Advancing ARGX-113 and ARGX-110 to clinical proof of concept

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4 December 2016

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Agenda

11:00 AM	**Introduction**
	- Hans de Haard, CSO argenx
11:10 AM	**ARGX-113 targeting FcRn**
	Advancing to clinical proof of concept in ITP
	- Nicolas Leupin, CMO argenx
	- Hans de Haard, CSO argenx
11:35 AM	**ARGX-110 targeting CD70**
	Phase 1 mono & combo therapy in TCL & AML
	- Nicolas Leupin, CMO argenx
	- Carsten Riether, University of Bern
12:15 AM	**Q&A**


Hans de Haard


Nicolas Leupin


Carsten Riether

Introduction

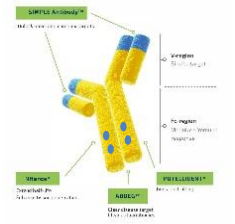
Creating value from highly differentiated antibodies

Rich proprietary pipeline

- Cancer & 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 - € 103Mio Sept 2016
  (AbbVie € 35MM April 2016, Private Placement € 30MM June 2016)
- > € 2B potential future income from partnerships

Proprietary pipeline in cancer and severe autoimmunity

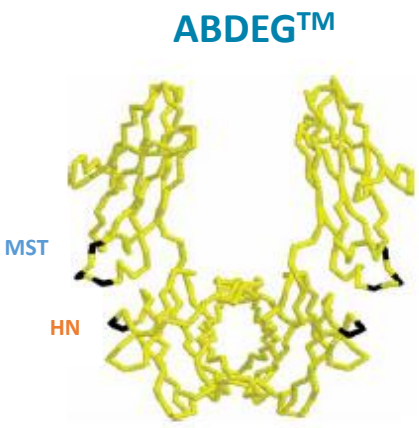
		Drug candidate	Target	Indication	Pre-clinical / Phase 1 / Phase 2
Autoimmune diseases		ARGX-113	FcRn	Myasthenia Gravis Immune Thrombocytopenia	4Q 2016 1Q 2017
Cancer immunotherapy		ARGX-110	CD70	T-Cell Lymphoma Acute Myeloid Leukemia	4Q 2016 4Q 2016
Metastatic cancer		ARGX-111	c-MET	Solid tumors Blood cancer	
		Discovery Undisclosed		Multiple	
Partnered, non-dilutive income	abbvie	ARGX-115	GARP	Cancer Immunotherapy	
	BIED ROCK BIO	ARGX-109 Gerilimzumab	IL-6	Autoimmunity	
	LEO	Undisclosed		Skin inflammation	
	Shire	Undisclosed		Undisclosed	

ARGX-113: Advancing to clinical proof of concept

ARGX-113: Lead program targeting autoimmune diseases

Mechanism of action – antagonizing FcRn

Proprietary Fc mutations

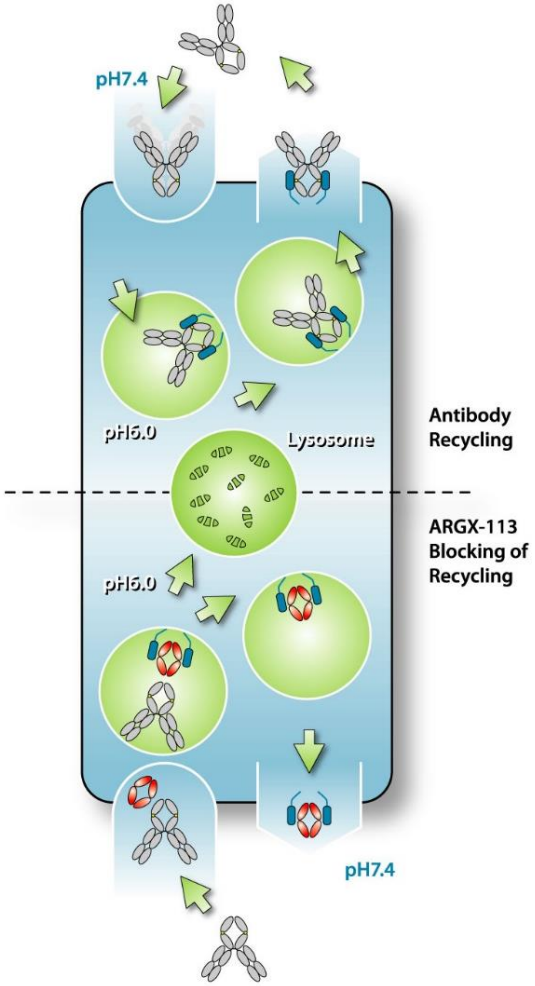


Engineering the Fc region of immunoglobulin G to modulate *in vivo* antibody levels

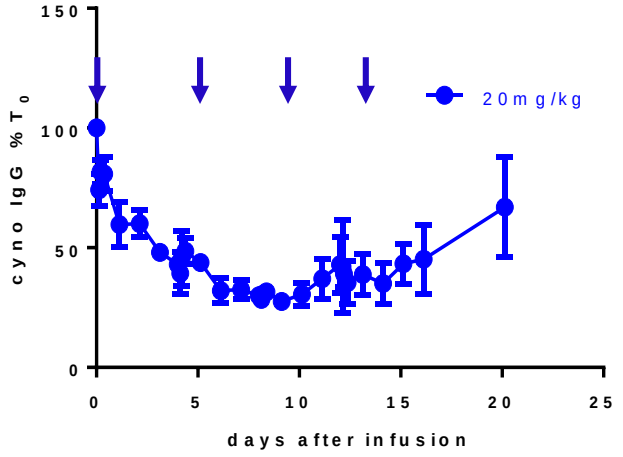
Carlos Vaccaro[1], Jinchun Zhou[1], Raimund J Ober[1,2] & E Sally Ward[1]

NATURE BIOTECHNOLOGY VOLUME 23 NUMBER 10 OCTOBER 2005

Block IgG recycling



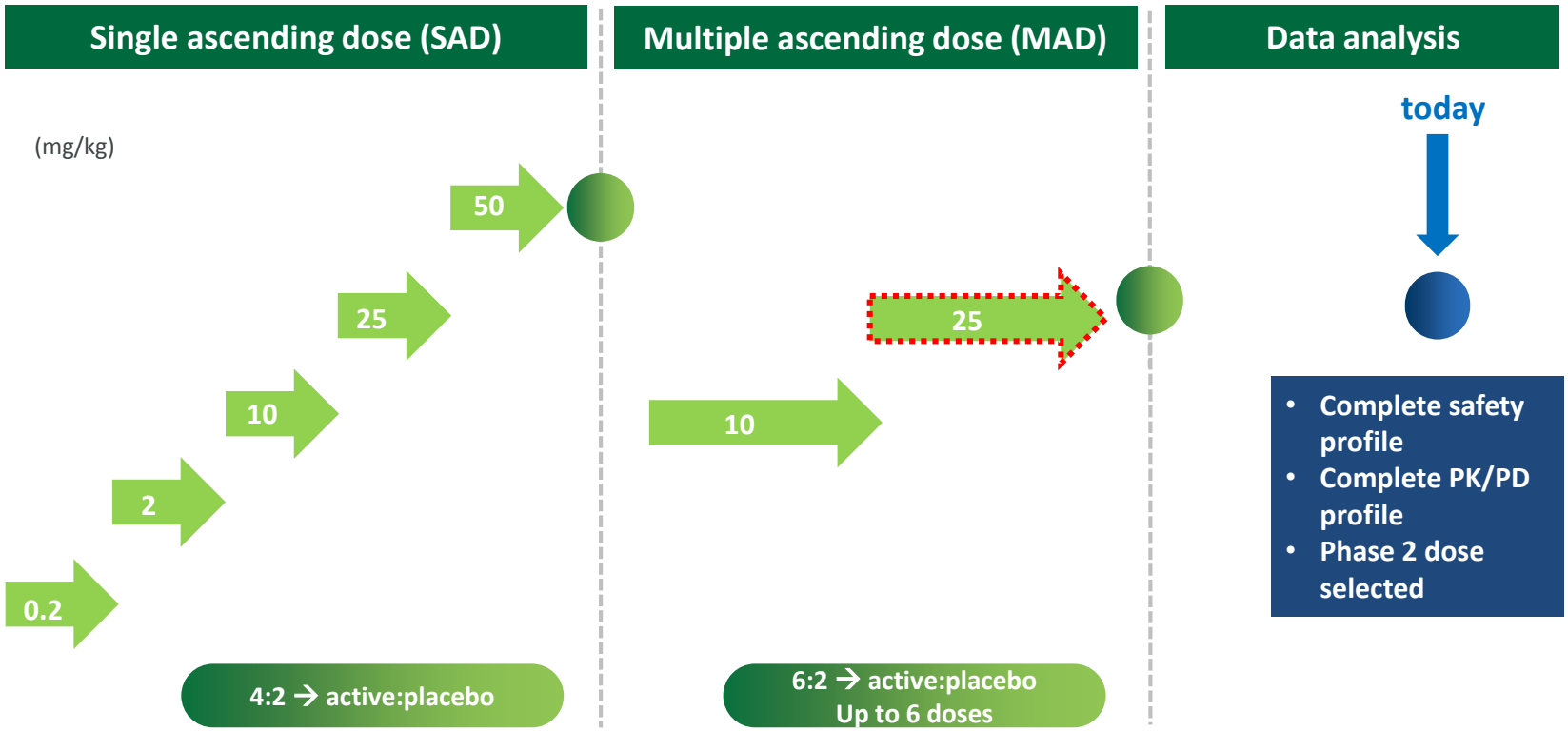
Repeat dose ARGX-113



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

ARGX-113: Favorable safety and tolerability profile observed

Phase I study design & status

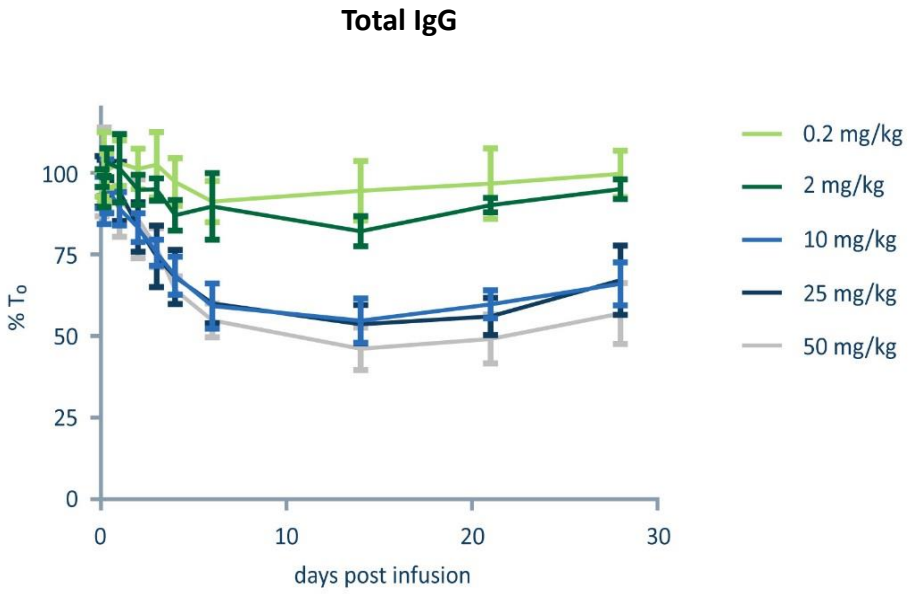


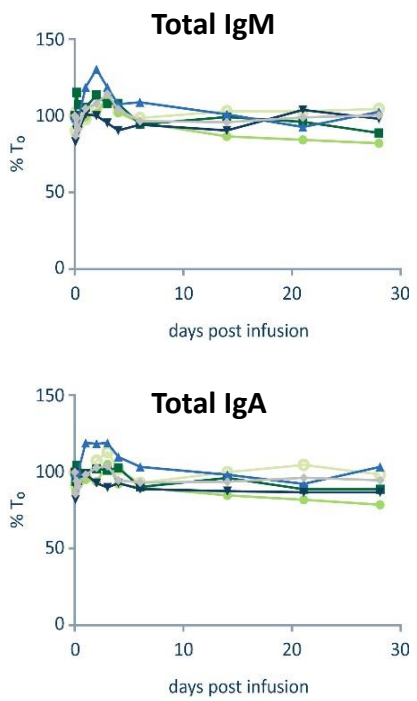
- Double-blind, placebo-controlled study in healthy volunteers
- SAD & MAD dosing completed according to plan (62 healthy volunteers in total)
- Favorable safety and tolerability profile observed

