 1 safety expansion
- H2: Phase 1 read out : safety & biological activity

ARGX-113

- H2: Start GLP Tox study

- H2: Start Phase 1 healthy volunteer study

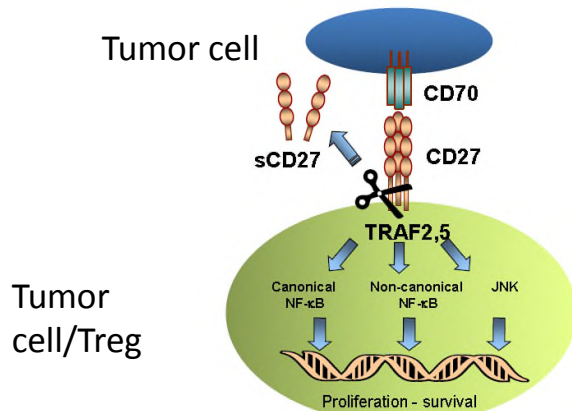
# ARGX-110: Anti-CD70 SIMPLE Antibody™



# ARGX-110: CD70, a promising immunotherapy target

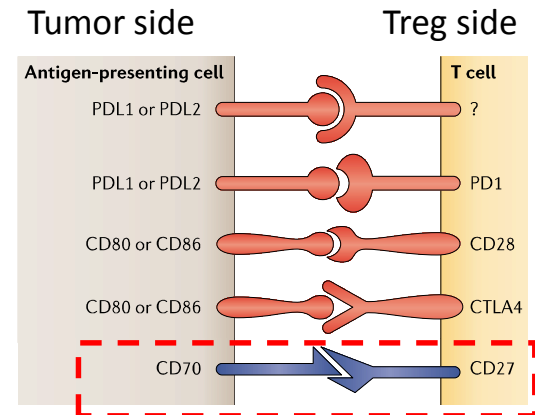
*CD70 is involved in tumor growth, enables immune escape and is highly tumor specific*

## 1. CD70 is a tumor/Treg growth signal



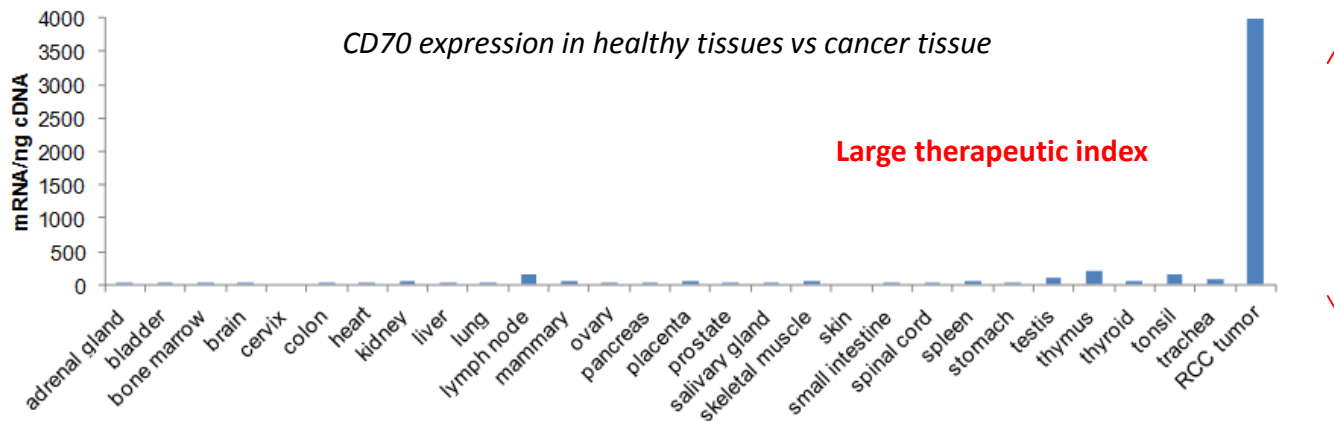
**Blocking CD70 deprives tumor of growth signal**

