

# argenx

## Full Year Results

### 2016

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Tim Van Hauwermeiren, CEO

Eric Castaldi, CFO

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15 March, 3 PM CET

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# Agenda

- Corporate introduction
- Recent news
- Upcoming news
- Financial news
- Q&A



# Introduction

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# Developing highly differentiated antibodies




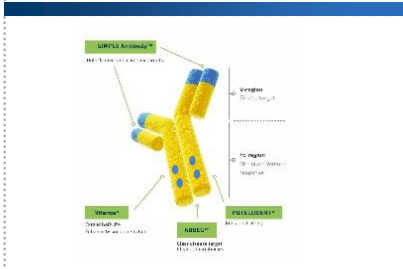
## Deep pipeline

- Cancer & severe autoimmune diseases
- 4 products in Phase I/II



## Validating strategic alliances

- Validation by industrial partners
- Access to novel targets via Innovative Access Program 



## Competitive technology suite

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



## Strong financials

- Strong cash position - €96.7 MM Dec 2016
- Supported by blue-chip biopharma investors

# Business model to maximize the value of our pipeline

## Generating differentiated antibody candidates...



## ...capturing value at optimal stages

Discovery		Preclinical development		Early & late clinical development		
Platform deals		Product deals outside strategic focus		Product deals large indications	Product portfolio progress to clinical PoC	
	<input checked="" type="checkbox"/>	ARGX-109		ARGX-115	<input checked="" type="checkbox"/>	ARGX-113 (Ph2 2017) <input type="checkbox"/>
	<input checked="" type="checkbox"/>	ARGX-112		ARGX-111	<input type="checkbox"/>	ARGX-110 (Ph2 2017) <input type="checkbox"/>
	<input checked="" type="checkbox"/>	ARGX-116				

Value inflection point

# Deep pipeline in cancer and severe autoimmunity

		Drug candidate	Target	Indication	Pre-clinical	Phase 1	Phase 2
Autoimmune diseases		ARGX-113	FcRn	Myasthenia Gravis			
				Immune Thrombocytopenia			
				Chronic autoimmune disease			
					2H 2017		
Cancer immunotherapy		ARGX-110	CD70	Acute Myeloid Leukemia			
				T-Cell Lymphoma			
Metastatic cancer		ARGX-111	c-MET	Solid tumors Blood cancer			
		Discovery Undisclosed		Multiple			
Partnered, non-dilutive income		ARGX-115	GARP	Cancer Immunotherapy			
		ARGX-109 Gerilimzumab	IL-6	Autoimmunity			
		ARGX-112	IL-22R	Skin inflammation			
		Multiple		Numerous rare diseases			
		ARGX-116	ApoC3	Dyslipidemia			



**ARGX-113: Advancing  
to clinical proof of  
concept**

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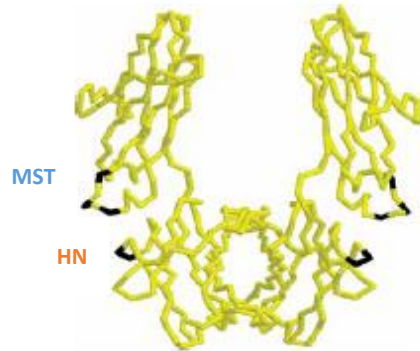
# ARGX-113: Lead program targeting autoimmune diseases

Mechanism of action – antagonizing FcRn

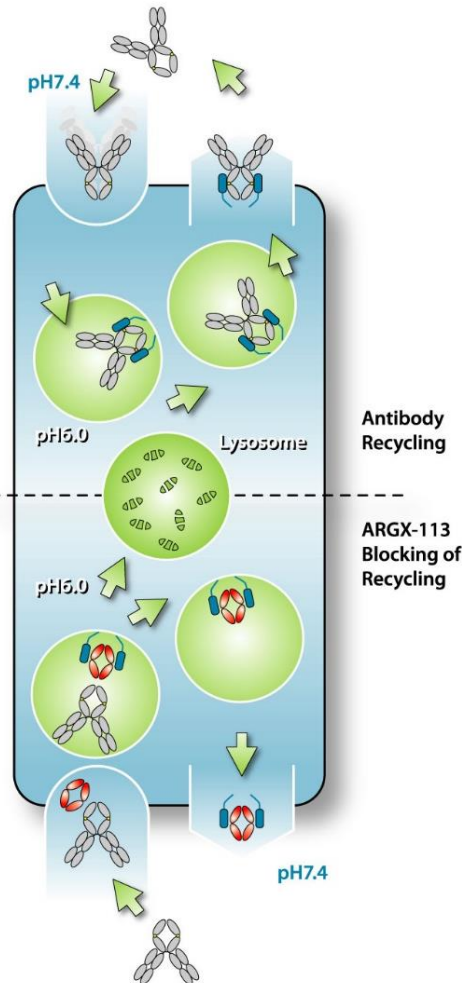
## Proprietary Fc mutations



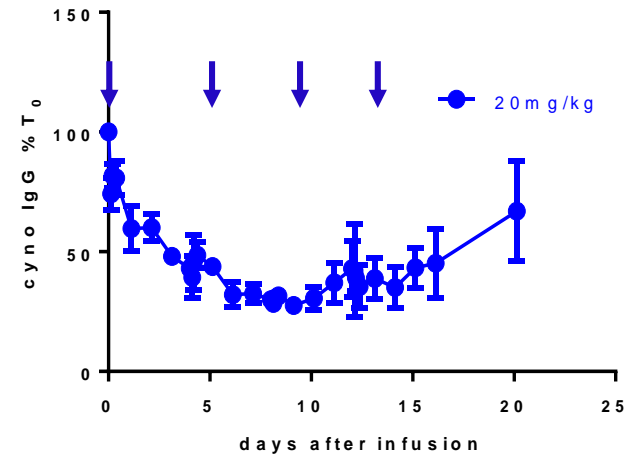
ABDEG™



## Block IgG recycling



## Repeat dose ARGX-113



- Observed saturation of PD effect at doses  $\geq 20$  mg/kg
- Repeat dosing > single dose



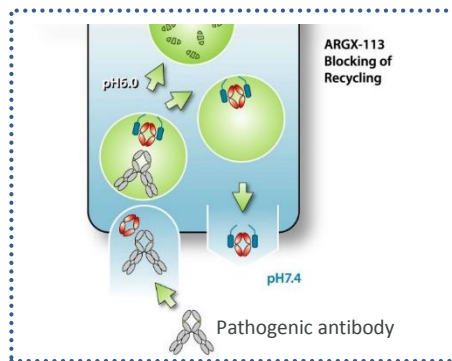
Engineering the Fc region of immunoglobulin G to modulate *in vivo* antibody levels

Carlos Vaccaro<sup>1</sup>, Jinchun Zhou<sup>1</sup>, Raimund J Ober<sup>1,2</sup>, Sally Ward<sup>1</sup>