Source: argenx data

ARGX-113: Selective IgG reduction

Single ascending dose escalation study (SAD) in healthy volunteers





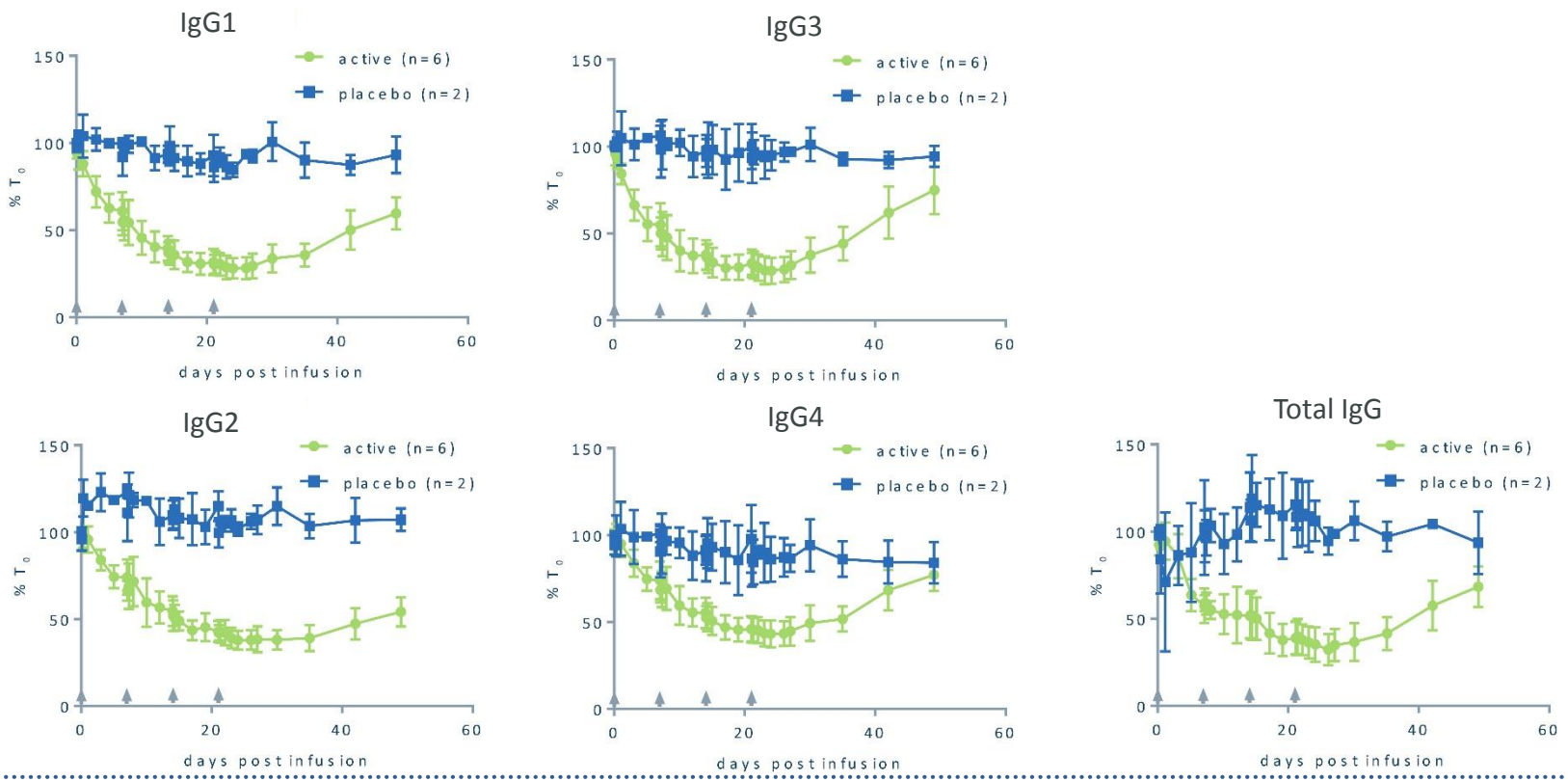
- Single 2h infusion: selective IgG reduction, not affecting IgM/IgA and albumin levels (not shown)
- Maximal PD effect (~50% IgG reduction) as of 6 days after infusion
- Low IgG levels maintained for several weeks
- Saturation of PD effect as of 10 mg/kg dose

Source: argenx data – blinded, uncleaned from HV study

ARGX-113: Potent reduction of IgGs across isotypes

PD data multiple ascending dose (MAD) study

Dosing: 10 mg/kg, every 7 days



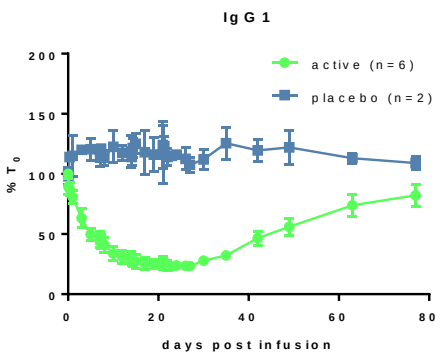
- Clinically meaningful IgG reduction: 50% achieved in 1 week; up to 85% maximum reduction
- After the last dosing, IgG levels remain reduced by 50% or more for a period of 3 weeks
- After the last dosing, IgG levels return to baseline in > 1 month

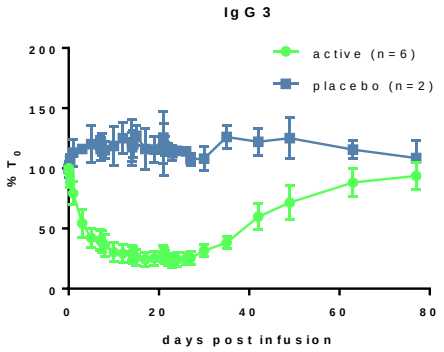
Source: argenx data – blinded, uncleaned from HV study

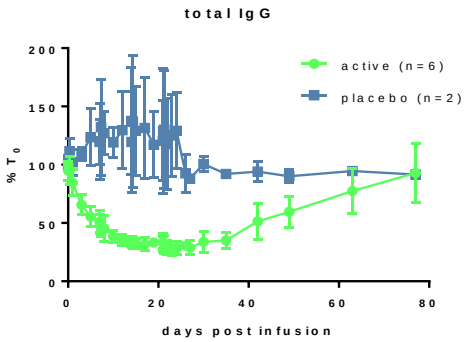
ARGX-113: Potent reduction of IgGs across isotypes

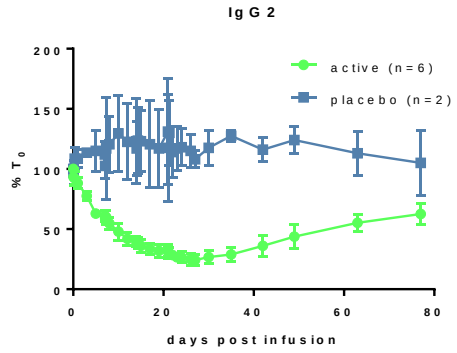
Similar PD pattern with higher concentration

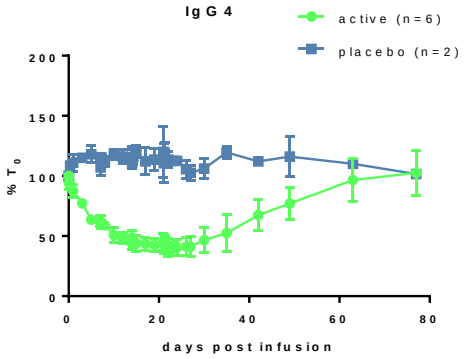
Dosing: 25 mg/kg, every 7 days











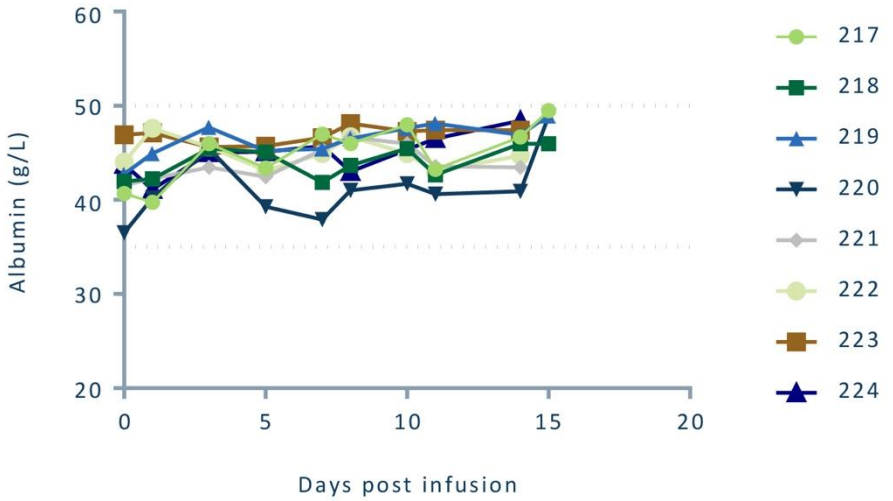
- Clinically meaningful IgG reduction: 50% achieved in 1 week; up to 85% maximum reduction
- After the last dosing, IgG levels remain reduced by 50% or more for a period of 3 weeks
- After the last dosing, IgG levels return to baseline in > 1 month

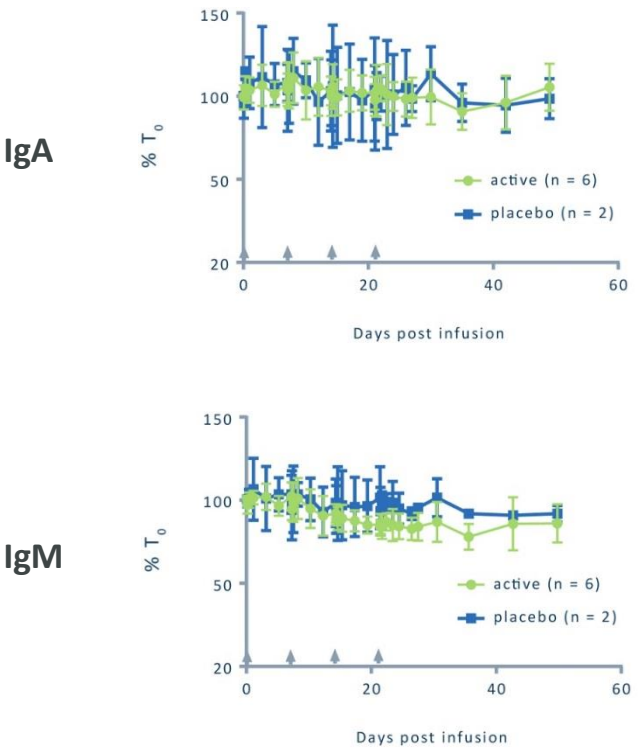
Source: argenx data – blinded, uncleaned from HV study

ARGX-113: Selective reduction of IgGs

Albumin, IgA and IgM levels not affected after multiple dosing

Dosing: 10 mg/kg, every 7 days





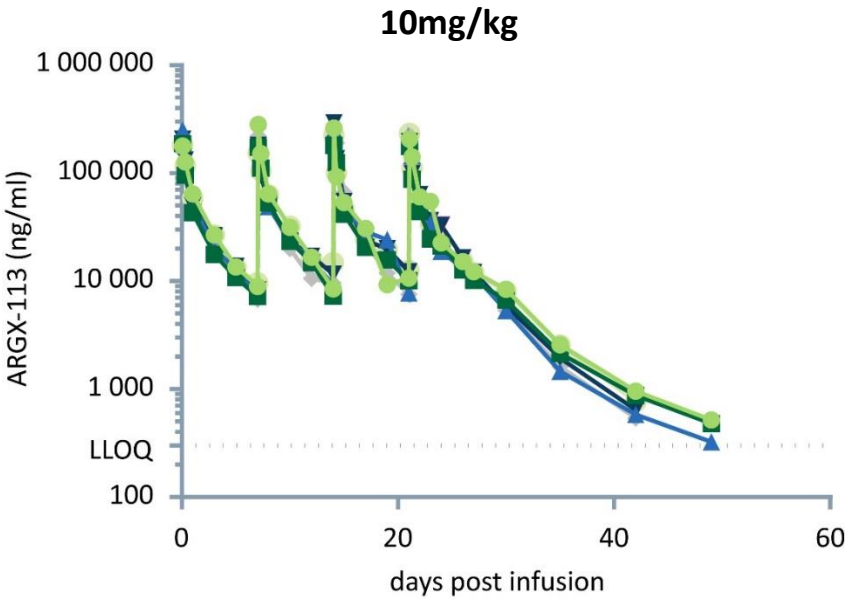
- Albumin, IgA and IgM levels not affected
- Comparable results for all dosing regimens

Source: argenx data – blinded, uncleaned from HV study

ARGX-113: Consistent clearance pattern with half-life 3-4 days

Similar PK pattern for 10mg/kg vs 25mg/kg

Dosing: every 7 days (6 healthy volunteers)



Parameter	Average
C_{max} (µg/ml)	195-202-237-204
$T_{1/2}$ (h)	95

- No significant increase in C_{max} following successive infusions
- PK pattern similar for all subjects
- Terminal half-life 3-4 days (similar to SAD)