## 2. CD70 enables tumors to escape immune surveillance



**Blocking CD70 deprives tumor of immune escape mechanism**

## 3. CD70 expression is highly tumor specific

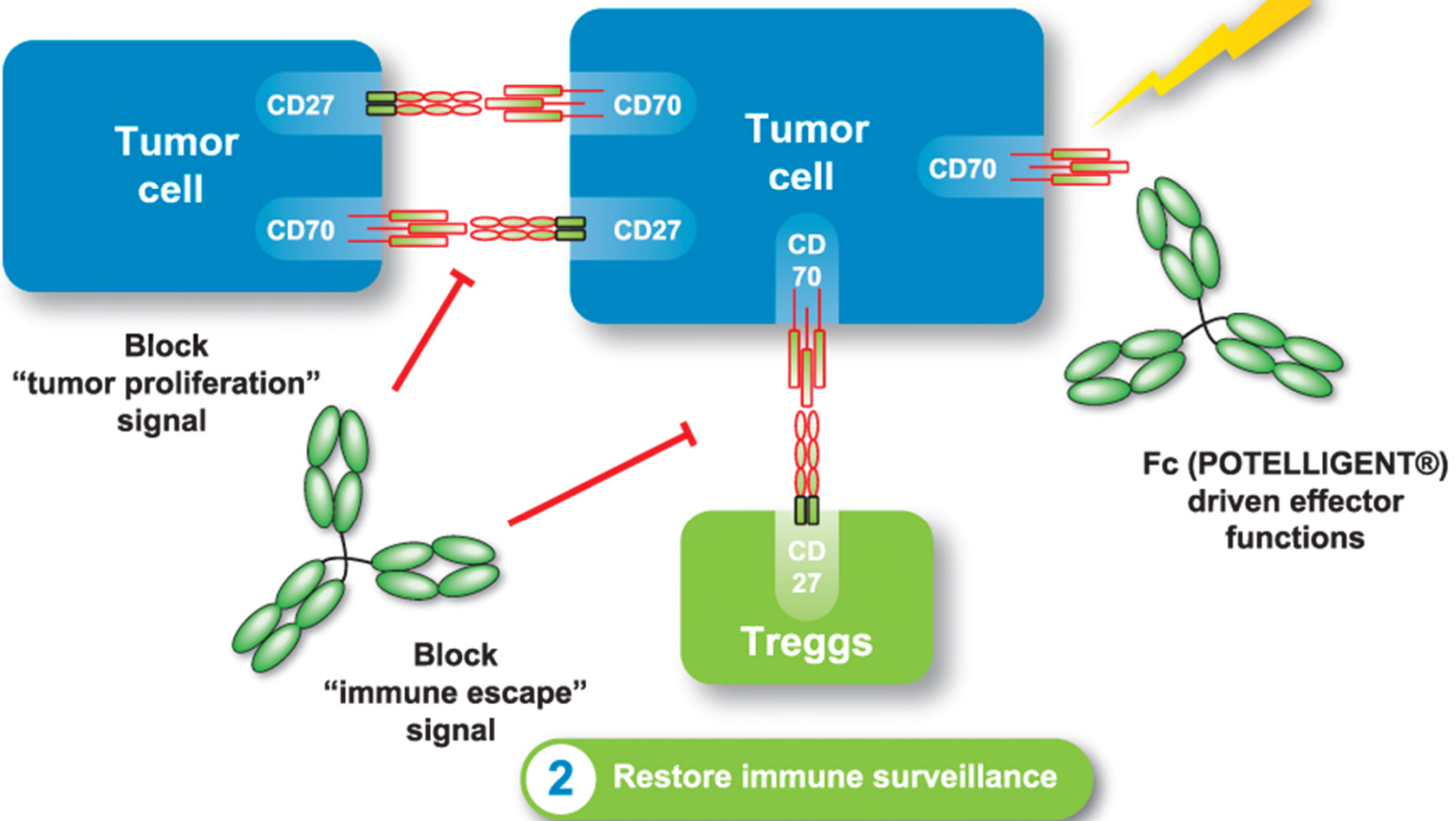


**Killing CD70+ cells should be safe**

# ARGX-110 targets CD70+ tumors via 3 modes of action

1 Block tumor growth

3 Kill tumor



# ARGX-110: Indications and market potential

*CD70 has potential across a broad range of malignancies*

CD70 expression**	
Solid tumors	CD70+ (frequency)
Renal cell	100%
Esophagus	67%
NSCLC	58%
Mesothelioma	57%
Head&Neck	50%
Melanoma	42%
Pancreas	27%
Ovarian	17%

Solid tumors	Indication	WW Incidence ('000)*	Potential entry point
	NSCLC	675	Neo-adjuvant
	Head & Neck	165	2nd line
	Ovarian	66	Platinum-refractory
	Renal	192	1st line combo with TKI
	Mesothelioma	9	2nd line (50%)
	▲ Perjeta® sells at \$71K per year; Herceptin® sells at \$54K per year (US)		

CD70 expression**	
Lymphomas	CD70+ (frequency)
Waldenström's	100%
Hodgkin's	96%
CTCL	83%
Mantle cell	80%
DLBCL	71%

Lymphomas	Indication	WW Incidence ('000)*	Potential entry point
	Waldenström's	4.2	salvage (100%)
	Hodgkin's	27	salvage therapy (~20%)
	Mantle cell	12	salvage therapy (~50%)
	T-cell	23.4	salvage therapy (~65%)
▲ Adcetris® sells at \$94.5K-121K per treatment course (US)			

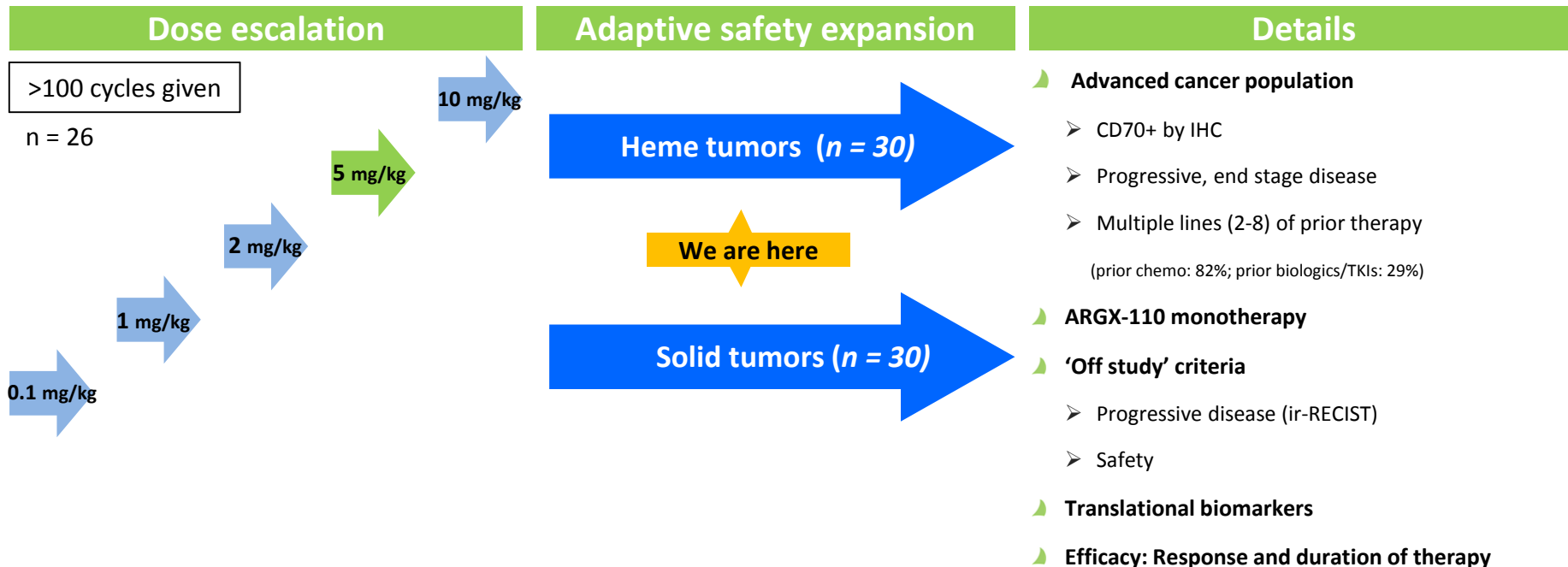
“...anti-CTLA4 and anti-PD-1 work almost exclusively in melanoma, kidney cancer and perhaps smoking-induced lung cancers. But if you want to treat the 90% of patients that have other solid tumors like ovarian, pancreatic, (...), esophageal cancer, you need to do something different” **Steven Rosenberg, NCI - BioCentury, Jan. 27, 2014**

\* Calculated as US incidence x 3; \*\* In-house data and literature  
 Grewal (2008) Expert Opin Ther Targets (3):341-351; Liu (2013) Onco Targets Ther. 6:615-619; Ho (2008) Blood. 112(12):4683-4689  
 Wang (2013); Herrinton (1993); www.LLS.org; www.cancer.org (ACS); Biocentury

# ARGX-110: Phase 1 trial overview

1Q 2013

2H 2015



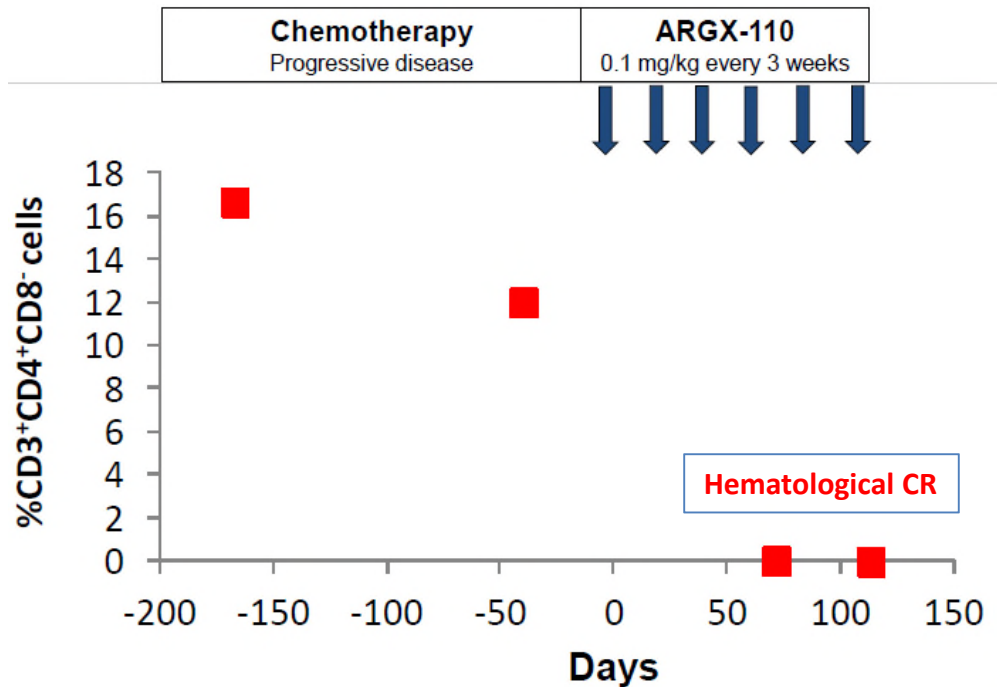
## Conclusions to date

- No dose-limiting tox or auto-immune related AEs observed
- About 50% of all comers are CD70 positive
- Biological activity observed in individual patients with TCL, Mesothelioma, Ovarian, Renal, H&N cancer, ...