NATURE BIOTECHNOLOGY | VOLUME 23 | NUMBER 10 | OCTOBER 2005

# ARGX-113: Pipeline-in-product opportunity

## Prioritizing IgG mediated diseases



### Solid biology rationale

Pathogenic IgGs proven to mediate disease



### Feasible for biotech

Orphan potential  
Economically viable  
Clinical & Regulatory path



### Proof of concept value

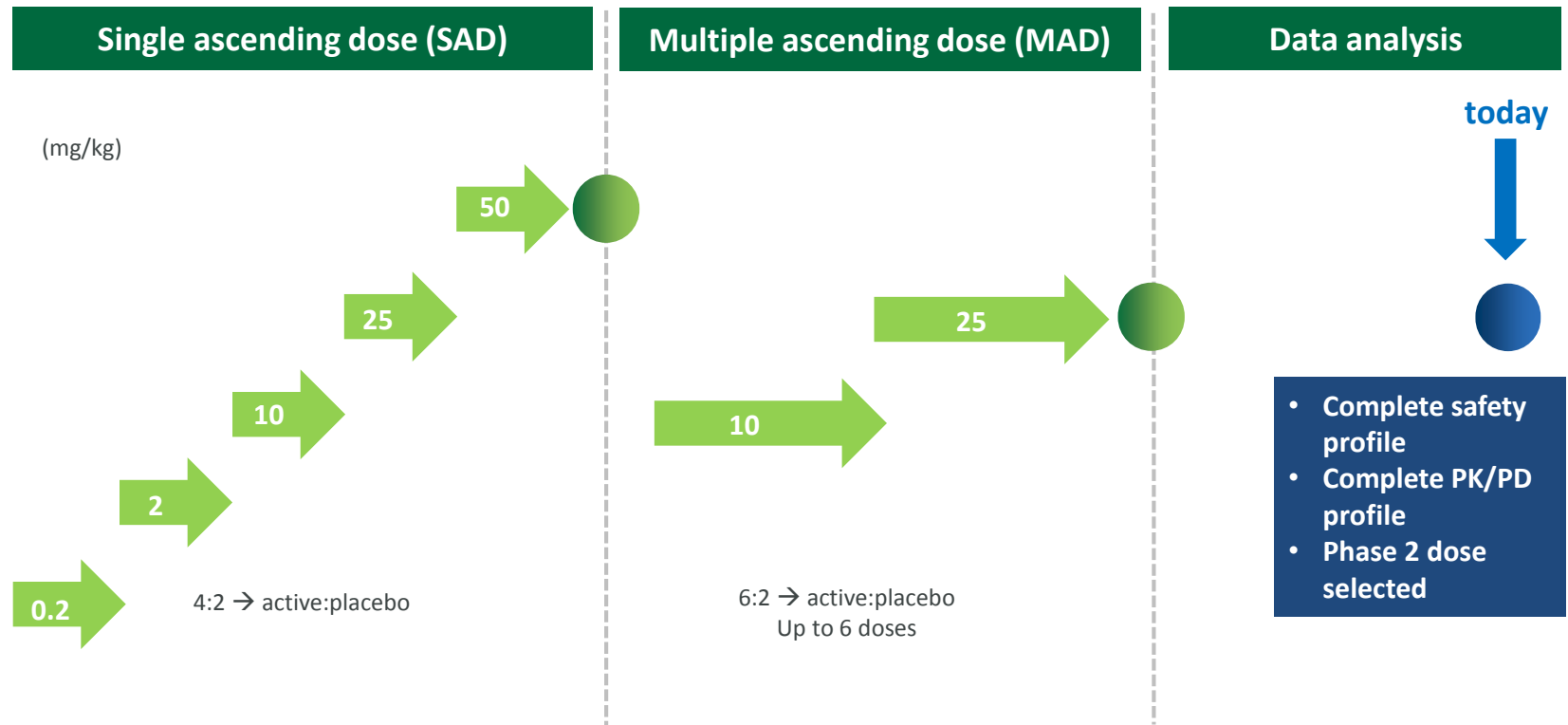
Spill-over effect into adjacent indications



- Myasthenia Gravis
- Immune Thrombocytopenia
- Pemphigus
- Bullous Pemphigoid
- Epidermolysis Bullosa Acquisita
- Scleroderma
- Anca Vasculitis
- Lupus
- Multiple Sclerosis
- Rheumatoid Arthritis
- Other

# ARGX-113: Favorable safety and tolerability profile observed

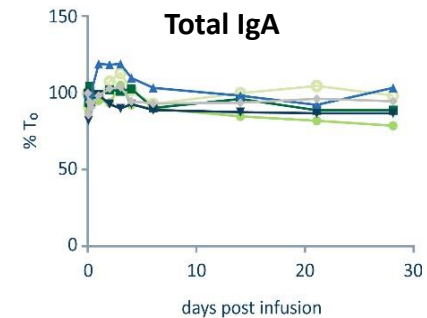
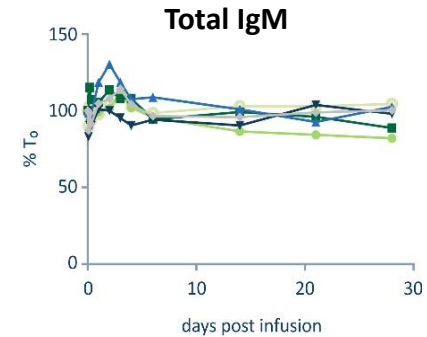
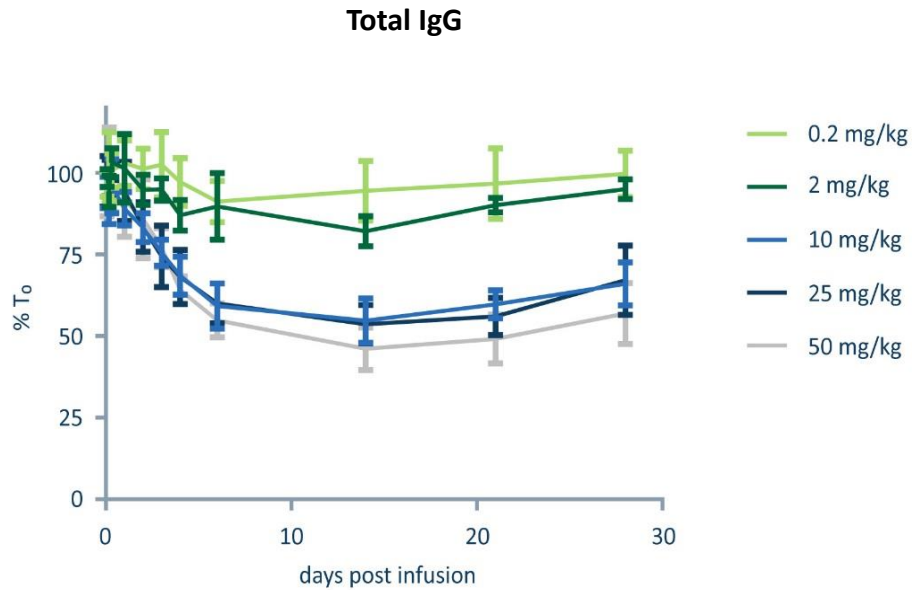
## Phase I study design & status



- Double-blind, placebo-controlled Phase I clinical trial in healthy volunteers
- SAD & MAD dosing completed according to plan (62 healthy volunteers in total)
- Reported to be well tolerated in single and multiple doses of up to 25 mg/kg