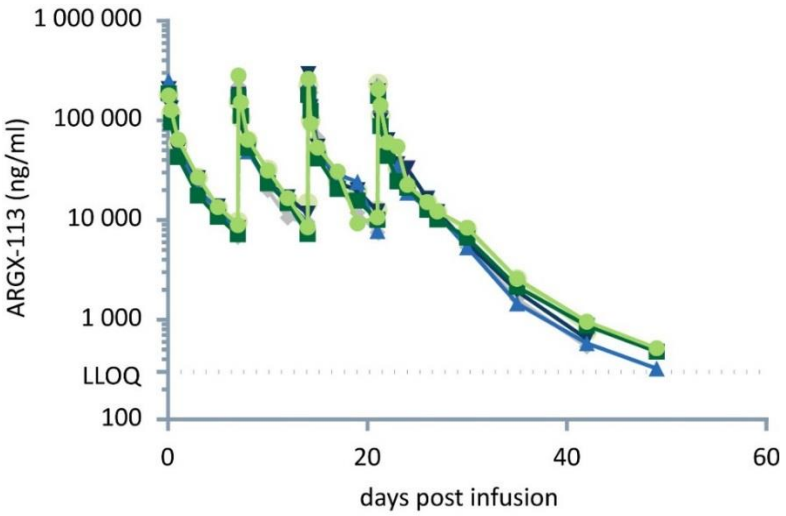
Source: argenx data – blinded, uncleaned from HV study

ARGX-113: Consistent clearance pattern with half-life 3-4 days

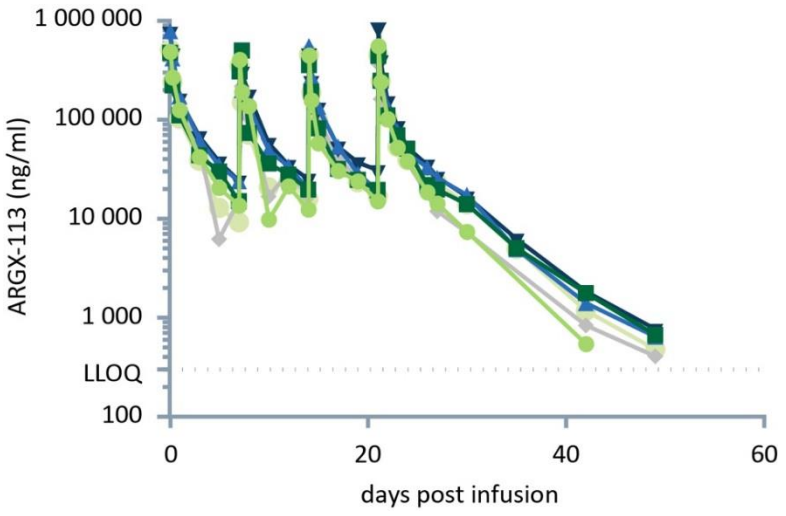
Similar PK pattern for 10mg/kg vs 25mg/kg

Dosing: every 7 days (6 healthy volunteers)

10mg/kg



25mg/kg



- Similar PK pattern for both concentrations
- Maximal PD effect at 10 mg/kg
- → '10 mg/kg every 7 days' **selected dosing regimen** for Phase II clinical trials

Source: argenx data – blinded, uncleaned from HV study

ARGX-113: Favorable safety profile

Across multiple doses and dosing regimes in 68 healthy volunteers

Single ascending dose escalation study (SAD), 0.2, 2.0, 10, 25 and 50 mg/kg

- No cutaneous reactions at injection site
- No infusion related reactions
- No severe or serious adverse event
- No adverse events leading to death

Multiple ascending dose escalation study (MAD), 10 mg/kg q4d and q7d

- No cutaneous reactions at injection site
- No infusion related reaction
- One severe adverse event*
- No adverse events leading to death

*One grade 3 adverse event was declared as serious adverse event, according to investigator likely to be unrelated to study drug

Preliminary, blinded results indicate that IV administration of single and multiple doses of ARGX-113 at doses up to 25 mg/kg is safe and generally well tolerated

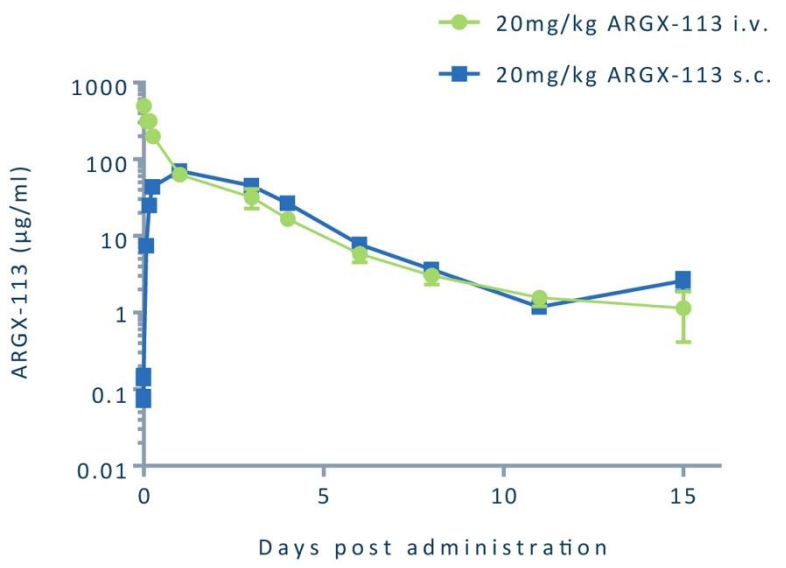
Source: argenx data – blinded, uncleaned from HV study

ARGX-113, further development

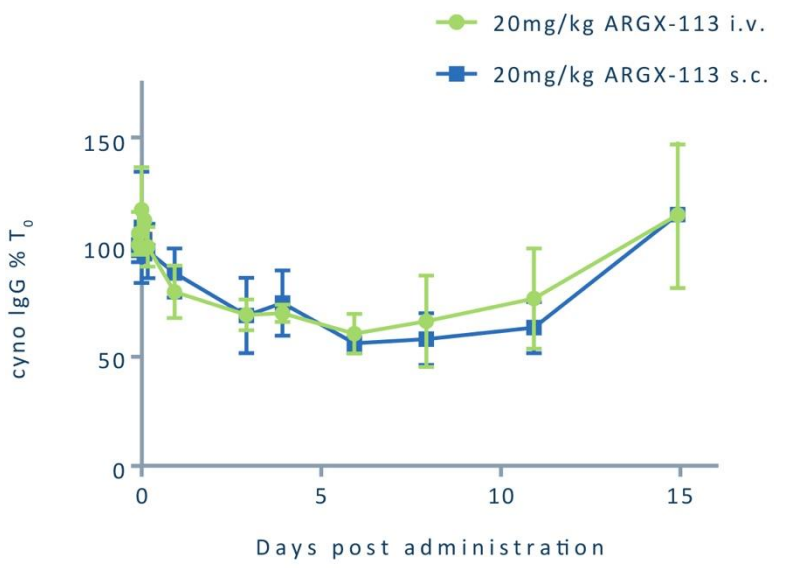
ARGX-113: Feasibility subQ dosing proven

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

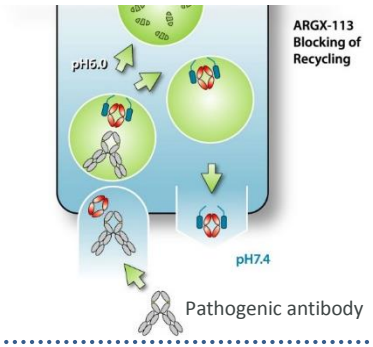


- IV versus subQ dosing:
  - Comparable half life
  - Favorable bio-availability of the compound in subQ dosing
  - Comparable reduction of IgG's with single dose; up to 50%

ARGX-113 in Immune Thrombocytopenia

ARGX-113: Pipeline-in-product opportunity

Prioritizing IgG mediated diseases



Solid biology rationale
Pathogenic IgG's proven to mediate disease

Feasible for biotech
Orphan potential
Economically viable
Clinical & Regulatory path clear

High proof of concept value
Spill-over effect into adjacent indications

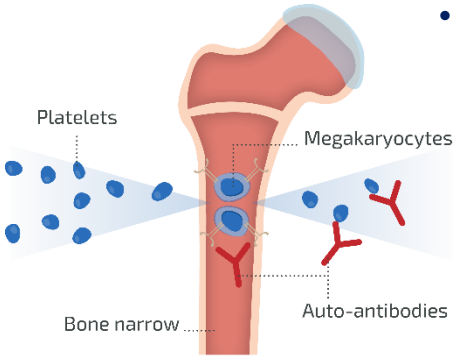
- Myasthenia Gravis
- Immune Thrombocytopenia
- Pemphigus
- Bullous Pemphigoid
- Epidermolysis Bullosa Acquisita
- Scleroderma
- Anca Vasculitis
- Lupus
- Multiple Sclerosis
- Rheumatoid Arthritis
- …

Source: argenx data

Immune thrombocytopenia: Fact sheet

Fatigue Emotional strain Impact on work Fear of bleeding Impact on social activities Bruising

- Rare disease
- Prevalence (US): 50,000 patients
- Female > male
- Highest incidence > 60 years of age



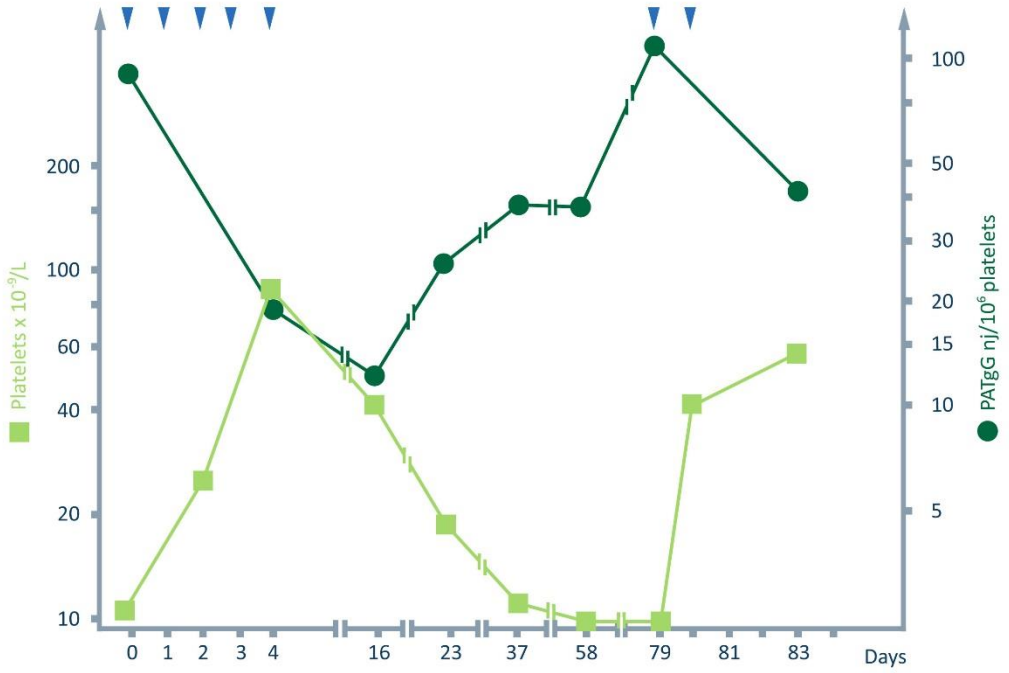
- Caused by auto-antibodies (auto-IgG's) destroying blood platelets:
  - Increased platelet removal
  - Reduced platelet production

- Treatment options:
  - Multiple iterations on corticosteroids & IVIg
  - Immunomodulatory agents
  - TPO-mimetics & splenectomy
- Side effects:

anaphylaxis anorexia backache cancer cataracts depression diabetes fatal hemolysis hepatitis hypertension infection infusion reactions leukoencephalopathy nausea osteoporosis psychosis renal sweating neutropenia thrombosis vomiting weakness

- ARGX-113
  - Potential breakthrough approach to clear pathogenic auto-IgG's
  - Addressing unmet need
    - Elimination of patient symptoms → achieve remission
    - Minimizing side effects of medication
  - Potential use in patients with inadequate response to steroids & in place of IVIg before second line agents

Autoantibody levels (IgGs) correlate with ITP disease score



▼ = IVIg treatment

● = AutoAb

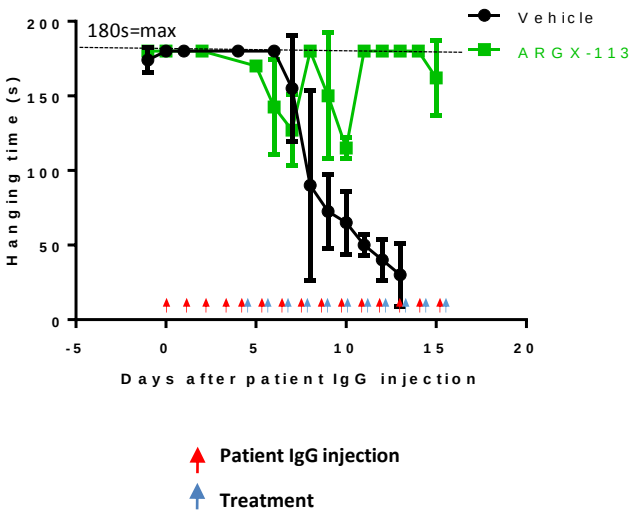
■ = Platelet counts

- ITP: autoantibodies inhibit platelet production and accelerate platelet destruction
- IVIg, plasmapheresis and immunoadsorption: proven clinical efficacy in ITP
- MoA IVIg: lowering autoantibodies results in platelet increase
- Plasmapheresis and immunoadsorption: identical MoA (data not shown)