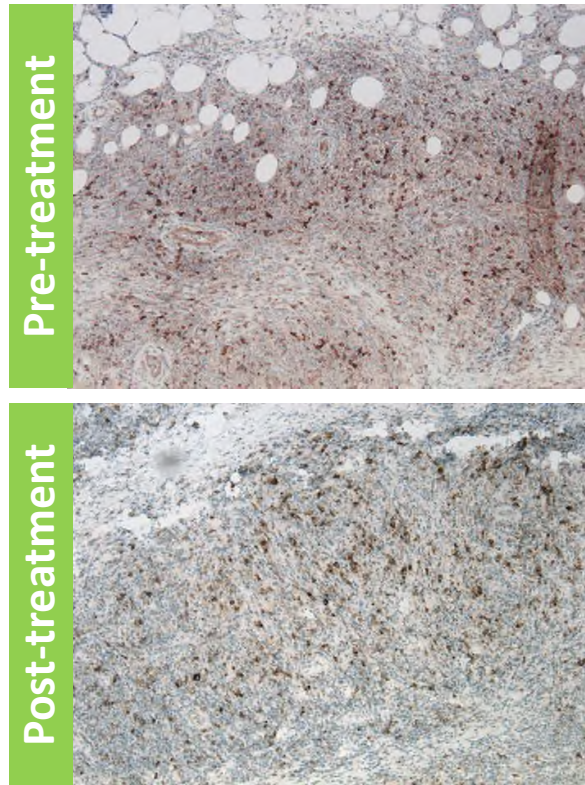
# ARGX-110: Initial observations of biological activity (1)

Complete hematological response with stable skin lesions observed in patient with Sézary syndrome

■ % malignant cells in patient blood



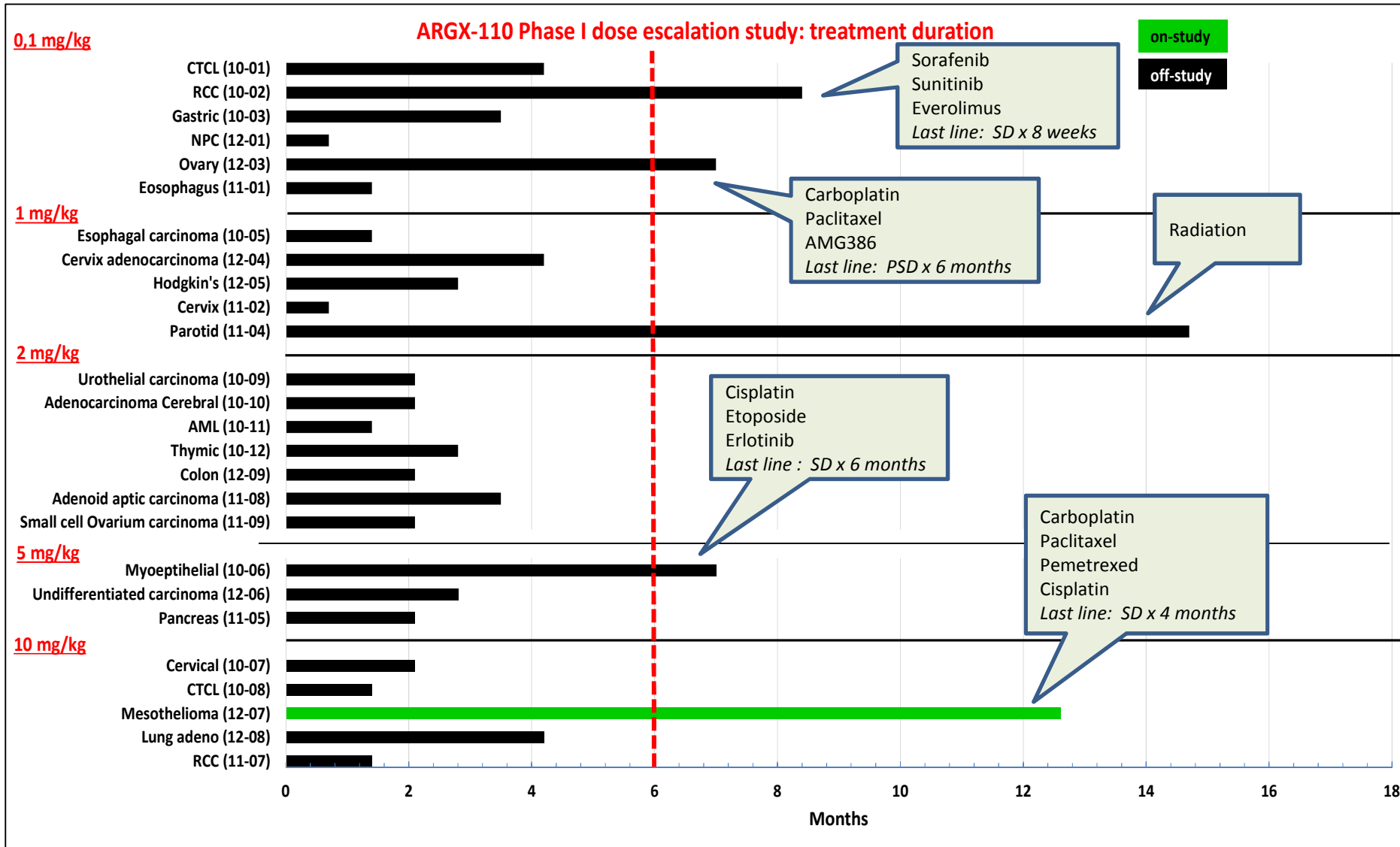
Status of skin lesions



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

Elimination of CD70 positive Sezary cells in 2<sup>nd</sup> CTCL-Sezary patient

# Dose escalation study: treatment duration



# ARGX-110: Expanding cancer immunotherapy


*Based on broad expression across a variety of tumors and favorable safety profile*

Phase 1	Ipilimumab (CTLA4)	Nivolumab (PD-1)	ARGX-110 (CD70)
<b>Dose (mg/kg)</b>	3	0.3 – 10	0.1 – 10
<b>Schedule</b>	Monthly X 4	Weekly X 8	Every 3 weeks
<b>CR</b>	1 DLBCL	1 CRC	1 T-cell lymphoma
<b>PFS6</b>	2/18	3/39	5/26
<b>Immune AEs</b>	<ul style="list-style-type: none"> <li>Colitis</li> <li>Endocrinopathies</li> </ul>	<ul style="list-style-type: none"> <li>Colitis</li> <li>Hypothyroidism</li> <li>Arthropathy</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>Combinability Potential</b>	<ul style="list-style-type: none"> <li>Limited due to systemic toxicity</li> </ul>		