# ARGX-113: Selective IgG reduction

Single ascending dose escalation study (SAD) in healthy volunteers

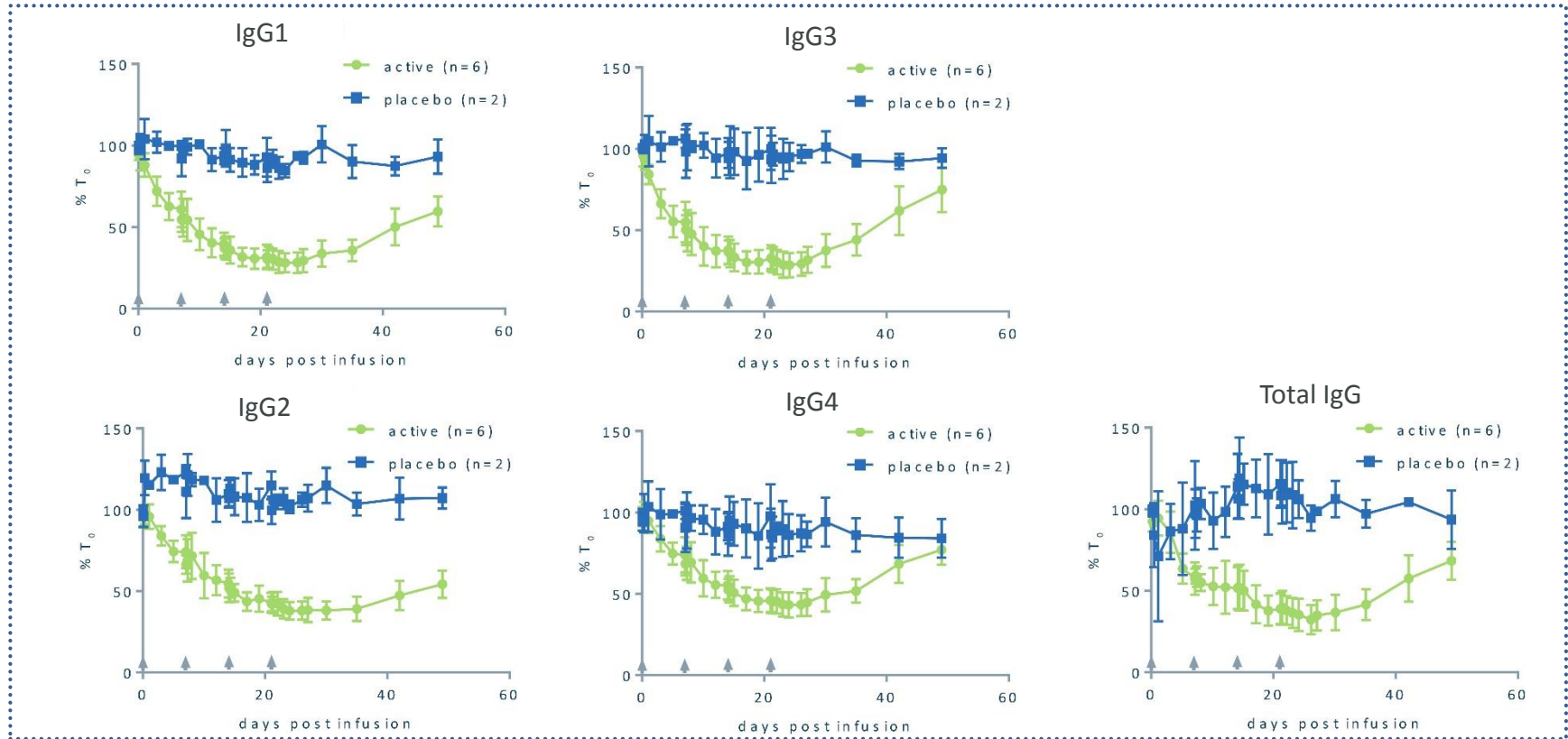


- Single 2h infusion: selective IgG reduction, not affecting IgM/IgA and albumin levels (not shown)
- Maximal PD effect (~50% IgG reduction) as of 6 days after infusion
- Low IgG levels maintained for more than four weeks
- Saturation of PD effect observed at 10 mg/kg dose

# ARGX-113: Potent reduction of IgGs across isotypes

PD data multiple ascending dose (MAD) study

Dosing: 10 mg/kg, every 7 days



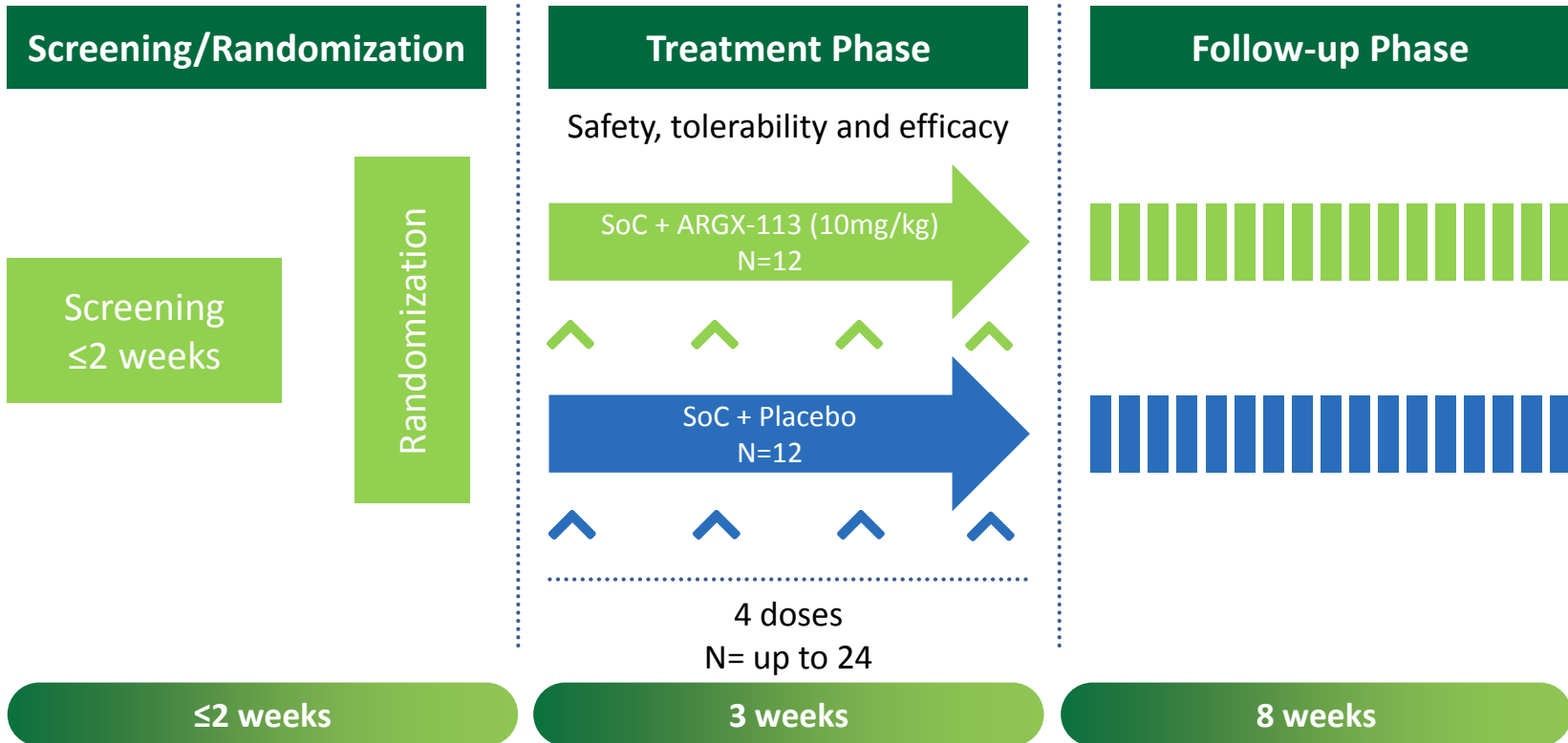
- Meaningful IgG reduction: 50% achieved in 1 week; up to 85% maximum reduction
- After the last dosing, IgG levels remain reduced by 50% or more for a period of 3 weeks
- After the last dosing, IgG levels return to baseline in > 1 month
- Comparable data for 25 mg/kg, every 7 days (data not shown)