Winiarski et al. 1983, Scand J Haematol

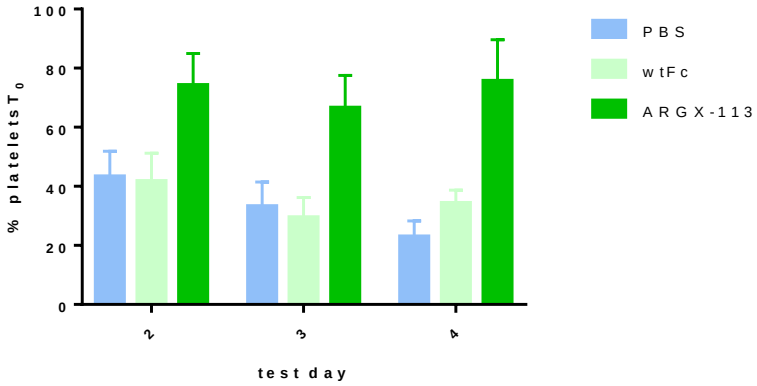
Proof of concept in mouse models for MG and ITP

Myasthenia Gravis



Model adapted from Huijbers et al. 2013, PNAS

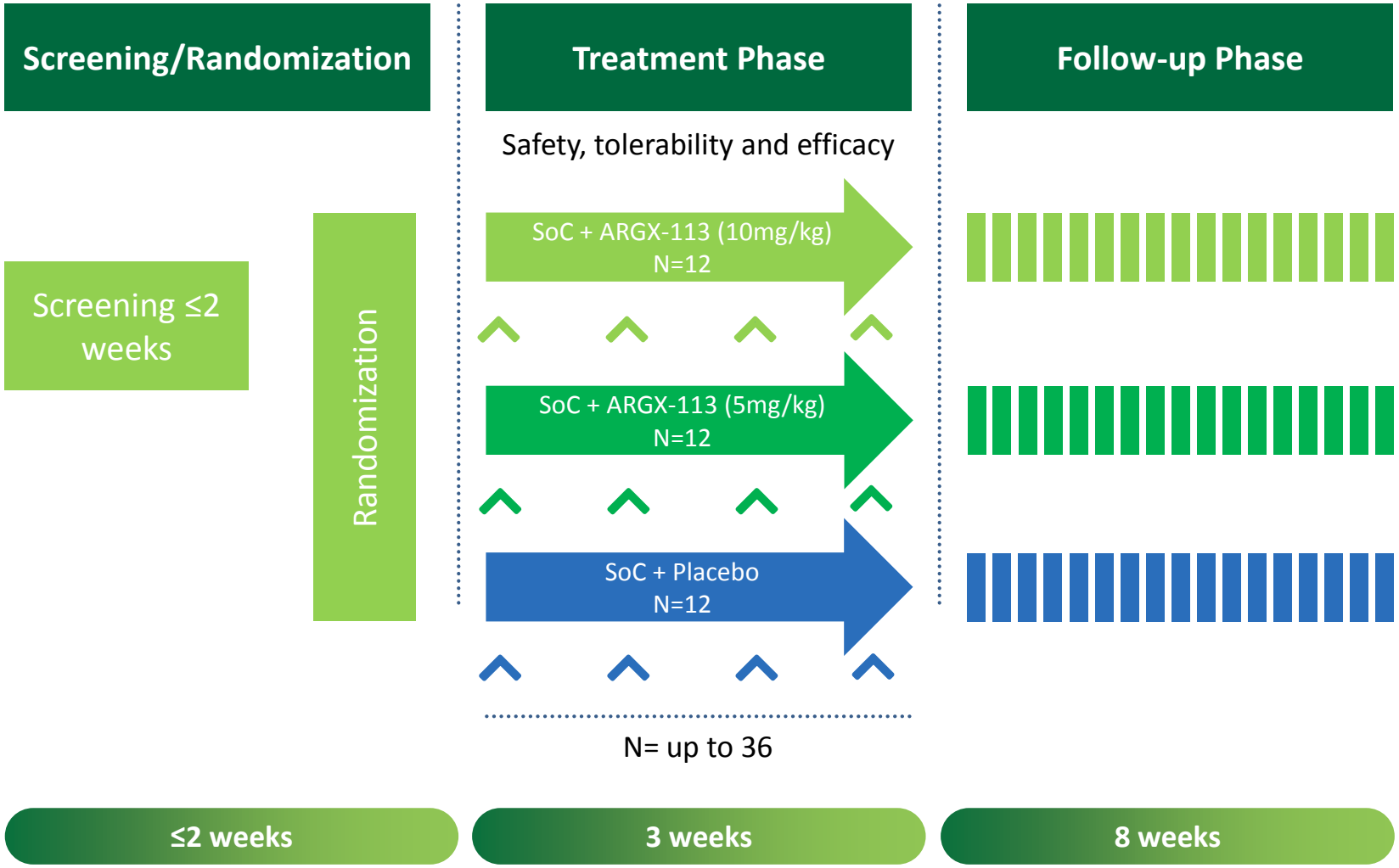
Immune thrombocytopenia



Model adapted from Jain et al. 2012, Arthritis Research & Therapy

- MG model: ARGX-113 maintains muscle strength in murine MuSK-MG antibody-transfer model
- ITP model: ARGX-113 ameliorates anti-platelet antibody-induced ITP in a pilot murine study

ARGX-113 in ITP: Phase II trial design



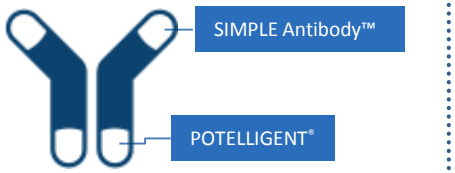
ARGX-113 in ITP: Objectives Phase II

Population	ITP patients with platelet levels < 30 X 10^9/L
Objectives	**Primary Objectives**: • Evaluate safety and tolerability **Secondary Objectives**: • Assess effect on platelet counts • Assess effect on use of rescue treatment • Assess pharmacokinetics (PK) • Assess pharmacodynamic (PD) effects • Evaluate immunogenicity

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

ARGX-110: targets CD70

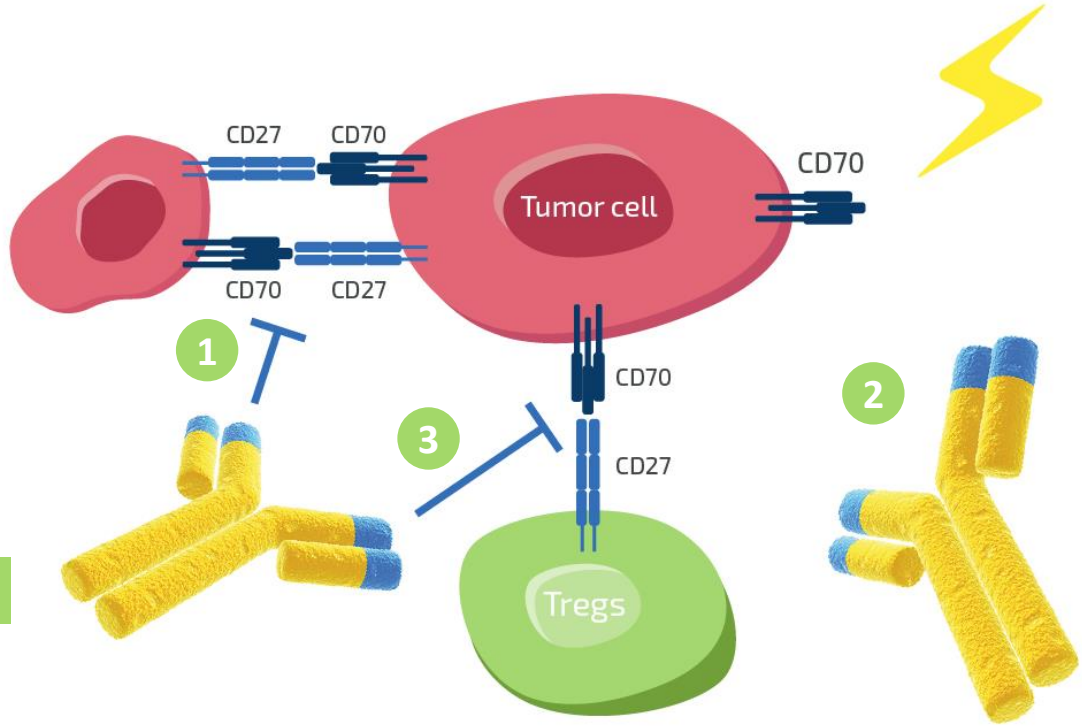
3 distinct modes of action to address tumor cell



1. Block tumor growth signal

2. Kill tumor

3. Restore immune surveillance

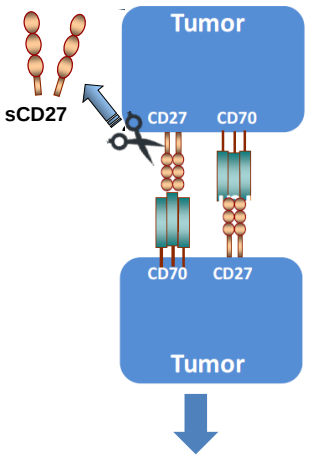


Prof. Ochsenbein won the 'Otto Naegeli Prize 2016', the most highly esteemed biomedical award in Switzerland.
"Of particularly great importance was the discovery that the interaction of CD70 with CD27 and subsequent signaling events has great therapeutic potential for the development of new, original methods of cancer treatment using immunotherapy."

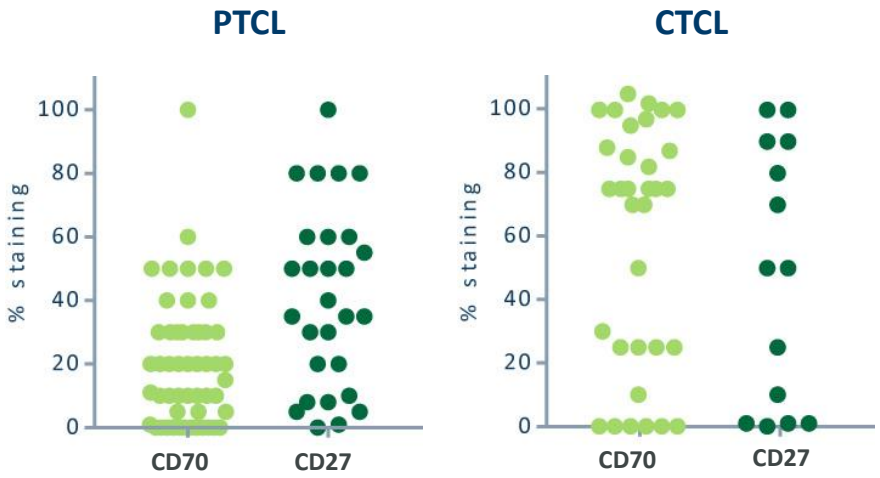
Silence et al. 2014, mAbs

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

CD70/CD27 on tumor cells

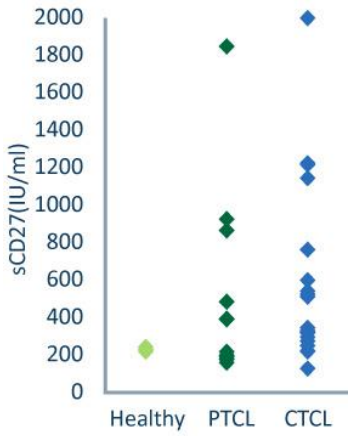


IHC of CD70/CD27 expression in TCL biopsies



Source: argenx data

sCD27 levels in TCL patient



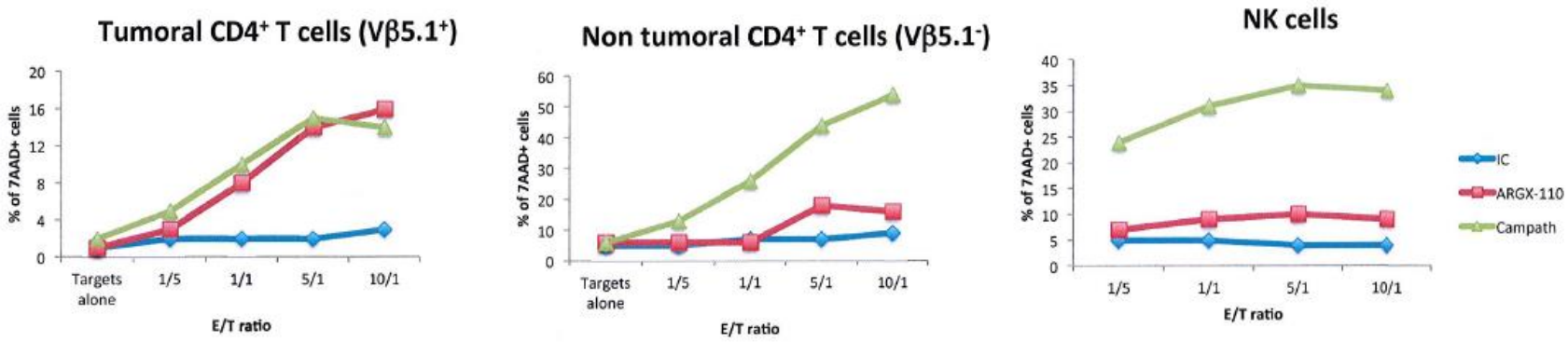
- CD70/CD27 strongly overexpressed across different TCL types
- Elevated sCD27 levels suggest strong pathway activity in TCL