	Current checkpoint inhibitors (CTLA4, PD-1)	ARGX-110 (CD70)
<b>Market Potential</b>	<ul style="list-style-type: none"> <li>Turning cancer into chronic disease               <ul style="list-style-type: none"> <li>\$24B/y for current indications</li> <li>\$35B/y if more solid and blood cancers can be addressed</li> </ul> </li> <li>Cancer therapy backbone in up to 60% of patients in next 10y vs &lt;3% today</li> </ul>	<ul style="list-style-type: none"> <li>CD70 overexpressed in most heme tumors</li> <li>CD70 overexpressed in range of solid tumors currently not addressed by CTLA4/PD-1/PD-L1</li> </ul>
<b>Pipeline</b>	<ul style="list-style-type: none"> <li>Combining immunotherapy strategies</li> <li>Need for novel immune checkpoint inhibitors: across more cancer indications and safer to combine</li> </ul>	<ul style="list-style-type: none"> <li>Safety profile supports combination therapy (e.g. with PD-1)</li> </ul>

*Immunotherapy – the beginning of the end for cancer, Citi Research by Andrew Baum.  
 <Yervoy Prescribing information, Ansell 2009; Brahmer 2010  
 ASCO Annual meeting 2014; abstract 3023*

# ARGX-110: Clinical development plan

Indication	Phase	Envisaged patient #	Envisaged primary end point	Expected study start
Lymphoma <i>e.g. T-cell or Mantle cell</i>	2	30	• Response rate	2H 2015
Waldenström's 	2	30	• Response rate	2H 2014
Combination therapy in solid tumor <i>e.g. Ovarian, H&amp;N, NSCLC</i>	1	30	• Safety • Translational Biomarkers	2H 2015

Data driven decision: expand WM or TCL/MCL to pivotal phase 2 (n=150)

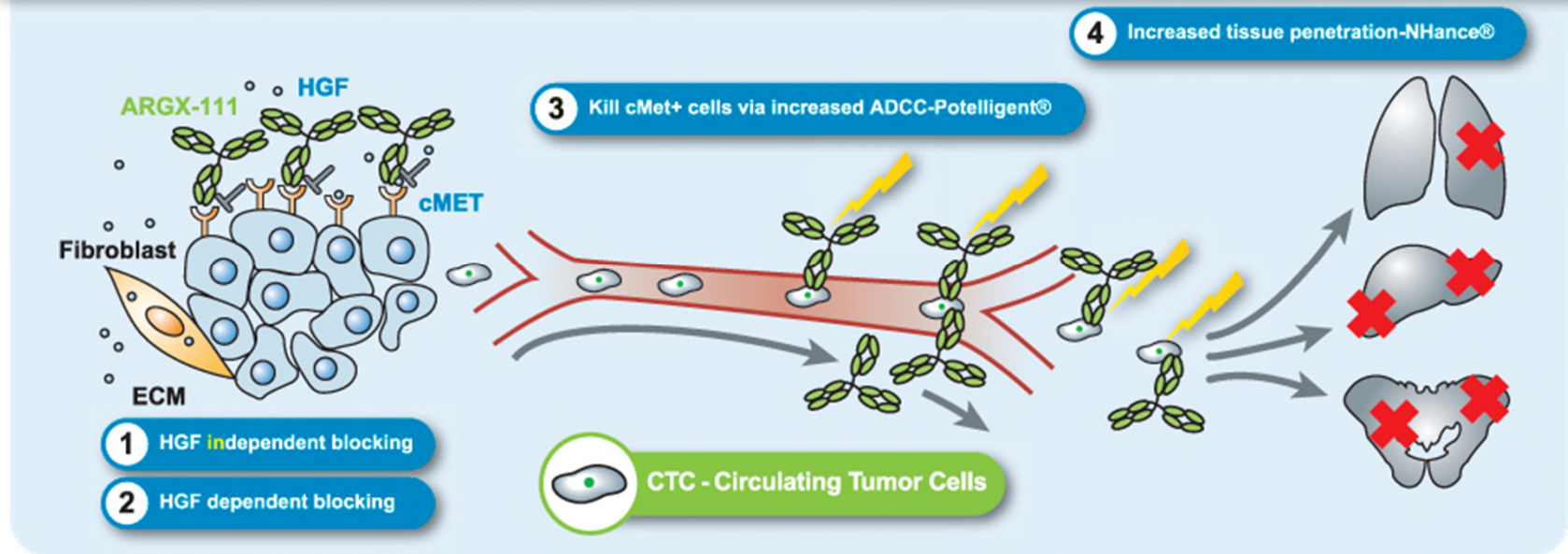
- In addition, the Company envisages undertaking a Phase 1 study in autoimmunity which is expected to start 2H 2015 (see appendix)



# ARGX-111: Anti-c-Met SIMPLE Antibody™

# ARGX-111 targets c-Met positive tumors and CTC's

## Different view on c-Met Biology



## 4 Modes of Action

- Best in class c-Met blocking - SIMPLE Antibody™
- Unique cell killing - POTELLIGENT®
- Unique tissue penetration - NHance®

## Different clinical development strategy

- Interfere early in cancer metastasis rather than dealing late with TKI resistance
- Adjuvant and neo-adjuvant therapy settings

# ARGX-111 blocks metastatic spread

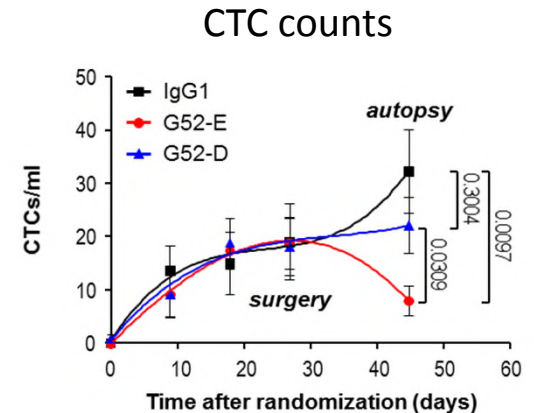
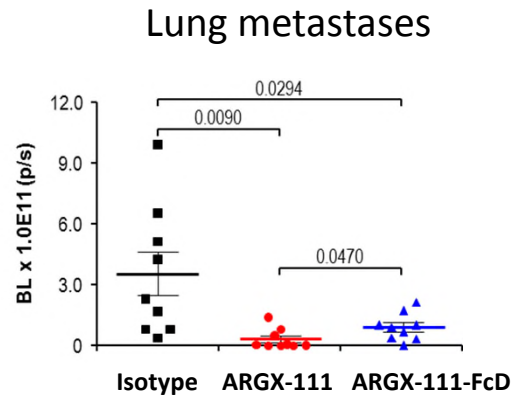
## Evaluation of lung metastasis from breast cancer (MDA-MB-231)