Source: argenx data – blinded, uncleaned from HV study

# ARGX-113 in MG: Phase II trial design

First patient dosed

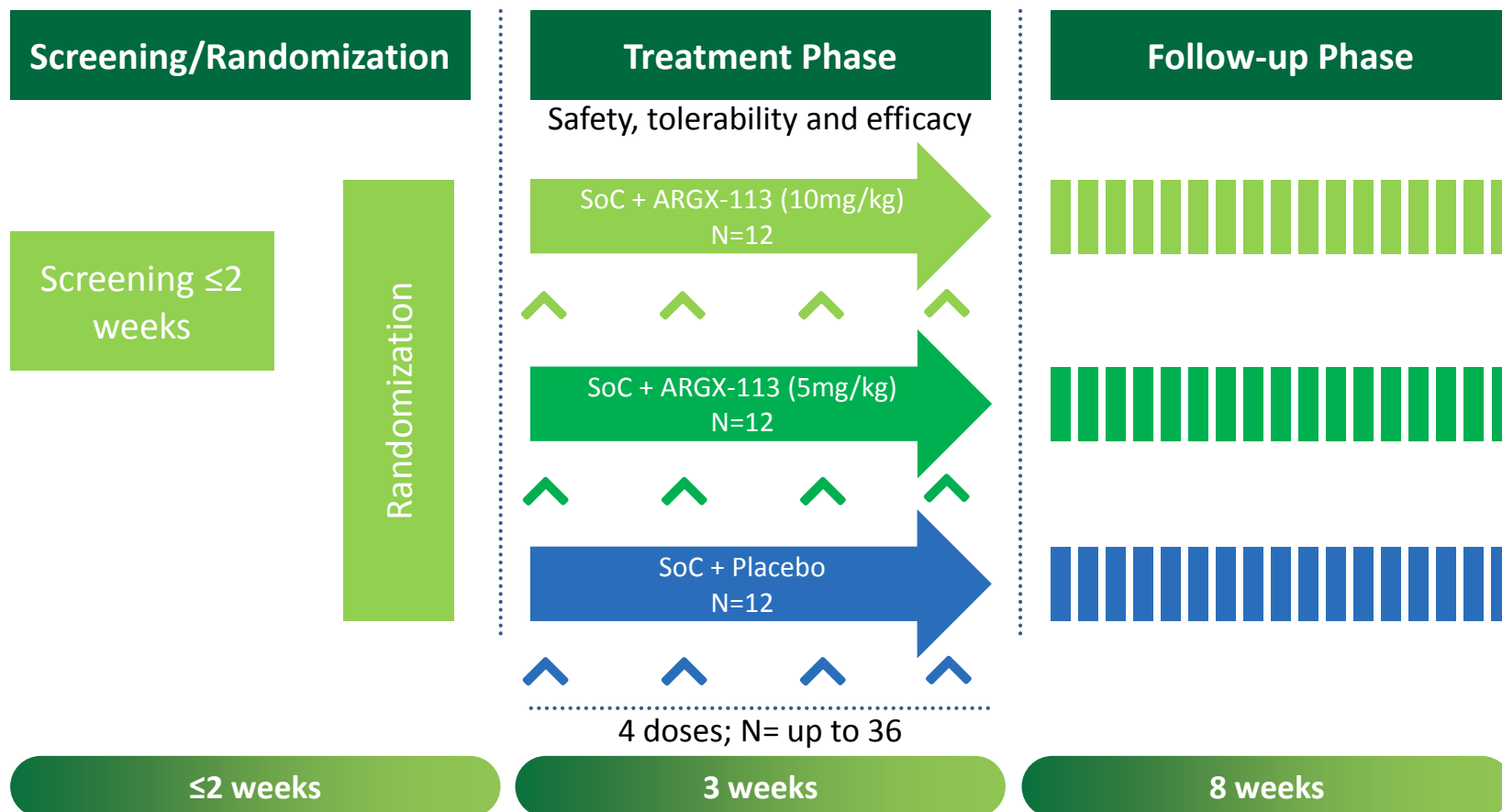
- Population: Autoimmune MG patients with generalized muscle weakness with total MG-ADL score  $\geq 5$  with more than 50% of this score attributed to non-ocular items



- Primary Objectives: Evaluate safety and tolerability
- Secondary Objectives: Evaluate efficacy, impact on quality of life and immunogenicity  
Assess pharmacokinetics (PK) pharmacodynamic (PD) marker

# ARGX-113 in ITP: Phase II trial design

- Population: ITP patients with platelet levels  $< 30 \times 10^9/L$

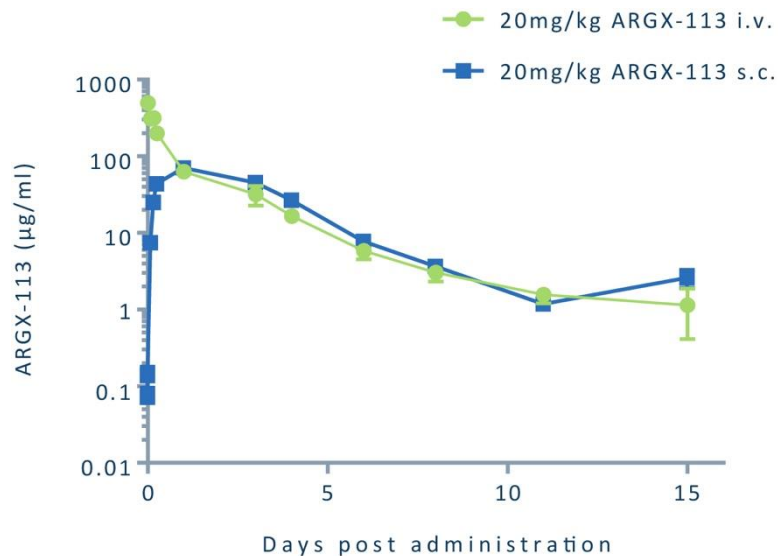


- Primary Objectives: Evaluate safety and tolerability
- Secondary Objectives: Evaluation of efficacy based on platelet counts, use of rescue treatment and bleeding events  
Assess pharmacokinetics (PK) and pharmacodynamic (PD) effect  
Evaluate immunogenicity

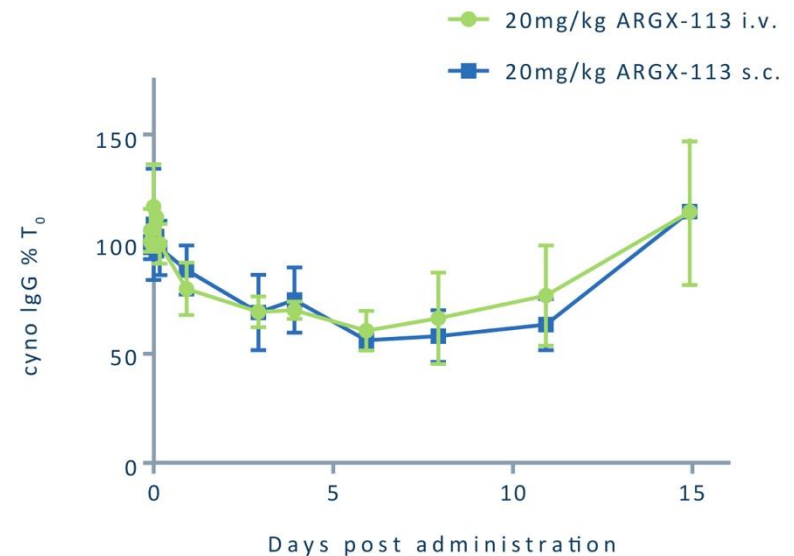
# ARGX-113: Feasibility subQ dosing

Cynomolgus PoC: comparable PD and PK profiles for IV and subQ administration

## PK single dose administration: IV vs subQ




## PD single dose administration: IV vs subQ



- IV versus subQ dosing in preclinical studies demonstrated:
  - Comparable half life
  - Favorable bio-availability of the compound in subQ dosing
  - Comparable reduction of IgGs with single dose; up to 50%