Grewal et al. 2008, Expert Opin Ther Targets

ARGX-110: depletion

Kills TCL tumor cells without affecting healthy cells

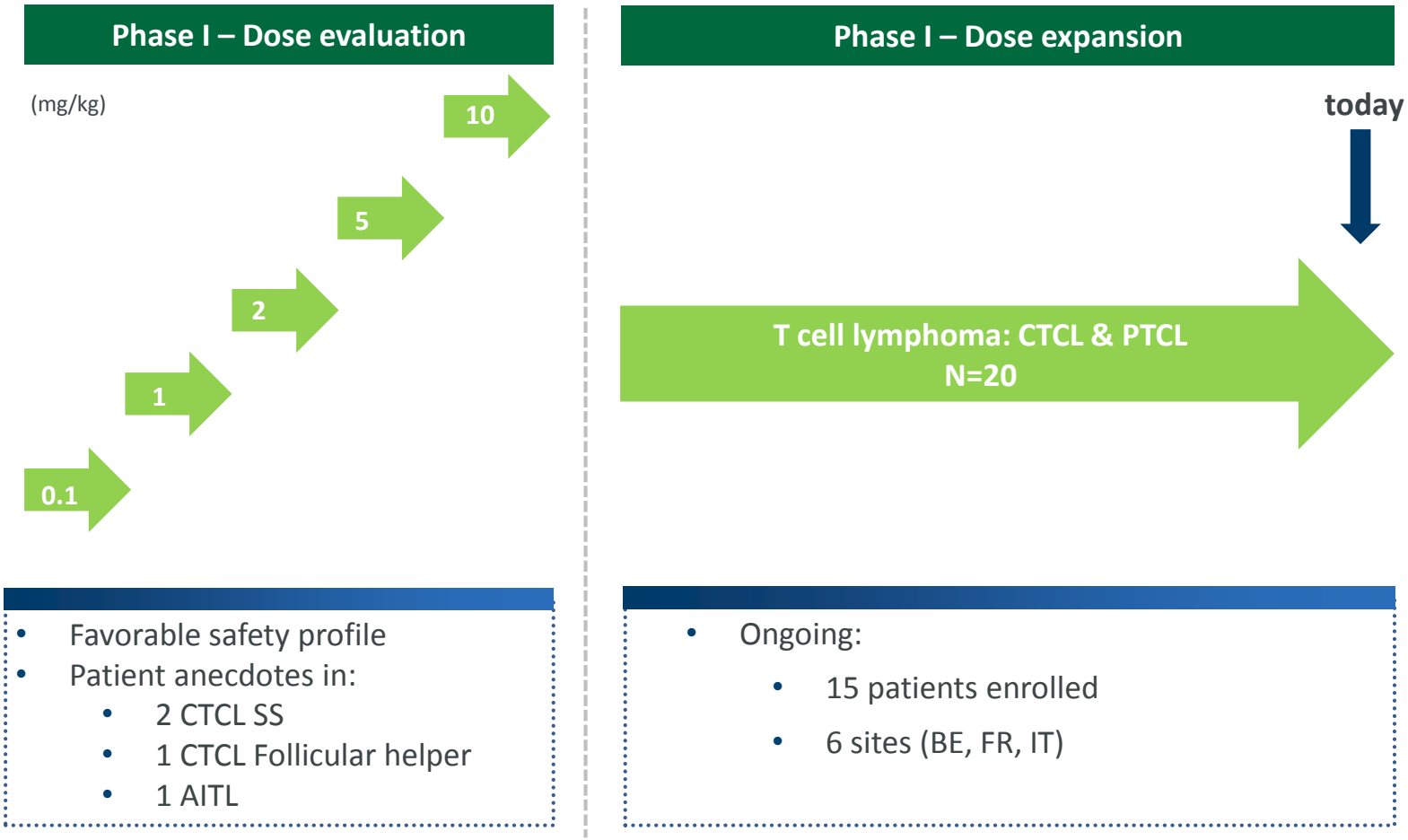
ARGX-110 equally effective as Campath but much more specific



- Campath: depleting both tumoral and non-tumoral T-cells & NK cells
- ARGX-110: selective killing of malignant Sézary CD4+ cells

ARGX-110 in TCL

ARGX-110: Phase I trial overview



- Favorable safety profile
- Patient anecdotes in:
  - 2 CTCL SS
  - 1 CTCL Follicular helper
  - 1 AITL

- Ongoing:
  - 15 patients enrolled
  - 6 sites (BE, FR, IT)

Overview CTCL patients

ARGX-110 Phase Ib

CTCL in Dose Escalation (0.1-10 mg/kg) and Expansion Cohort 1 (5 mg/kg)

Indication	Dose mg/kg	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C20	Best response
CTCL	0.1														SD in skin; CR in blood
CTCL	10														PD based on blood assessment
CTCL	5														SD in skin; decrease skin lesions in # and size

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

Indication	Stage	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C20	Best response
CTCL-MF	T4, N0, M0, B0														SD in skin, mSWAT ↑18%
CTCL-MF/SS + (PTCL-NOS)	T4, N3, M0, B0														SD nodal, PD skin ↑63.5%
CTCL-SS	T4, N3, M0, B1														PD?, mSWAT ↑4%
CTCL-MF	T4, Nx, M0, B0														SD nodal and skin, mSWAT ↓42%
CTCL-SS	T4, Nx, M0, B2														PR in skin, SD nodal and blood, mSWAT ↓50% C4
CTCL-MF	T2, N0, M0, B0														PR in skin, mSWAT ↓62% C6
CTCL-SS	T2, Nx, M0, B2														PD
CTCL-TFH like	T2, N0, M0, B0														PD in skin ↑56%
CTCL-panniculitis like	T3, N0, M0, B0														PR in skin by PET/CT
CTCL-MF	T4, Nx, M0, B0														PD

Source: argenx data - uncleaned

Definition of Global response in CTCL

Global Score*	Definition	Skin	Nodes	Blood	Viscera
CR	Complete disappearance of all clinical evidence of disease	CR	All categories have CR/NI		
PR	Regression of measurable disease	CR	All categories do not have a CR/NI and no category has a PD		
		PR	No category has a PD and if any category involved at baseline, at least one has a CR or PR		
SD	Failure to attain CR, PR, or PD representative of all disease	PR	No category has a PD and if any category involved at baseline, no CR or PR in any		
		SD	CR/NI, PR, SD in any category and no category has a PD		
PD	Progressive disease		PD in any category		
Relapse	Recurrence disease in prior CR		Relapse in any category		

Olsen et al., Journal of Clinical Oncology 2011

Definition of Global response in skin

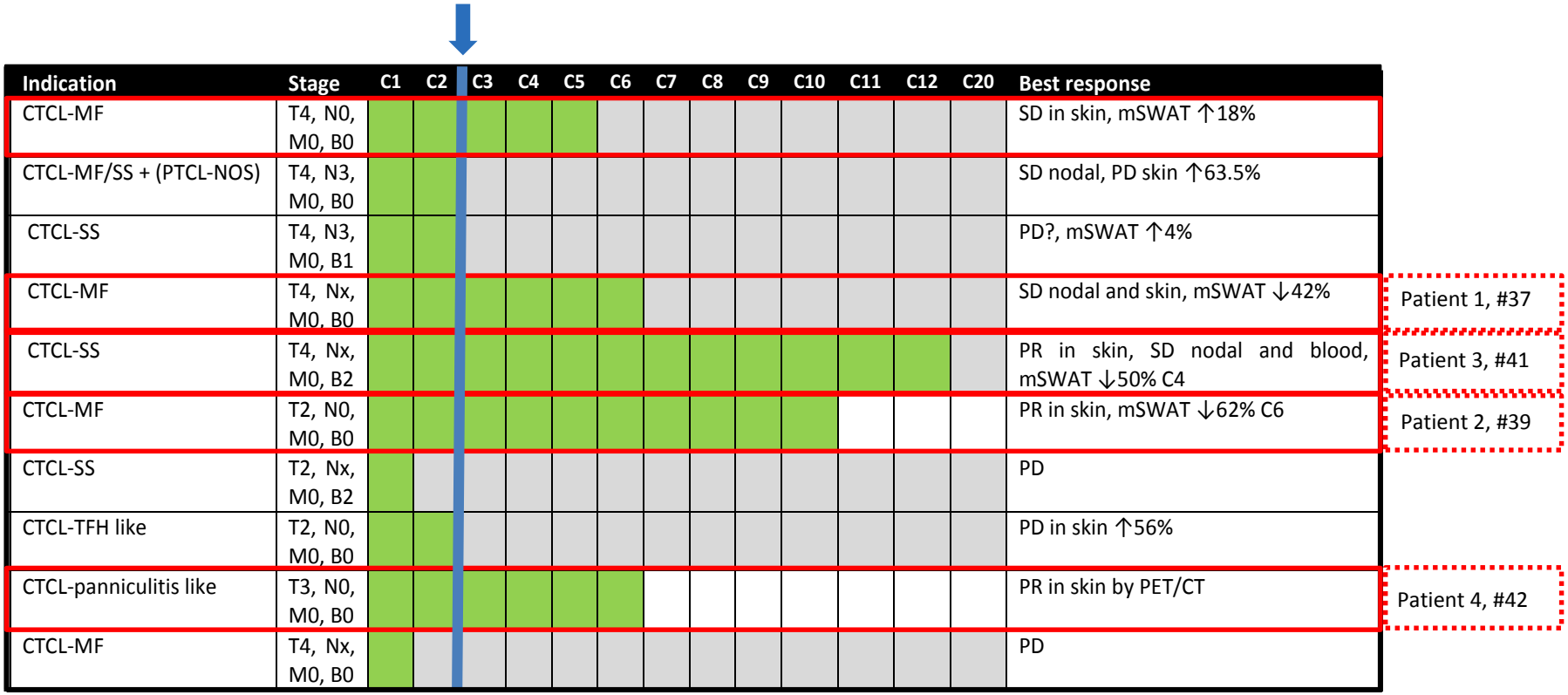
Response	Definition
Complete response	100% clearance of skin lesions
Partial response	50%-99% clearance of skin disease from baseline without new tumors (T_3) in patients with T_1, T_2 or T_4 only skin disease
Stable disease	< 25% increase to < 50% clearance in skin disease from baseline without new tumors (T_3) in patients with T_1, T_2, or T_4 only skin disease
Progressive disease[†]	≥ 25% increase in skin disease from baseline or New tumors (T_3) in patients with T_1, T_2 or T_4 only skin disease or Loss of response: in those with complete or partial response, increase of skin score of greater than the sum of nadir plus 50% baseline score
Relapse	Any disease recurrence in those with complete response