### neoadjuvant animal model\*

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

**Surgery**

**Autopsy**

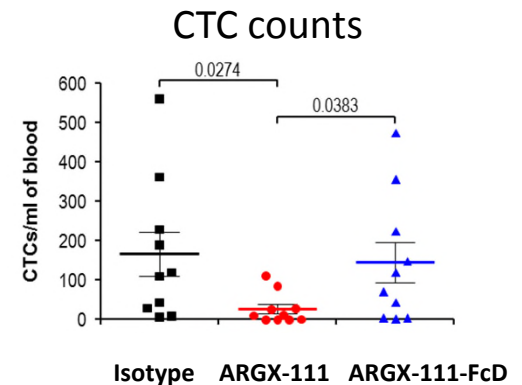
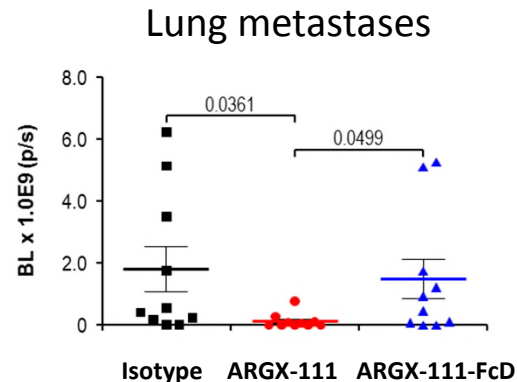


### adjuvant animal model

**Surgery**

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

**Autopsy**



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

# ARGX-111: Phase 1 trial overview

1Q 2014

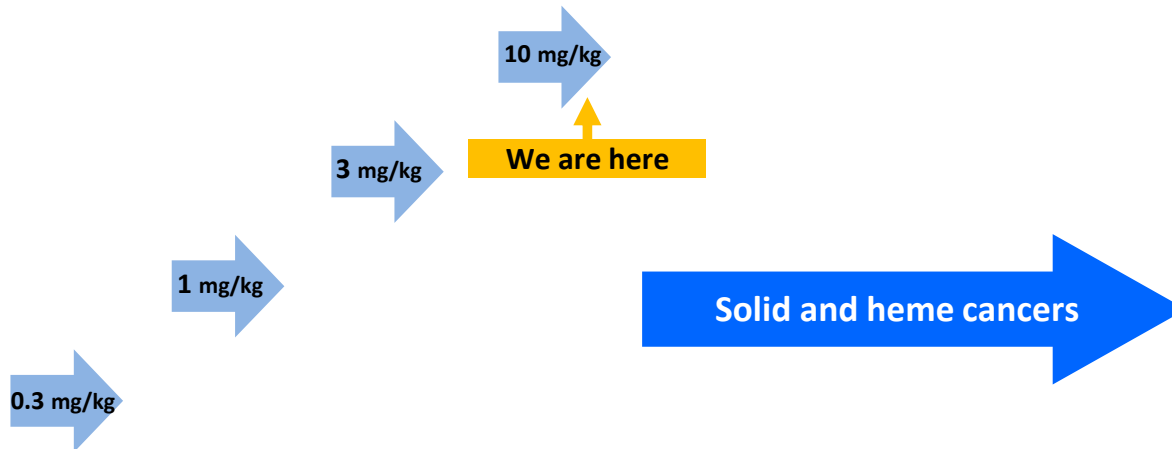
1H 2015

2H 2015

Dose escalation

Adaptive safety expansion

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**

## Conclusions to date

- ▶ ~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

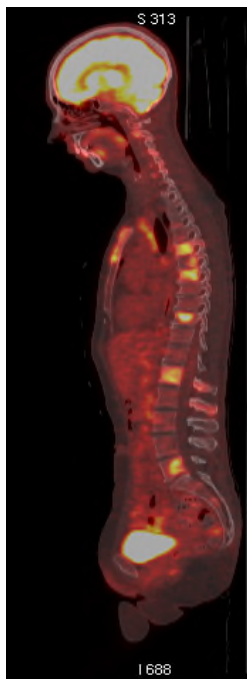
# ARGX-111: Initial signs of biological activity

## Background

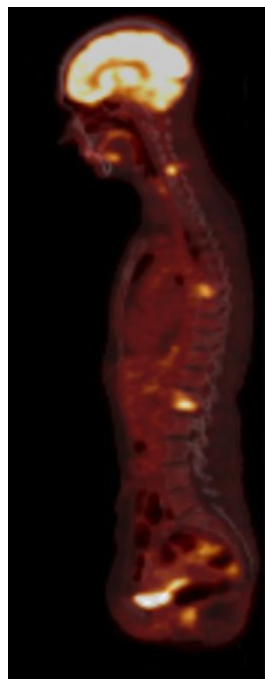
- ▶ Biological activity observations: Mixed response for individual patient with bone metastasis
  - ▶ 50 year old Gastric Cancer patient with bone metastases
  - ▶ Multiple lines of previous treatment; including surgery and 2 lines of triplet chemotherapy
  - ▶ PET scan observation of biological activity (see right) confirmed on repeat imaging
  - ▶ Good performance (clinical) status maintained throughout treatment period

## Early sign of biological activity

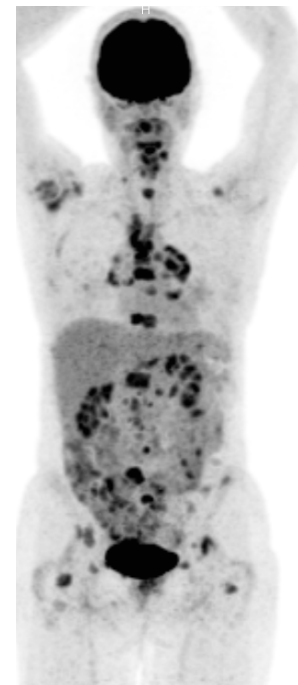
Baseline PET scan



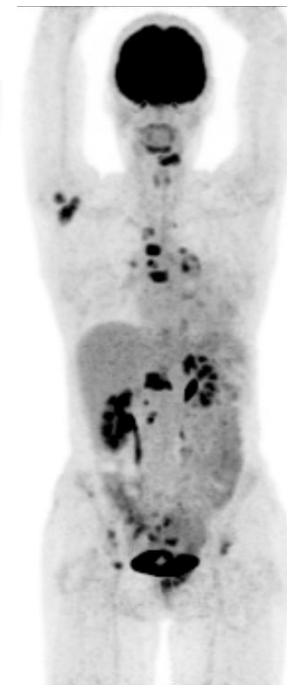
Improvement after 4 doses



Baseline PET scan



Improvement after 4 doses



Mixed response for patient for bone metastasis on PET scan

# ARGX-111: Clinical development plan

## Deliverables and next steps Phase 1

- ▶ Dose escalation completed - expected 2H 2014
- ▶ Expanded safety data - expected 2H 2015
- ▶ Preliminary efficacy data (CTC elimination and reduction of metastasis) - expected 2H 2015
- ▶ IHC method ready for Phase 2 validation