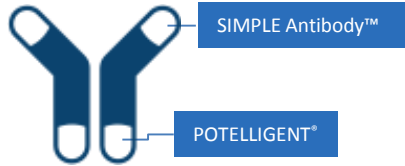


ARGX-110: Phase I/II  
mono & combo  
therapy

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# ARGX-110: targets CD70

3 distinct modes of action to address tumor cell



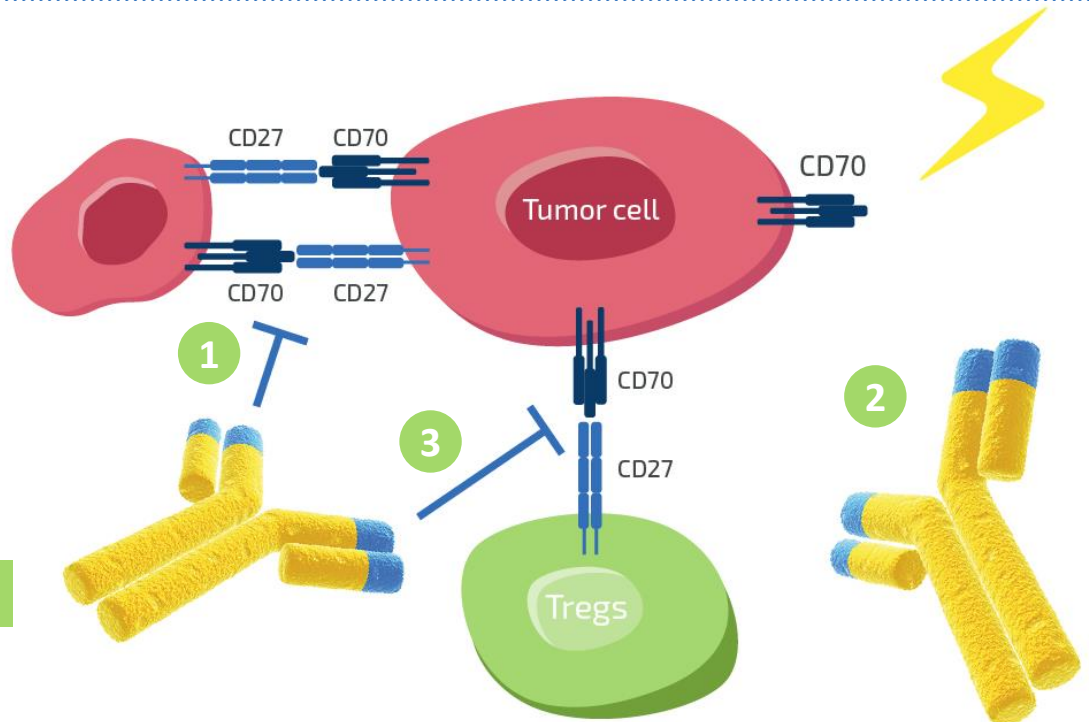
1. Block tumor growth signal



2. Kill tumor



3. Restore immune surveillance



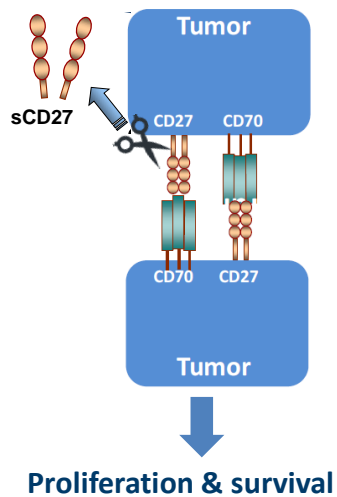
*Prof. Ochsenbein won the 'Otto Naegeli Prize 2016', the most highly esteemed biomedical award in Switzerland.*

*"Of particularly great importance was the discovery that the interaction of CD70 with CD27 and subsequent signaling events has great therapeutic potential for the development of new, original methods of cancer treatment using immunotherapy."*

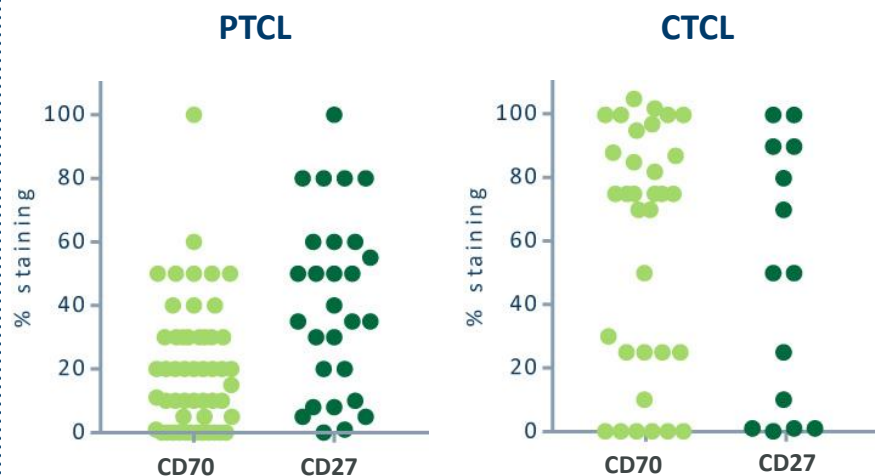


# ARGX-110: CD70/CD27 pathway highly relevant in TCL

## CD70/CD27 on tumor cells

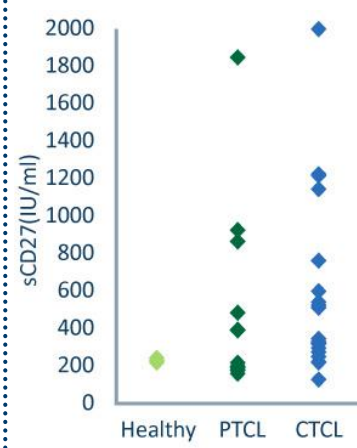


## IHC of CD70/CD27 expression in TCL biopsies



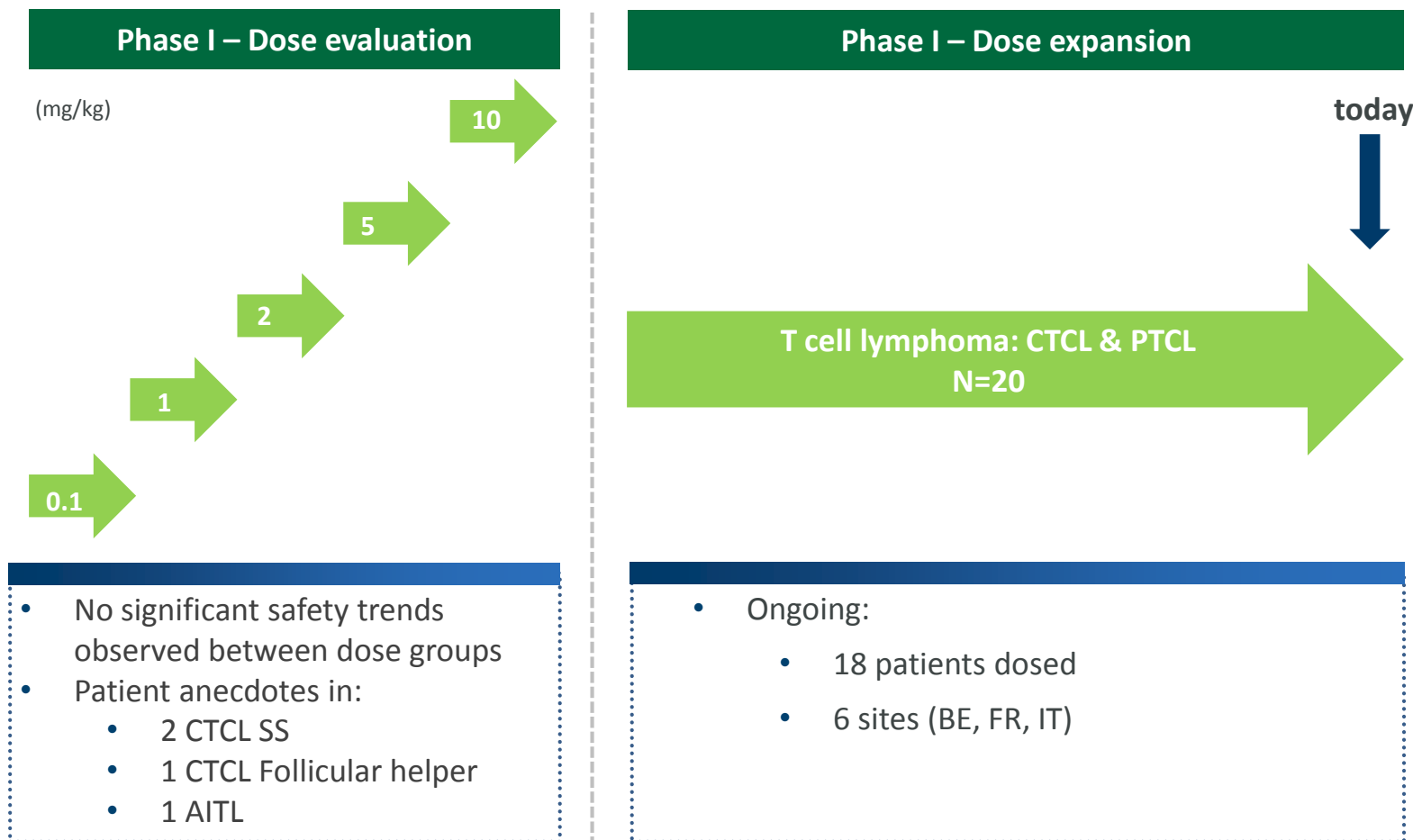
Source: argenx data

## sCD27 levels in TCL patient



- CD70/CD27 strongly overexpressed across different TCL types
- Elevated sCD27 levels suggest strong pathway activity in TCL