Olsen et al., Journal of Clinical Oncology 2011

Overview CTCL patients

ARGX-110 Phase Ib

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



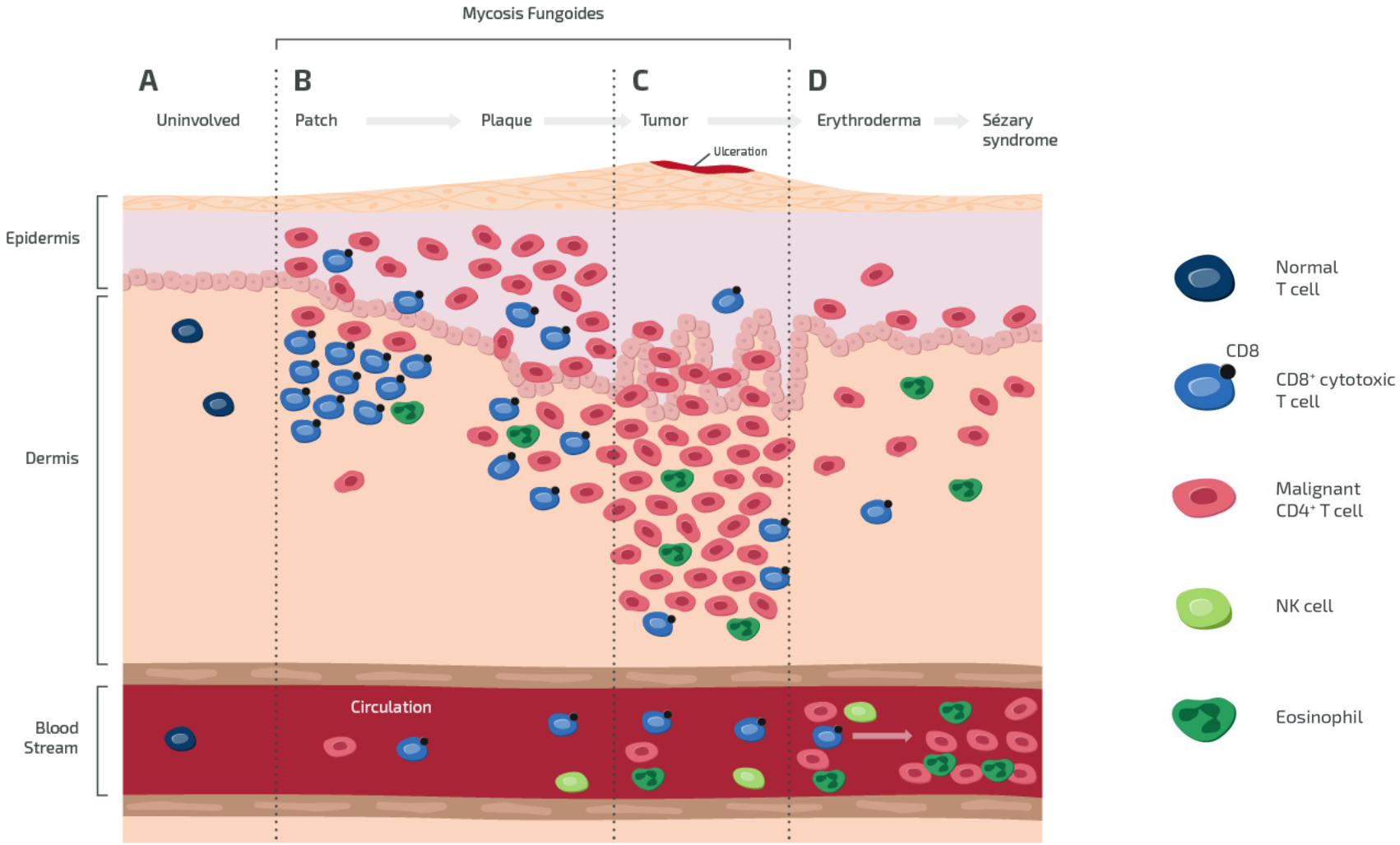
Indication	Stage	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C20	Best response	
CTCL-MF	T4, N0, M0, B0														SD in skin, mSWAT ↑18%	
CTCL-MF/SS + (PTCL-NOS)	T4, N3, M0, B0														SD nodal, PD skin ↑63.5%	
CTCL-SS	T4, N3, M0, B1														PD?, mSWAT ↑4%	
CTCL-MF	T4, Nx, M0, B0														SD nodal and skin, mSWAT ↓42%	Patient 1, #37
CTCL-SS	T4, Nx, M0, B2														PR in skin, SD nodal and blood, mSWAT ↓50% C4	Patient 3, #41
CTCL-MF	T2, N0, M0, B0														PR in skin, mSWAT ↓62% C6	Patient 2, #39
CTCL-SS	T2, Nx, M0, B2														PD	
CTCL-TFH like	T2, N0, M0, B0														PD in skin ↑56%	
CTCL-panniculitis like	T3, N0, M0, B0														PR in skin by PET/CT	Patient 4, #42
CTCL-MF	T4, Nx, M0, B0														PD	

- 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

Source: argenx data - uncleaned

Cutaneous TCL

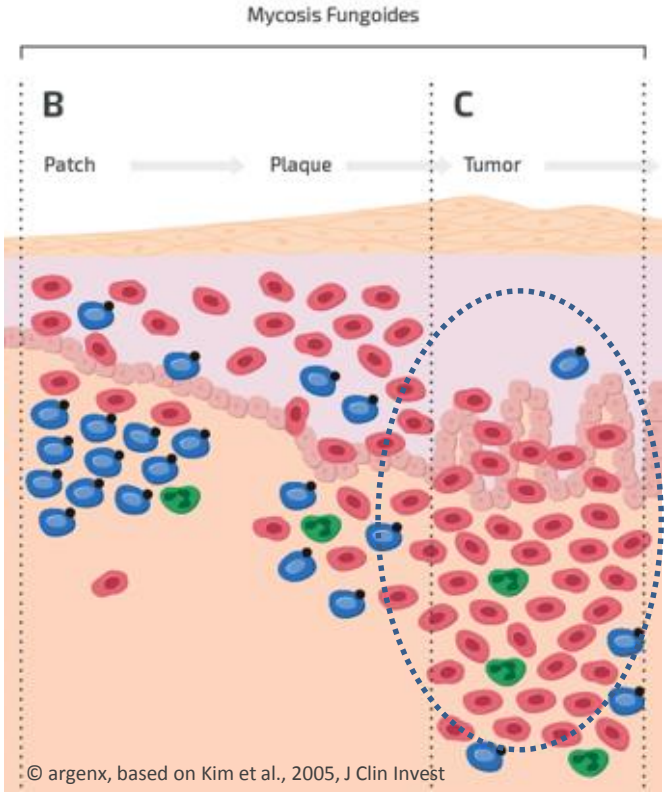
Progression from Patch to Sézary Syndrome



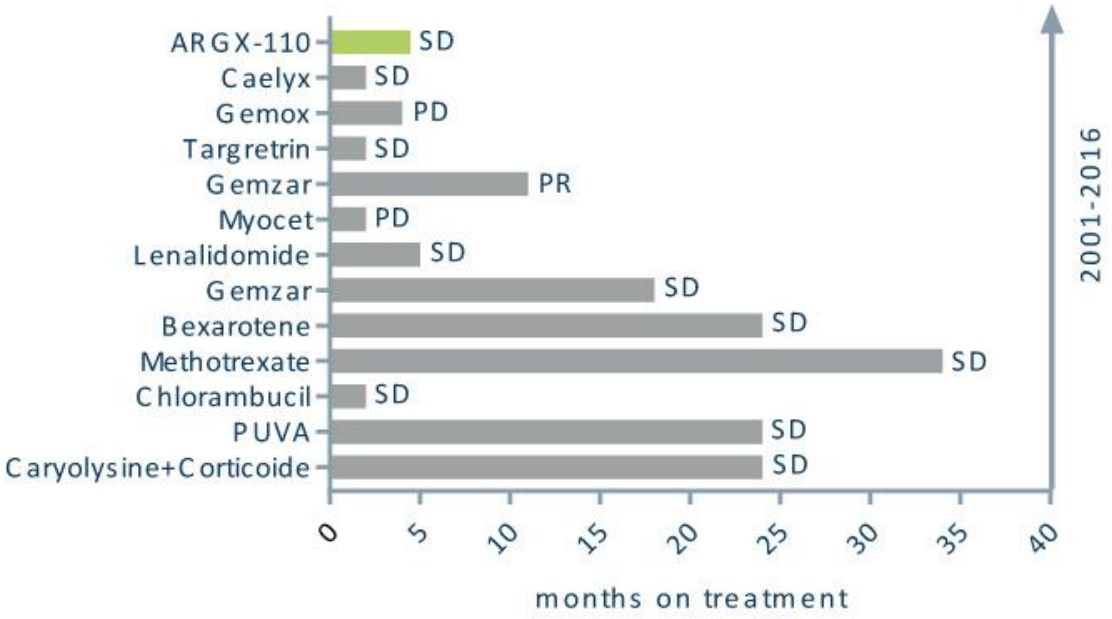
ARGX-110: Activity in heavily treated TCL patients

Patient 1 (2101): Cutaneous TCL – Mycosis fungoides (MF)

Patient	67 year old man with CTCL-MF, diagnosed on 21 Jan 2001
Tumor	Skin T4, Nx, M0, B0 (Stage IIIA)
Nr doses	6, off study because of QTc prolongation



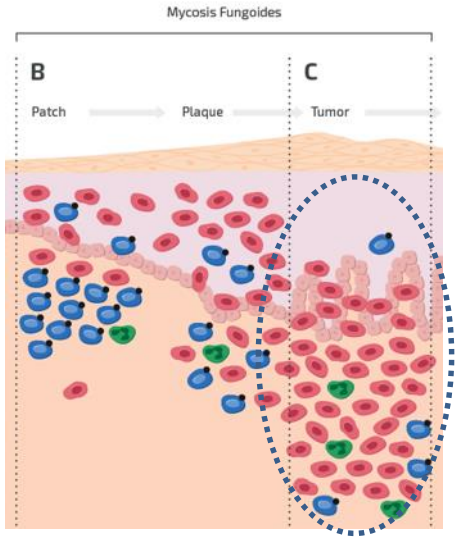
Treatments and best response



Source: argenx data –patient anecdotes - uncleaned

Malignant cells in the skin disappear after one dose

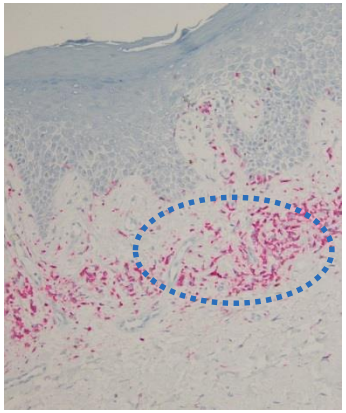
Patient 1 (2101): Cutaneous TCL – Mycosis fungoides (MF)



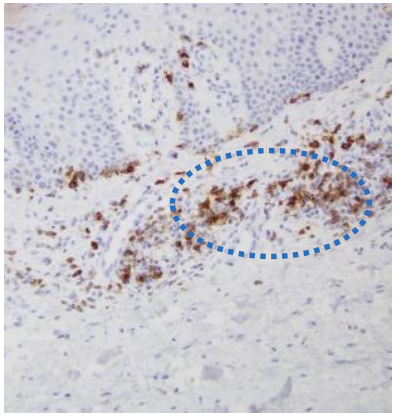
ARGX-110 treatment results in:

- decrease of CD4$^+$ malignant T-cells
- depletion of CD70$^+$ malignant T-cells
- infiltration of CD8$^+$ T-cells

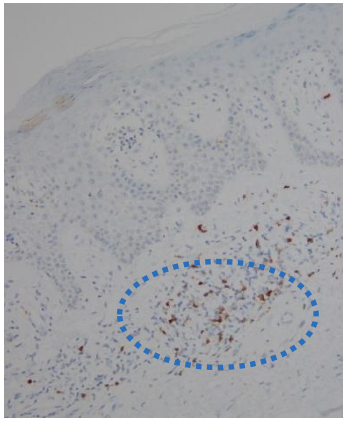
CD4$^+$ – pre



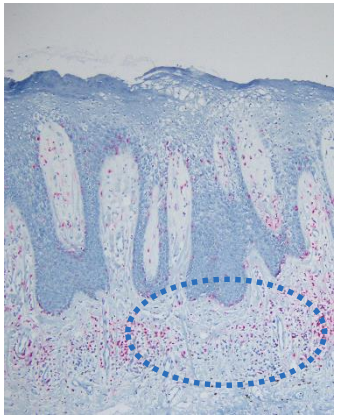
CD70 – pre



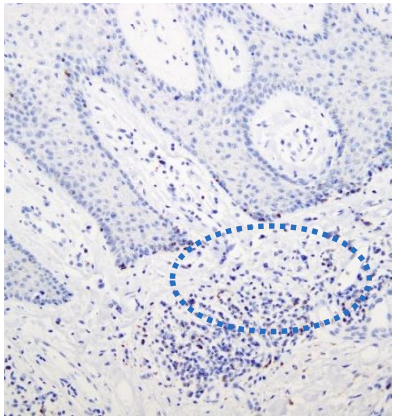
CD8$^+$ – pre



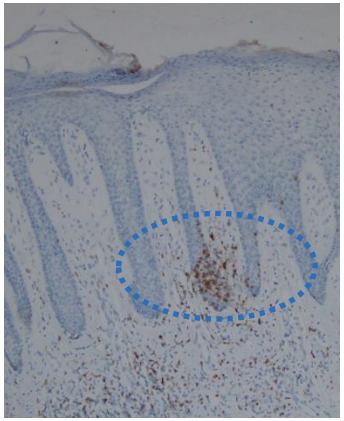
CD4$^+$ – post (C2)



CD70 – post (C2)



CD8$^+$ – post (C2)



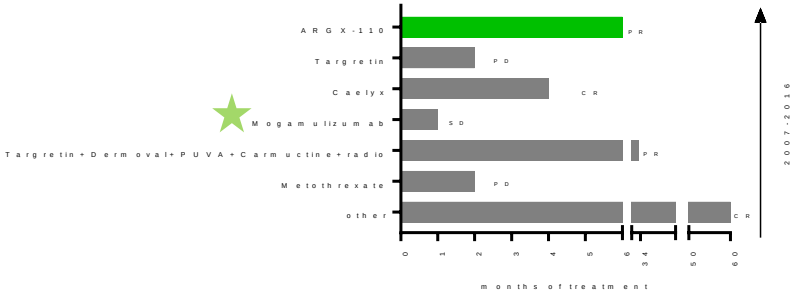
Source: argenx data –patient anecdotes - uncleaned

Partial response: improved mSWAT and skin lesions

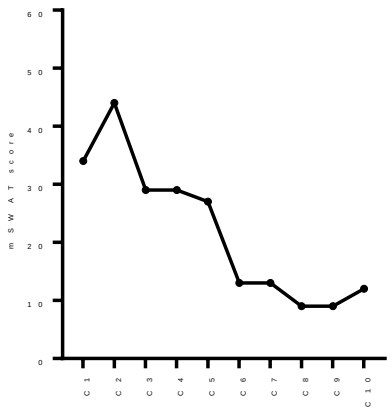
Patient 2 (2103): Cutaneous TCL – Mycosis fungoides (MF)