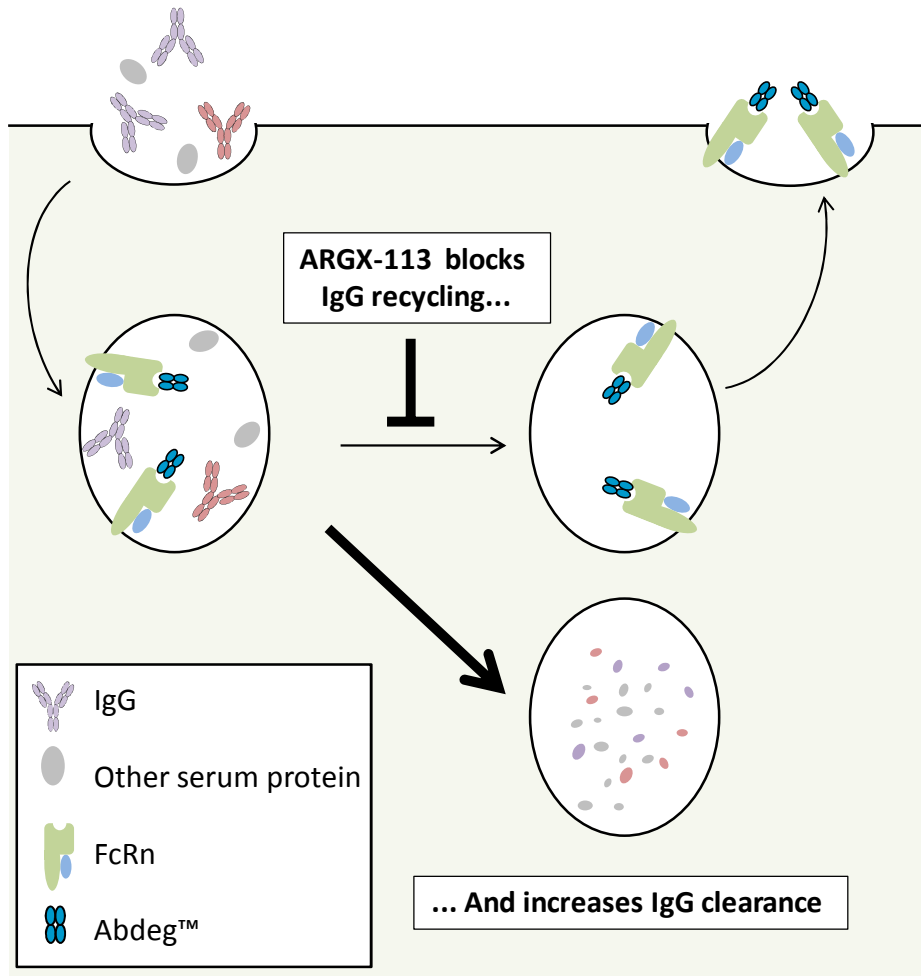
## Clinical development plan

- ▶ Further development currently envisaged as combination therapy
- ▶ Potential indications: neo-adjuvant therapy breast cancer; 2<sup>nd</sup> line therapy gastric cancer
- ▶ Together with potential partner
- ▶ Expected to start 2H 2015

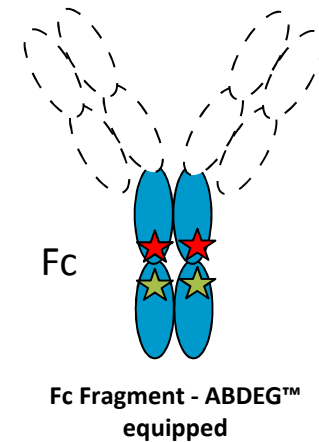
# ARGX-113: Antibody fragment (Fc) to block FcRn

# ARGX-113 blocks FcRn, accelerating antibody clearance

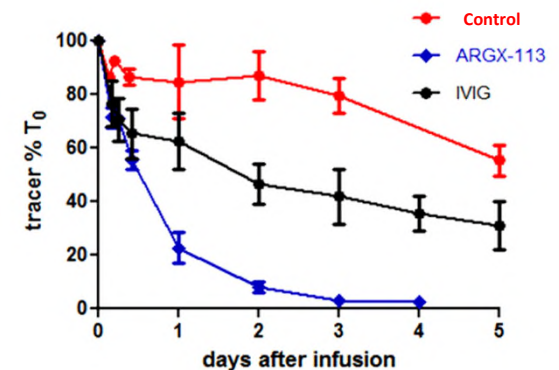
## Mode of action



## Design



## Therapeutic effect

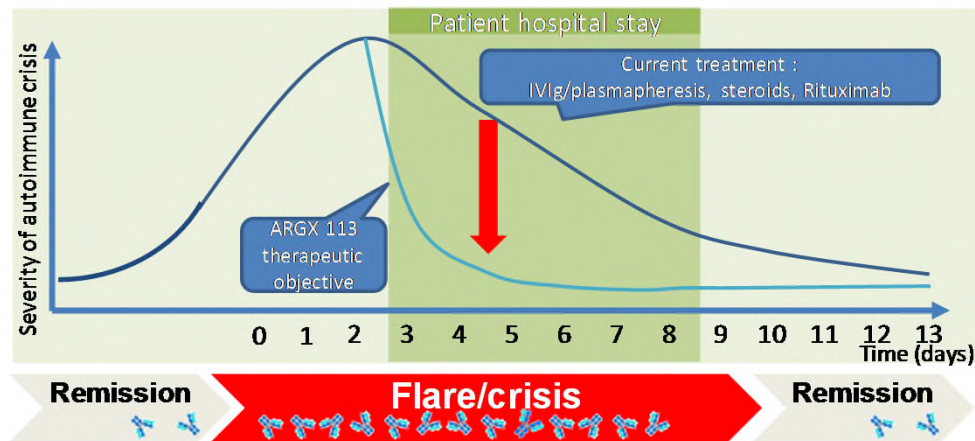


Comparison of tracer antibody clearance capacity of ARGX-113 vs IVIG (cynomolgus monkey model)



# ARGX-113: Management of acute severe autoimmune disease by rapid clearance of autoantibodies

## ARGX-113 can address acute autoimmune flares



## ARGX-113: indications and market potential

Orphan indications	Prevalence per 100,000 (US)
Myasthenia gravis	20 - 50
Skin blistering diseases	18 (Pemphigus)
Idiopathic Thrombocytopenia Purpura	9.5

- 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%)