# ARGX-110: Phase I trial overview



# Overview CTCL patients

## ARGX-110 Phase Ib

### CTCL in Expansion Cohort 2 (1 mg/kg q3w)

Patient / indication	Number of treatment cycles received <sup>1</sup>																Best response <sup>2</sup>
	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	
CTCL follicular T helper like																	Progressive disease
CTCL panniculitis*																	Partial response
CTCL-MF/SS (+PTCL-NOS <sup>3</sup> )																	Stable disease
CTCL-MF																	Stable disease
CTCL-MF																	Stable disease
CTCL-MF*																	Partial response
CTCL-MF																	Progressive disease
CTCL-SS																	Progressive disease
CTCL-SS																	Partial response
CTCL-SS																	Progressive disease

Data presented @ ASH, Dec 2017

1 Each cycle is three weeks.  
 2 Based on the modified Severity Weighted Assessment Tool, or mSWAT, a widely-used method for scoring of skin lesions in CTCL. The mSWAT score takes into account the number and severity of skin lesions as well as the total body surface area affected. A stable disease score is given if the mSWAT score does not increase by more than 25%. A partial response is deemed to have occurred with a 50% reduction in the mSWAT score. A complete response requires a 100% reduction in mSWAT score.  
 3 NOS: not other specified. PTCL-NOS is the most common TCL subtype.  
 \* Patient currently on study.

- Encouraging signs of clinical activity in expansion cohort 2: 2/10 SD and 3/10 PR
- Patients on study up to cycle 12
- 2/3 SD in dose escalation cohort



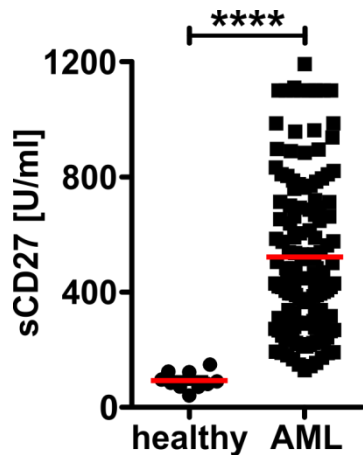
**ARGX-110 in AML**

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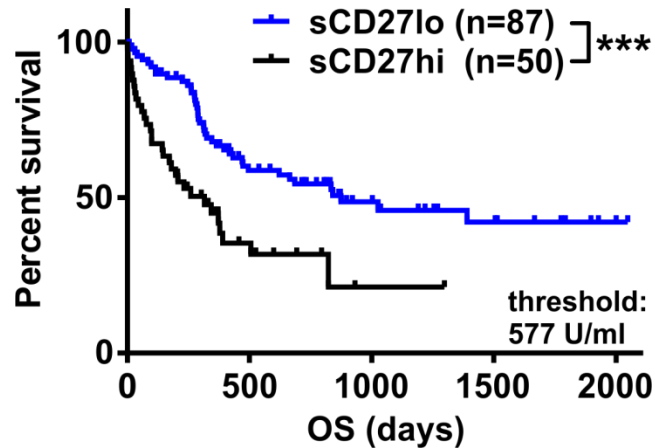
# ARGX-110: Rationale in AML

Indication for CD70/CD27 signaling in AML patients

## sCD27 serum levels



## sCD27 serum levels → poor prognosis



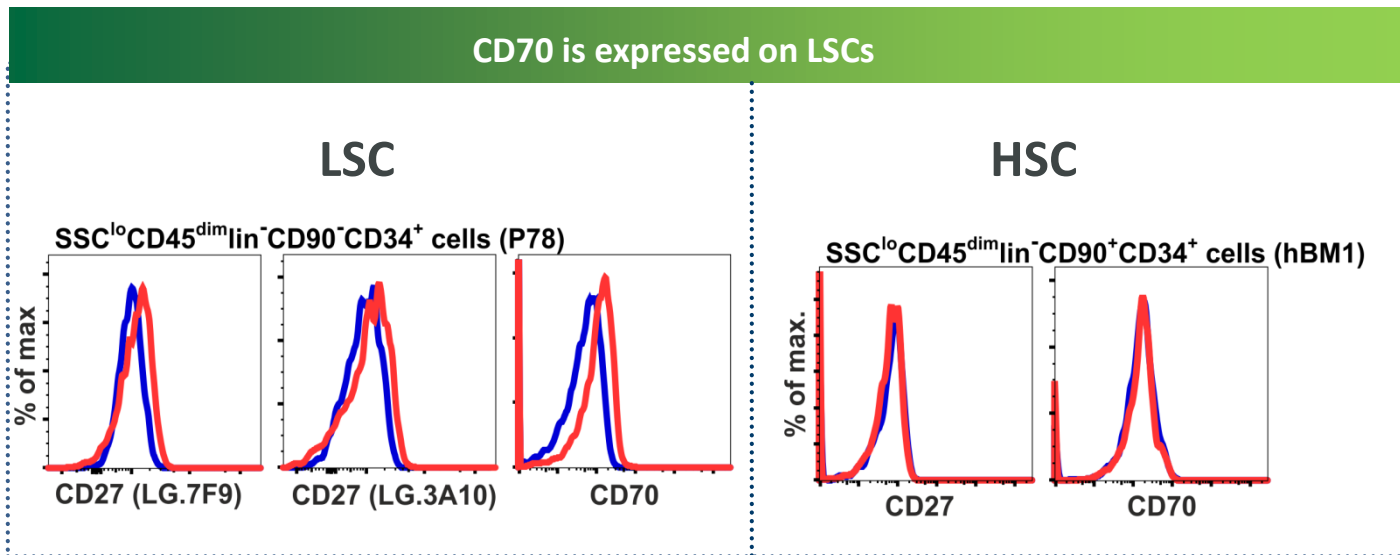
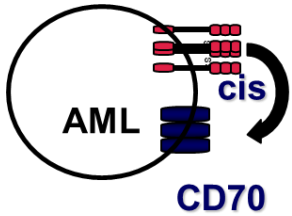
parameter	HR (95% CI)	p-value
sCD27	2.17 (1.34-3.50)	0.0016
risk group	1.69 (1.29-2.38)	0.0024
age	1.03 (1.01-1.05)	0.0050
BM blast %	0.99 (0.98-1.00)	0.1259
blood blast %	1.00 (0.99-1.01)	0.9329
blood leukocyte #	1.00 (0.99-1.01)	0.6558

- sCD27 serum levels:
  - biomarker for active CD70/CD27 signaling in vivo
  - increased in serum of AML patients
  - independent negative prognostic marker across entire patient population



# ARGX-110: Rationale in AML

CD70/CD27 biology highly involved in newly diagnosed AML

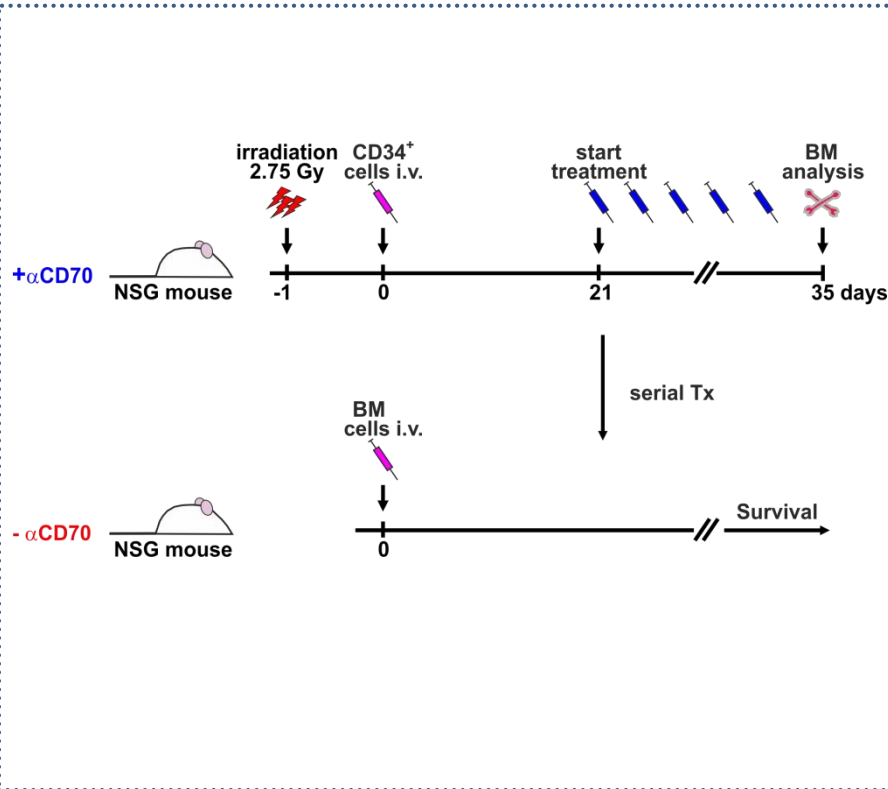


- CD70/CD27 selectively overexpressed on LSCs and not on hematopoietic stem cells (HSC)
- CD70 expressed on ~100% of AML blasts, majority of malignant cells are CD70/CD27 double-positive
- ARGX-110: selective targeting of LSCs