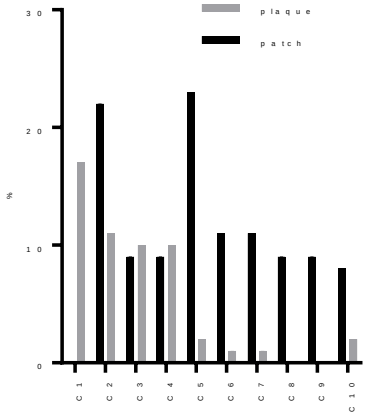
Patient	79 year old female with CTCL-MF, diagnosed 2007
Tumor	Skin T2, N0, M0, B0 (stage IB)
Doses	10, ongoing, 1 mg/kg q3w

Treatments and best response

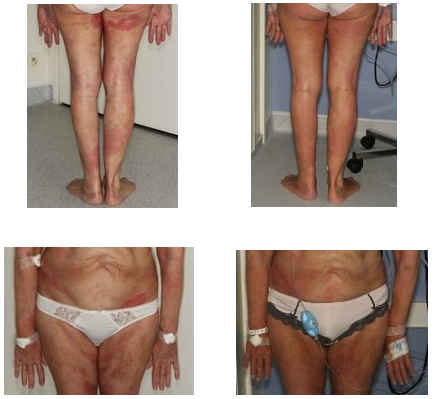


Reduced mSWAT score and total body lesions





Pre C1 C6



Pictures kindly provided by investigator

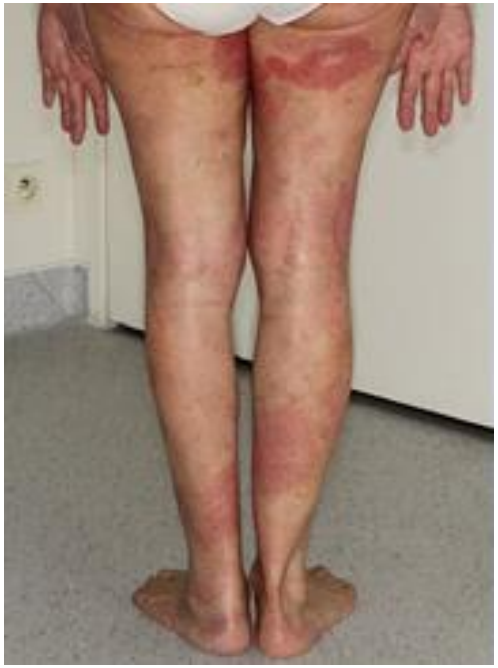
- Cutaneous tumor lesions decrease in surface area; 60% reduction of mSWAT and a partial response (PR)
- Cutaneous tumor lesions improve from plaques to patches

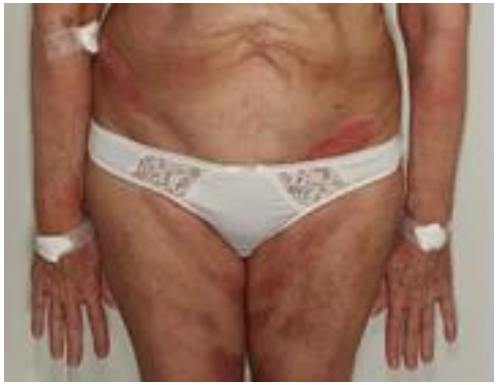
Source: argenx data –patient anecdotes - uncleaned

Partial response

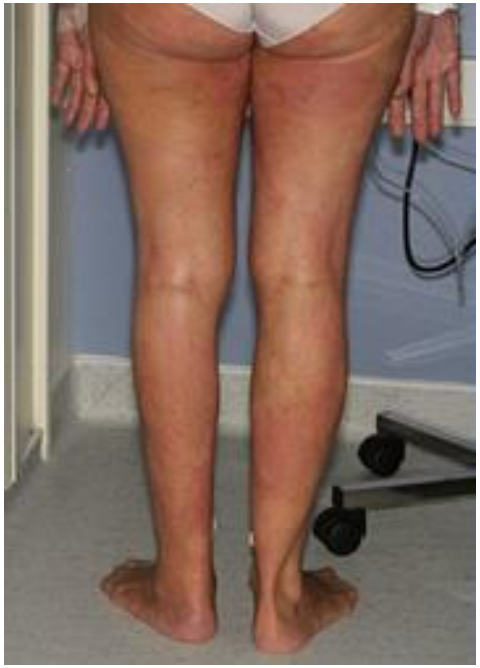
Patient 2 (2103): Cutaneous TCL – Mycosis fungoides (MF)

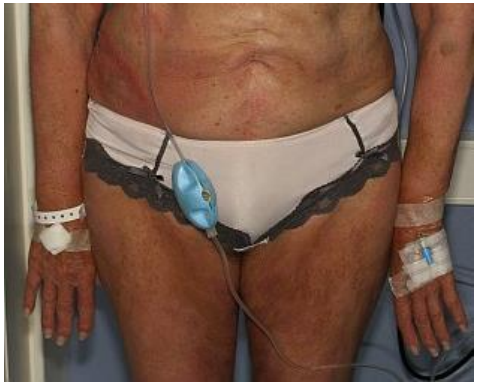
Pre - C1





Post - C6





Pictures kindly provided by investigator

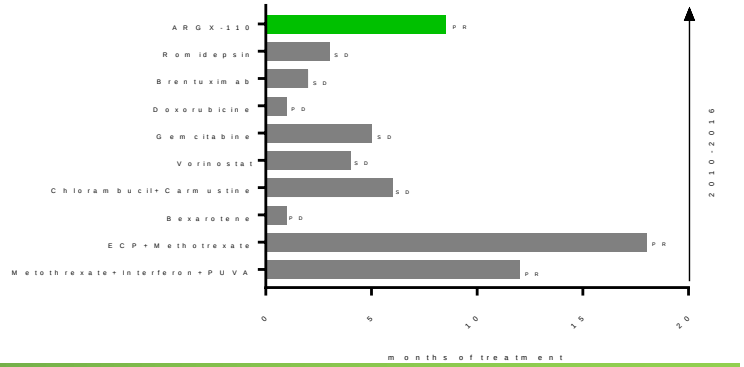
Source: argenx data –patient anecdotes - uncleaned

Stable disease: Improved mSWAT and skin lesions

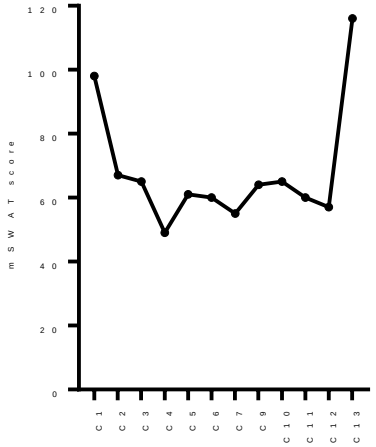
Patient 3 (2102): Cutaneous TCL – Sézary-Syndrome (SS)

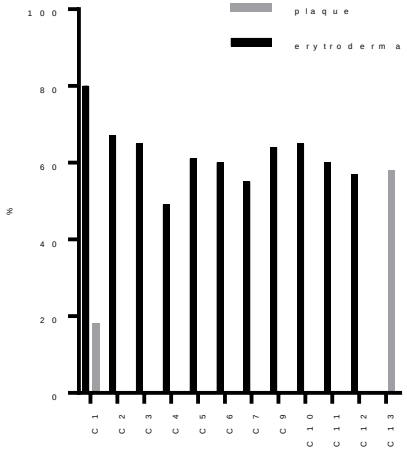
Patient	55 year old female with CTCL-SS, diagnosed 2010
Tumor	Skin T4, Nx, M0, B2 (stage IV)
Doses	12, 1 mg/kg q3w, off study due to PD

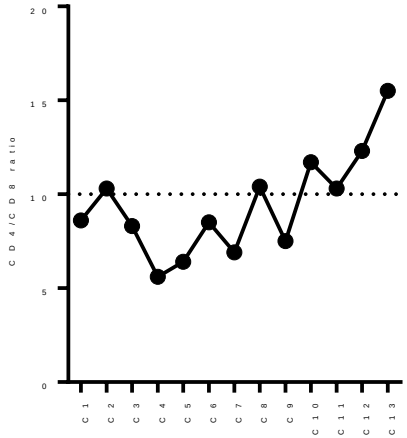
Treatments and best response



mSWAT score, total body lesions and CD4/CD8 ratio in blood







- PR in skin
- SD in nodes and blood
- Best response PR

- Cutaneous tumor lesions decrease in surface area; 50% reduction of mSWAT and a partial response (PR)
- Cutaneous tumor lesions improve from plaques to erythroderma, but increased plaque at PD

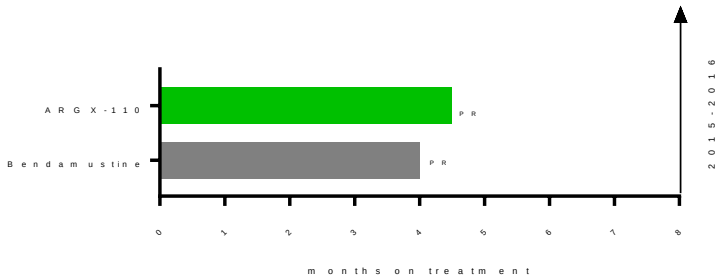
Source: argenx data –patient anecdotes - uncleaned

Partial respons: improvement subcutaneous lesions

Patient 4 (2203): Cutaneous TCL – Panniculitis like

Patient	84-year old female, diagnosed June 2015
Tumor	Skin T3, Nodal N0, Visceral M0, Blood B0
Nr doses	6, ongoing

Treatments and best response



Overview

	Prescreen	C1	C2	C3	C4	C5	C6	C7
FDG-PET global response in skin			C2D20 SD		C4D1 SD		C6D1 PR	
IHC CD70%	Fresh, cutaneous 51-75%, 3+, mc					No tumor cells detected		

Source: argenx data –patient anecdotes - uncleaned

ARGX-110: TCL patients Ph I study

Favorable safety profile

Grade 3-4 toxicities in TCL

AE	0.1 mg/kg	1 mg/kg	5 mg/kg	10 mg/kg
Anemia			4*	
Thrombocytopenia			2	
Febrile neutropenia			1	
Confusion			1	
General degradation	1			
Fever & shivers		1		
Inferior limbs Edema				1
Scrotal Edema				1
Pseudomonas infection		1		
QTC prolongation		1		
Vasculopathy **			1	
Total N patients (#21)	1	14	5	1

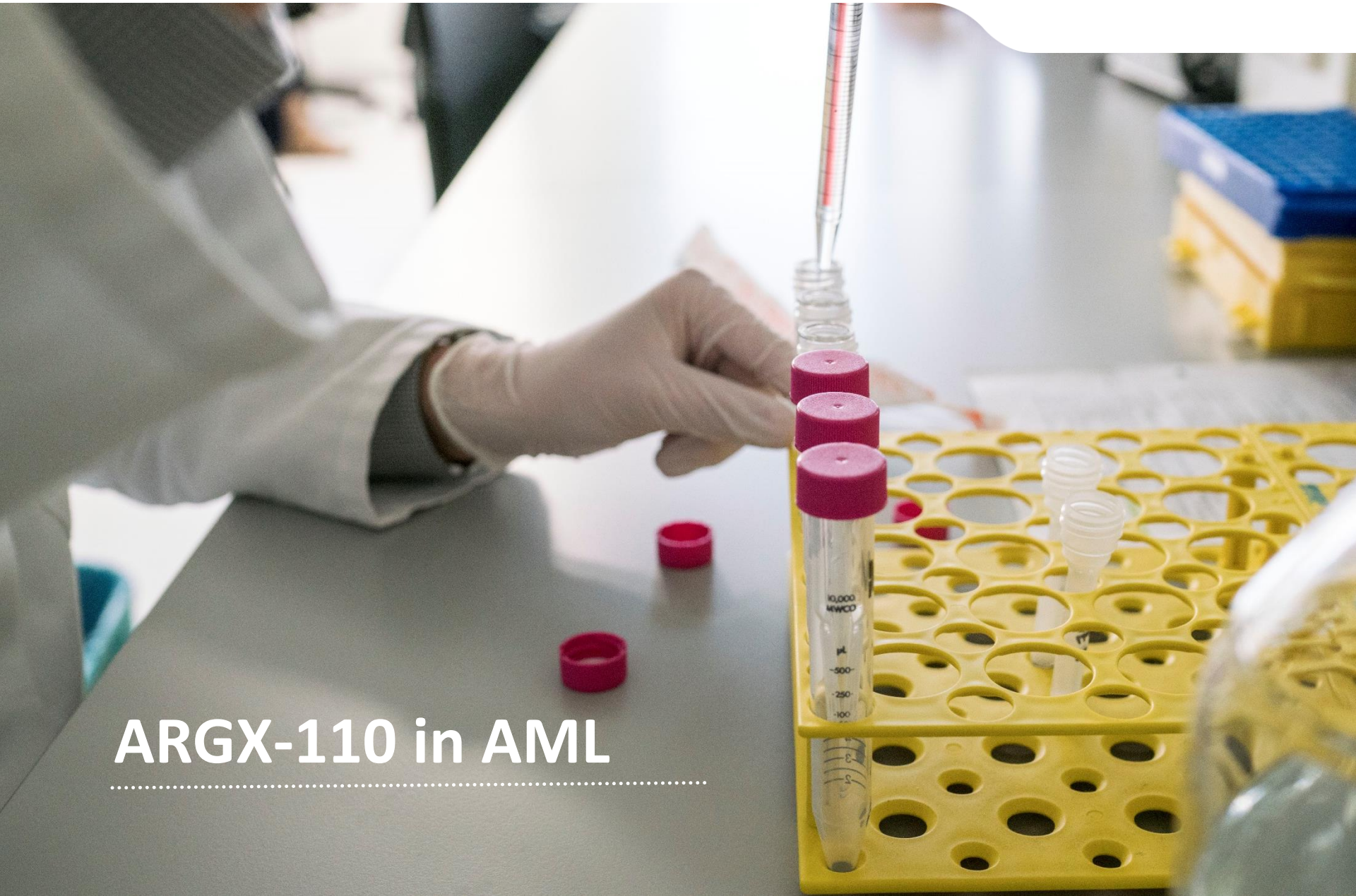
- Favorable safety profile for heavily pretreated TCL patient population
- No major trends in terms of safety between the main dose groups (1mg/kg and 5mg/kg)
- Overall two grade 5 toxicities observed: 1 at 5mg/kg (pneumonia) and 1 at 10mg/kg (sepsis)