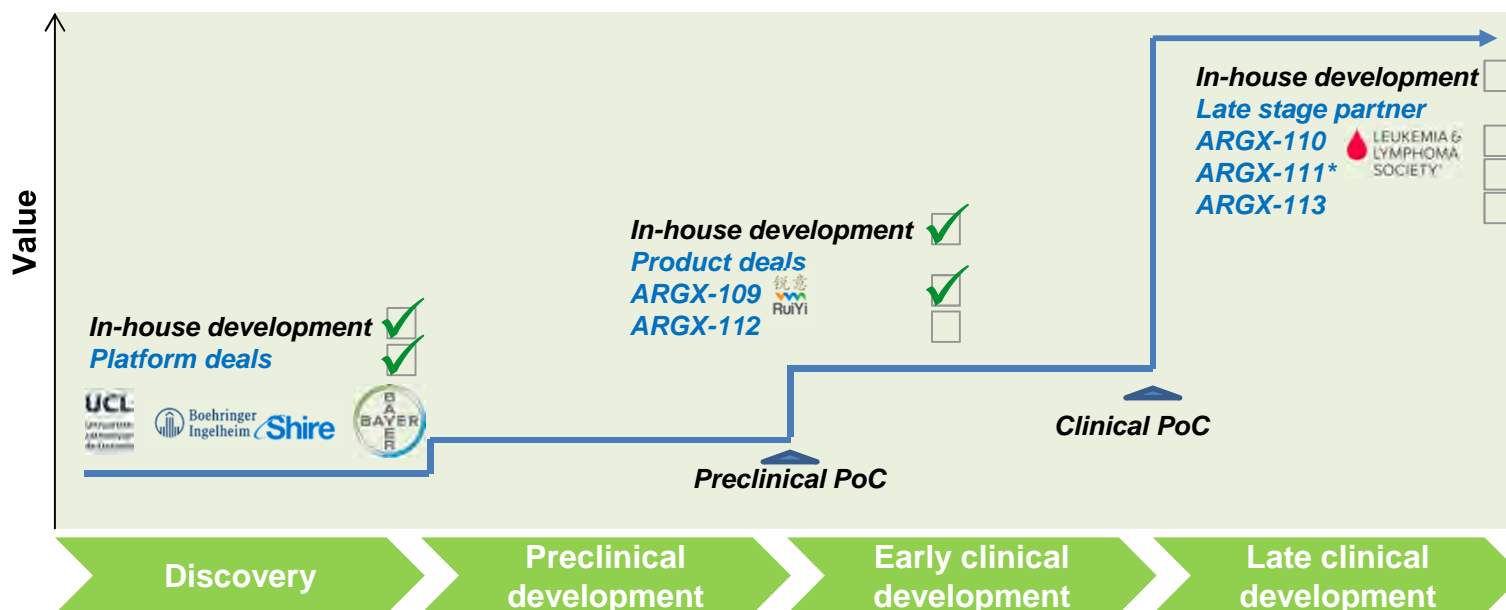
# Current Alliances and Partnering Strategy

# Business model fuelled by productive platform

## Generating a portfolio of differentiated product candidates

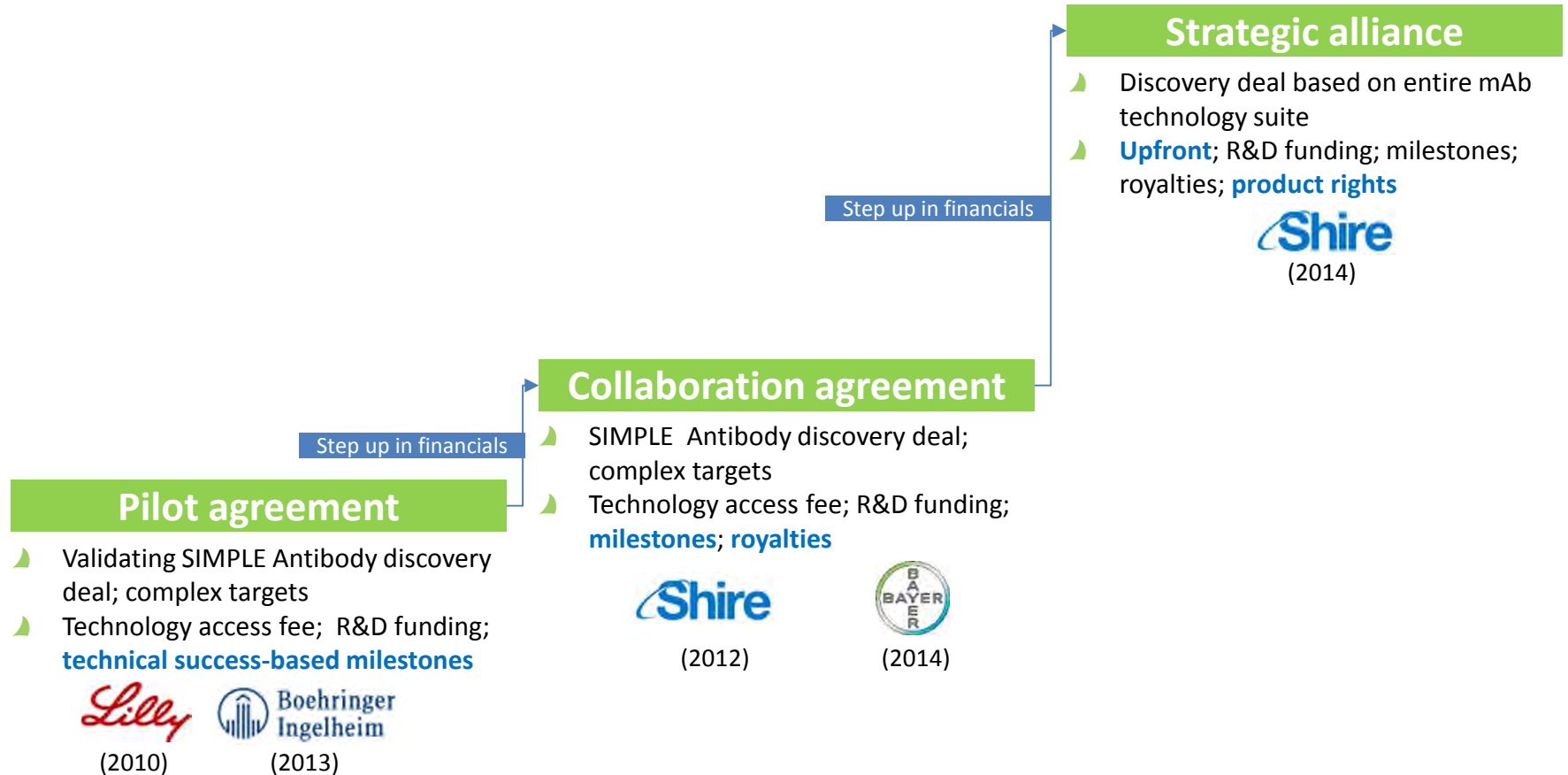


## Partnering at each stage in the value chain



\* Partner after Phase 1

# Building select, deep strategic alliances on the back of success



➤ €12.9 million in cumulative revenue from partnerships, grants and tax incentives to date