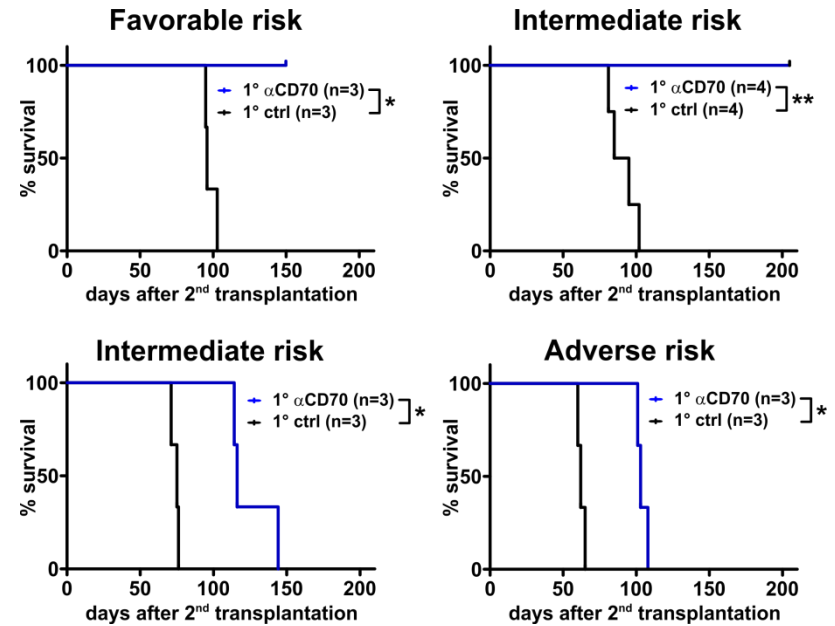


# ARGX-110: Periodic treatment

Long-term effects *in vivo*



BM of  $\alpha$ CD70-treated contain fewer cells that transmit the disease (LSCs) in vivo

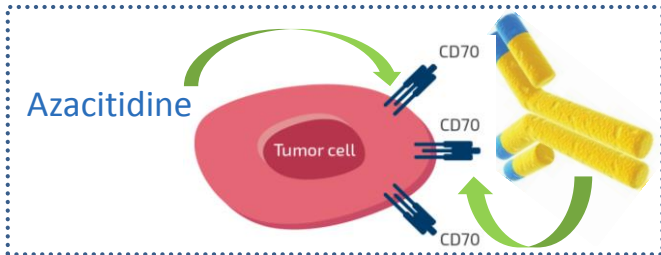


- Increased survival after secondary transplantation of AML BM cells from primary recipients transiently treated with  $\alpha$ CD70 Ab
- Increased survival observed for AML blasts taken from all 3 AML risk categories



# Phase I/II Combo ARGX-110 & Azacitidine: trial design

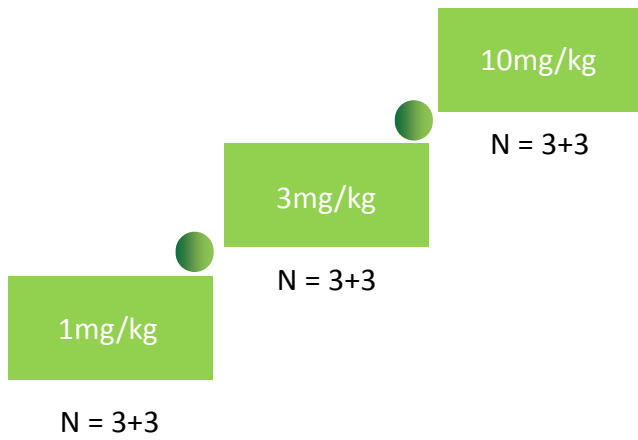
First patient dosed



## Phase I – Dose escalation

Safety and tolerability

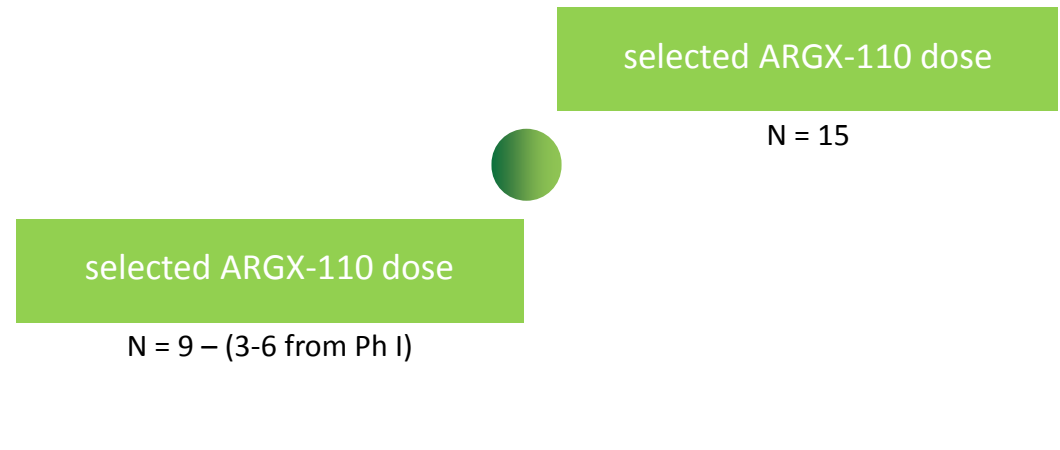
Vidaza = 75 mg/m<sup>2</sup> (standard of care)



N = up to 18

## Phase II – Proof of concept

Efficacy



N = up to 24

- Population: untreated AML & high risk of myelodysplastic syndrome, eligible for AZA
- Design: open-label, non-controlled, non-randomized



**ARGX-115**

**Cancer Immunotherapy**

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# AbbVie option deal

## Key elements

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### Financial terms

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- \$ 40MM upfront
- Preclinical milestones 2x \$10MM
- Up to \$ 625MM development, regulatory and commercial milestones
- Tiered, up to lower teens royalty payments on net product sales

### Deal highlights

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- Responsible for delivering IND data package
- GARP-based research programs creating further product opportunities
- Retains rights to combine ARGX-115 with own pipeline programs
- Co-promotion rights in EU/Swiss Economic Area



- Option to exclusive development and commercialization license
- Further GARP-based research funding once first preclinical milestone met
- Right to license additional therapeutic programs resulting from this research - additional milestone and royalty payments on resulting products



# Financials

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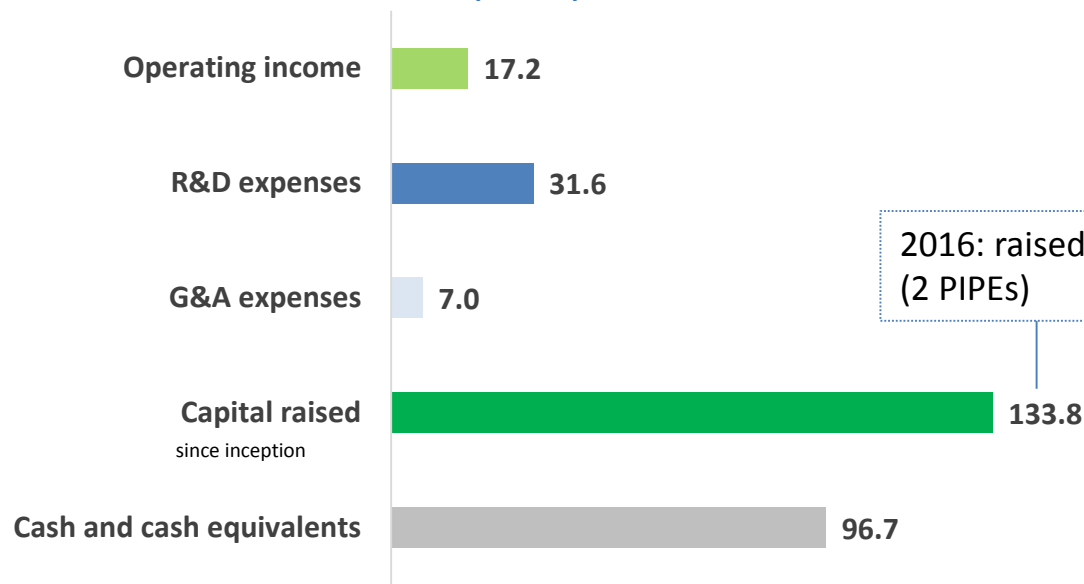
## argenx HY 2016 financials

in thousands of €	Year ended December 31, 2015	Year ended December 31, 2016	Variance
Revenue	6,854	14,713	7,859
Other operating income	3,101	2,439	(662)
<b>Total operating income</b>	<b>9,955</b>	<b>17,152</b>	<b>7,197</b>
Research and development expenses	(20,635)	(31,557)	(10,922)
General and administrative expenses	(4,925)	(7,011)	(2,086)
<b>Operating loss</b>	<b>(15,605)</b>	<b>(21,416)</b>	<b>(5,811)</b>
Financial income	112	73	(39)
Exchange gains/(losses)	181	(31)	(212)
<b>Total comprehensive loss</b>	<b>(15,312)</b>	<b>(21,374)</b>	<b>(6,062)</b>
Net increase (decrease) in cash, cash-equivalents and current financial assets *	(13,645)	54,402	68,047
<b>Cash, cash-equivalents and current financial assets at the end of the period</b>	<b>42,327</b>	<b>96,729</b>	<b>54,402</b>

(\*) compared to year end 2014 and 2015 respectively

# Well capitalized to execute strategic plan

## Operating income, expenses & capital raised Year ended December 31, 2016 (MEUR)

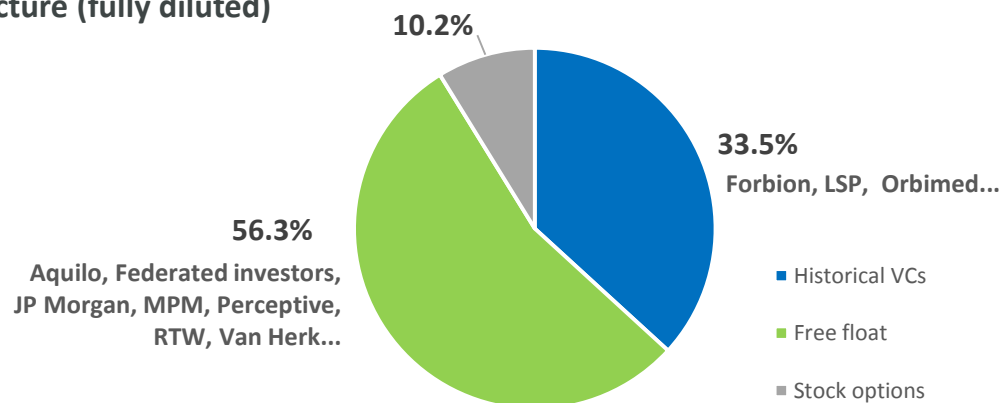


2016: raised € 46MM  
(2 PIPEs)



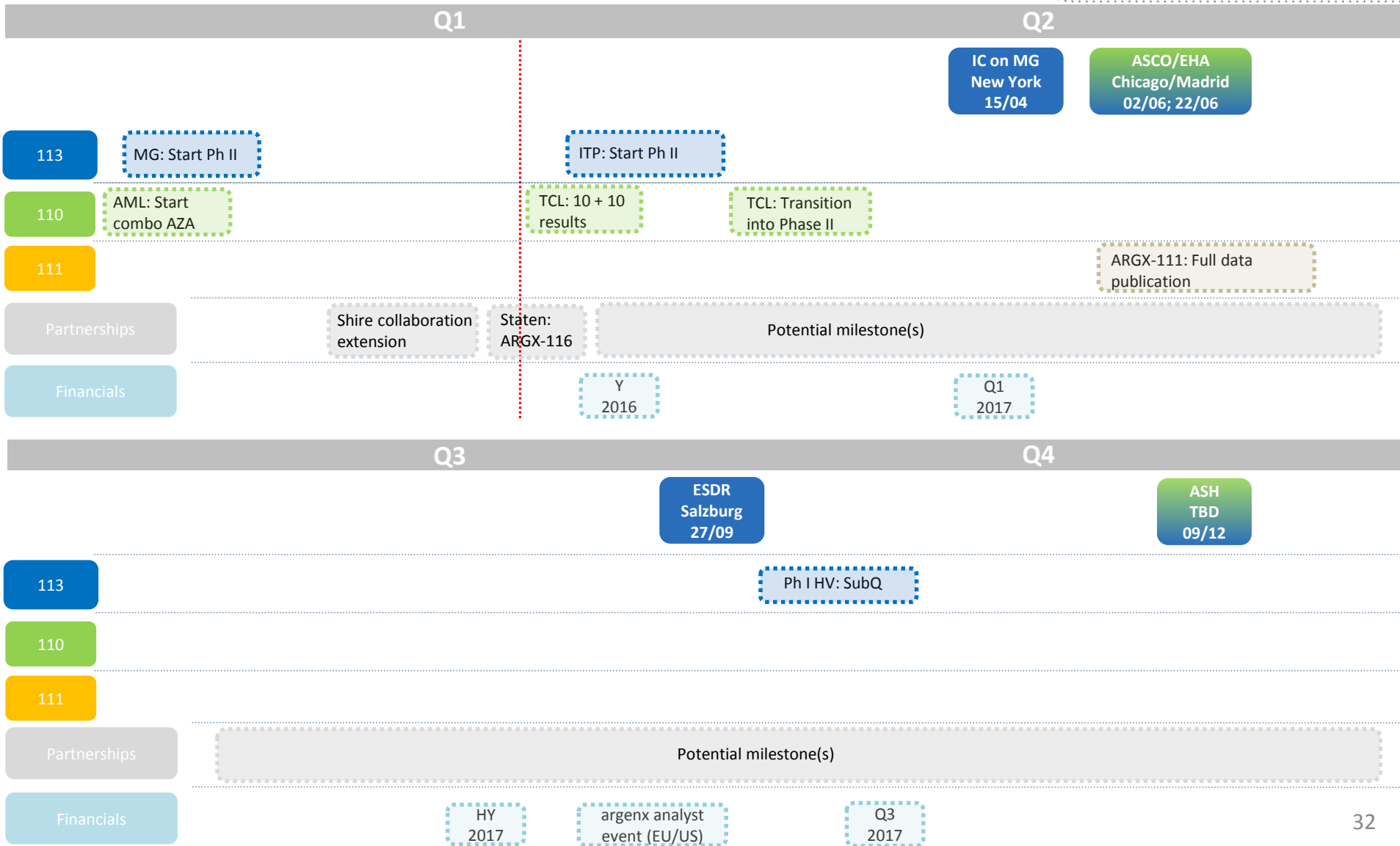
58 employees  
. 48 R&D  
. 10 G&A

## Shareholder structure (fully diluted) Jan 2017



Outstanding shares: 20,126,479  
Market Cap: ~ € 333M

# Communications plan 2017







**Thank you!**

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