➤ >€1.3B\* potential cumulative revenues from existing partnerships

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

# Corporate Overview

# Experienced management team

Name	Nationality	Function	Credentials
<b>Tim van Hauwermeiren</b> (M. Eng, eMBA)		<b>Chief Executive Officer</b>	<ul style="list-style-type: none"> <li>&gt; 18yr BD and GM experience; strong deal sheet incl. \$265m deal with Boehringer Ingelheim; &gt; €200m financing track</li> <li>Procter &amp; Gamble; Ablynx</li> </ul>
<b>Hans de Haard</b> (PhD, Prof)		<b>Chief Scientific Officer</b>	<ul style="list-style-type: none"> <li>&gt; 23yr mAb discovery experience, serial pioneer of mAb platforms (Dyax Fab library, Nanobody® and SIMPLE Antibody™); 7 mAbs in the clinic – one approved</li> <li>Akzo Nobel; TargetQuest; Unilever; Ablynx</li> </ul>
<b>Torsten Dreier</b> (PhD)		<b>Chief Development Officer</b>	<ul style="list-style-type: none"> <li>&gt; 17yr of mAb pre-clinical development; 6 mAbs in clinic incl. 1st BITE® Blinatumumab®</li> <li>Micromet; Ablynx</li> </ul>
<b>Alain Thibault</b> (MD)		<b>Chief Medical Officer</b>	<ul style="list-style-type: none"> <li>&gt; 18yr of clinical oncology experience; 3 products on the market: Xeloda®, Yondelis®, Zaltrap®, several in development</li> <li>NCI; Roche; J&amp;J; Regeneron</li> </ul>
<b>Eric Castaldi</b> (M. Fin)		<b>Chief Financial Officer</b>	<ul style="list-style-type: none"> <li>&gt;25yr of finance experience; raised over €400 mio through public and private financing rounds</li> <li>My Kinda Town, Safety Kleen Corporation, NICOX</li> </ul>
<b>Michael Saunders</b> (PhD, eMBA)		<b>Sr Director Targets and Programs</b>	<ul style="list-style-type: none"> <li>&gt; 21yr of industry experience in NCE and NBE drug discovery; strong track record of target selection, program and alliance mgmt; 4 IND's</li> <li>GSK; Devgen; consultant</li> </ul>
<b>Debbie Allen</b> (PhD)		<b>VP Business Development</b>	<ul style="list-style-type: none"> <li>&gt; 25yr of mAb experience, Humira® inventor, 15yr in BusDev</li> <li>Cambridge Antibody Technology; architect of CAT-HGS alliance (BENLYSTA®) BD consultant to Glycart, others: Roche-Glycart deal</li> </ul>
<b>Koos Rasser</b> (PhD, JD)		<b>IP Counsel</b>	<ul style="list-style-type: none"> <li>&gt; 32yr patent experience, including in-house (Global Head IP at Procter &amp; Gamble) and law firm (Howrey LLP)</li> <li>Organon; Schering-Plough; Biogen IDEC; Millennium</li> </ul>

# Our products are 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-111, ARGX-113
  - ▶ Pending claims in EU, other major territories
- 

- ▶ **Patents currently expected to expire in 2028-2033 window**

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- ▶ **Under our industrial partnerships, only non-exclusive licenses have been granted to our technology platforms**

# Strategic objectives

## ▶ **Progress ARGX-110**

- ▶ Phase 2 monotherapy in Waldenström's in collaboration with LLS
- ▶ Phase 2 monotherapy in 2<sup>nd</sup> hematological indication (potentially in T-cell lymphoma or Mantle cell lymphoma)
- ▶ Phase 1b combination therapy in solid tumors
- ▶ Phase 1 monotherapy in autoimmune indication (envisaged to be vasculitis)

## ▶ **Progress ARGX-111**

- ▶ Phase 1b monotherapy expansion and completion to establish proof of mechanism

## ▶ **Progress ARGX-113**

- ▶ Phase 1 healthy volunteer study
- ▶ Phase 2 in autoimmune patients

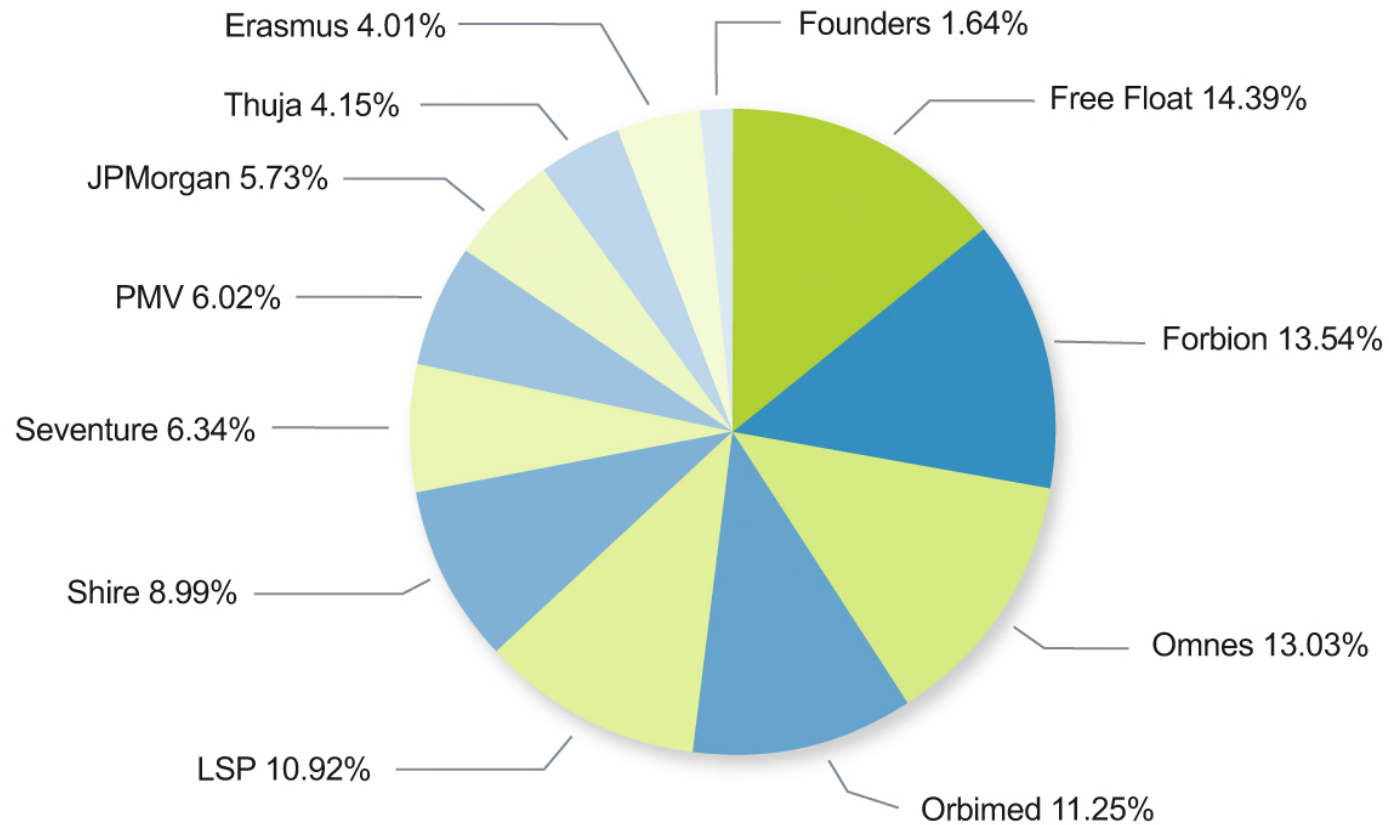
## ▶ **Advance and expand preclinical product pipeline**

## ▶ **Facilitate access to novel targets and technologies**

## ▶ **General corporate purposes**



# Shareholding




# Recent and anticipated news flow

2014

2015

ARGX-110

- Start Phase 1 safety expansion
- Partnership with  **Waldenström's Phase 2 open**
- 





- H1: Phase 1 safety expansion recruited
- H2: Phase 1 read out: safety & biologic activity**
- H2: first patient in 2<sup>nd</sup> hematological Phase 2
- H2: first patient in solid tumor combination therapy Phase 1

ARGX-111

- Start Phase 1 dose escalation
- Dose selected

- H1: Start Phase 1 safety expansion
- H2: Phase 1 read out : safety & biological activity**

Corporate development

- Two technical success milestones 
- Signed SIMPLE Antibody™ discovery deal with Bayer** 
- Signed strategic alliance with Shire** 
- Deliver pilot 

- ARGX-113 first patient in healthy volunteer study



## BEZOEK ONS OP STAND #5023

DAG VAN DE TIPS - ZATERDAG 4 OKTOBER 2014 - Ghelamco Arena Gent