* 1 patient 3 AE anemia and 2 AEThrombocytopenia
** Undosed patient

Source: argenx data – uncleaned

Proprietary pipeline in cancer and severe autoimmunity

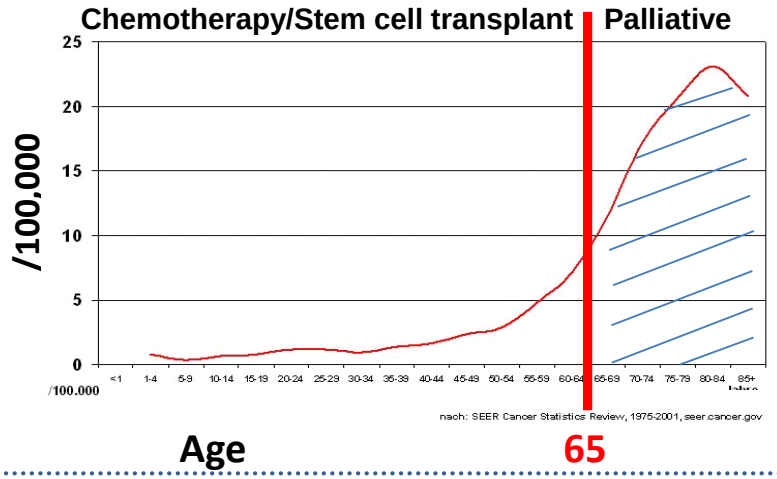
		Drug candidate	Target	Indication	Pre-clinical / Phase 1 / Phase 2
Autoimmune diseases		ARGX-113	FcRn	Myasthenia Gravis	4Q 2016
				Immune Thrombocytopenia	1Q 2017
Cancer immunotherapy		ARGX-110	CD70	T-Cell Lymphoma	4Q 2016
				Acute Myeloid Leukemia	4Q 2016
Metastatic cancer		ARGX-111	c-MET	Solid tumors Blood cancer	
		Discovery Undisclosed		Multiple	
Partnered, non-dilutive income	abbvie	ARGX-115	GARP	Cancer Immunotherapy	
	BIED ROCK BIO	ARGX-109 Gerilimzumab	IL-6	Autoimmunity	
	LEO	Undisclosed		Skin inflammation	
	Shire	Undisclosed		Undisclosed	



ARGX-110 in AML

Acute Myeloid Leukemia (AML): high unmet need

AML incidence and treatment paradigm



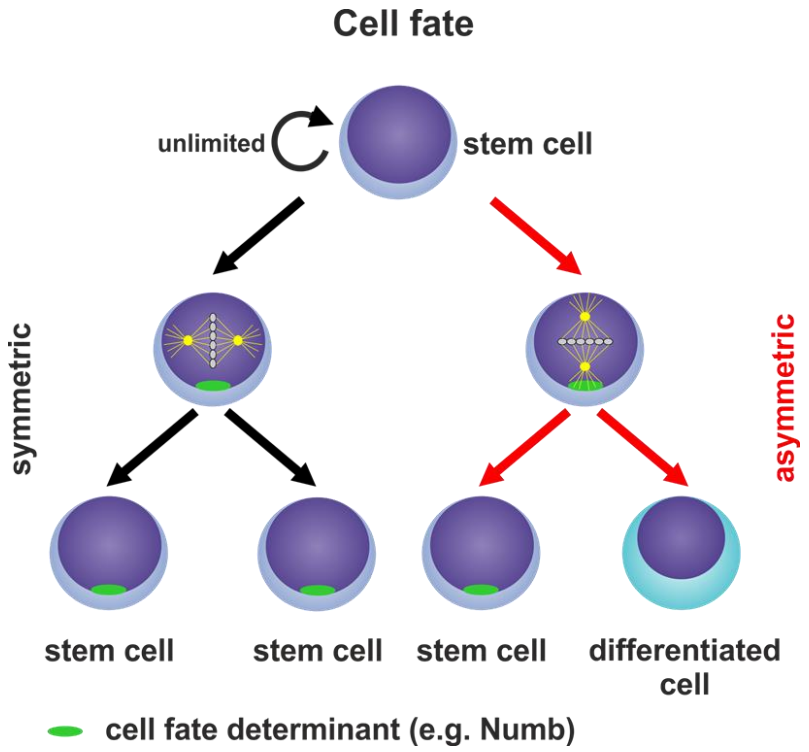
Epidemiology

- Worst 5Y survival rate of heme malignancies
- 3.8/100'000 per year, median age: 70, incidence increases with age
- 5-year survival when adverse risk: 5-20% (25-30% of pts)

Very high unmet medical need

- Younger patients effectively treated with transplant and chemotherapy
- Older patients (>65) unfit for transplant receive palliative treatment (40% of pts on Azacitidine)

AML: Leukemic stem cells responsible for disease relapse

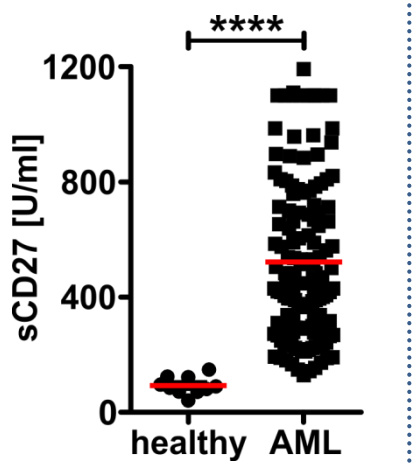


- Accumulation of blasts in bone marrow and blood → drop in red blood cells, platelets, and normal white blood cells
- Leukemic stem cells (LSCs = AML stem/progenitor cells) are responsible for disease relapse

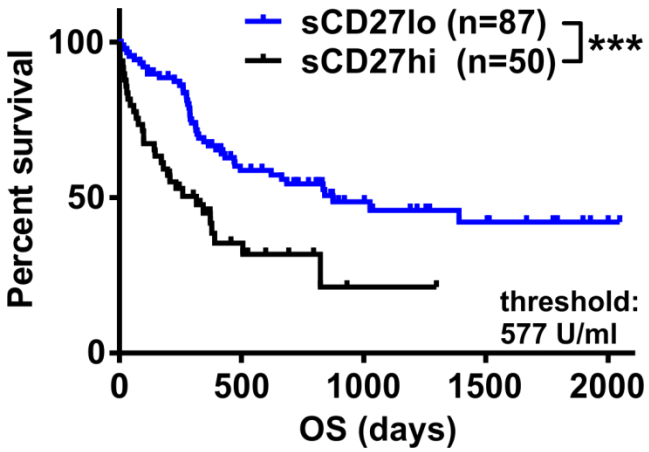
ARGX-110: Rationale in AML

Indication for CD70/CD27 signaling in AML patients

sCD27 serum levels



sCD27 serum levels → poor prognosis



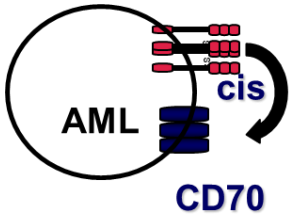
parameter	HR (95% CI)	p-value
sCD27	2.17 (1.34-3.50)	0.0016
risk group	1.69 (1.29-2.38)	0.0024
age	1.03 (1.01-1.05)	0.0050
BM blast %	0.99 (0.98-1.00)	0.1259
blood blast %	1.00 (0.99-1.01)	0.9329
blood leukocyte #	1.00 (0.99-1.01)	0.6558

- 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

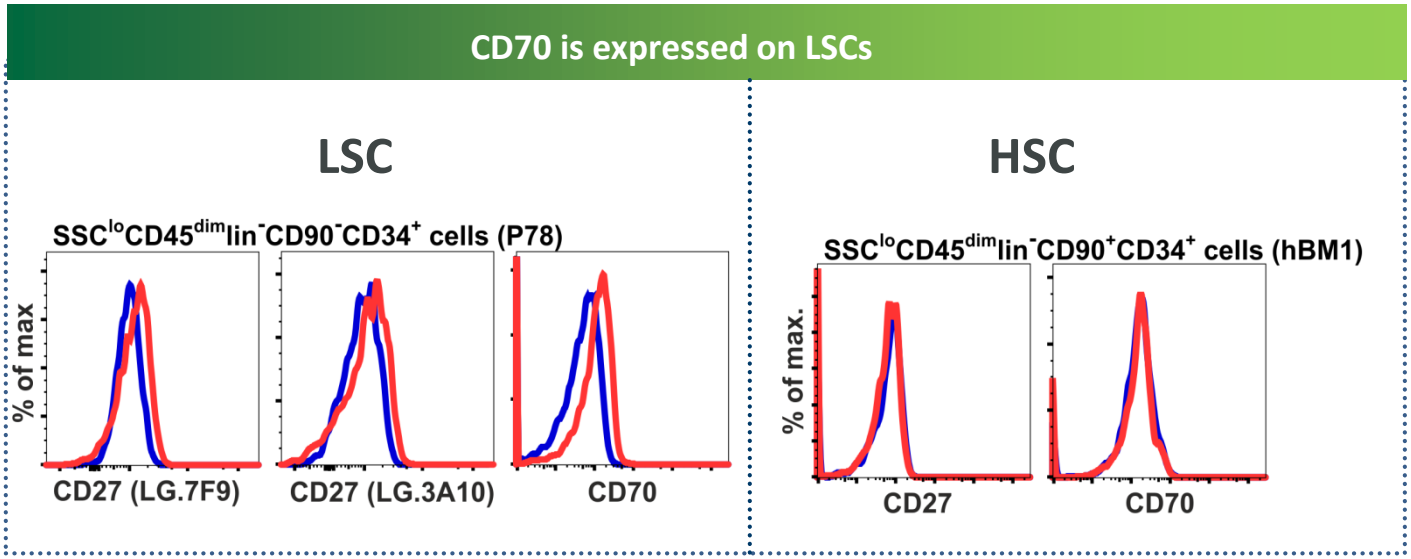
Riether et al, Journal of Experimental Medicine, 2016

ARGX-110: Rationale in AML

CD70/CD27 biology highly involved in newly diagnosed AML



CD70 is expressed on LSCs

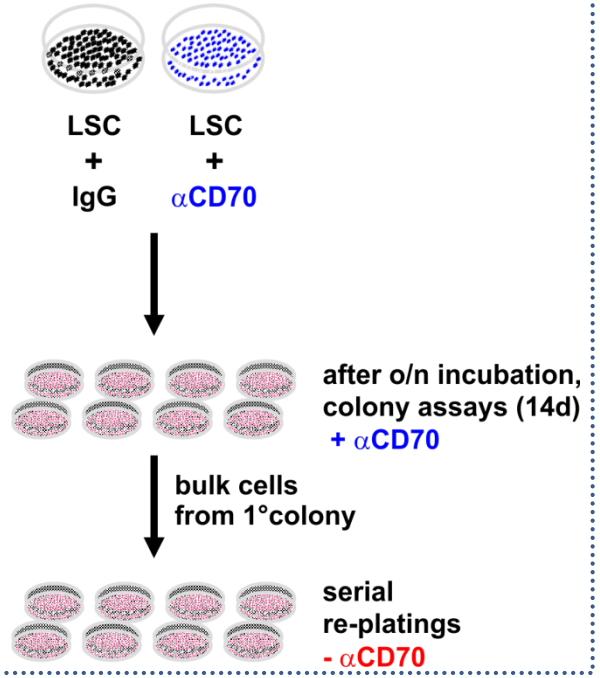


- CD70/CD27 selectively overexpressed on LSCs and not on hematopoietic stem cells (HSC)
- CD70 expressed on ~100% of AML blasts, majority of malignant cells are CD70/CD27 double-positive
- ARGX-110: selective targeting of LSCs

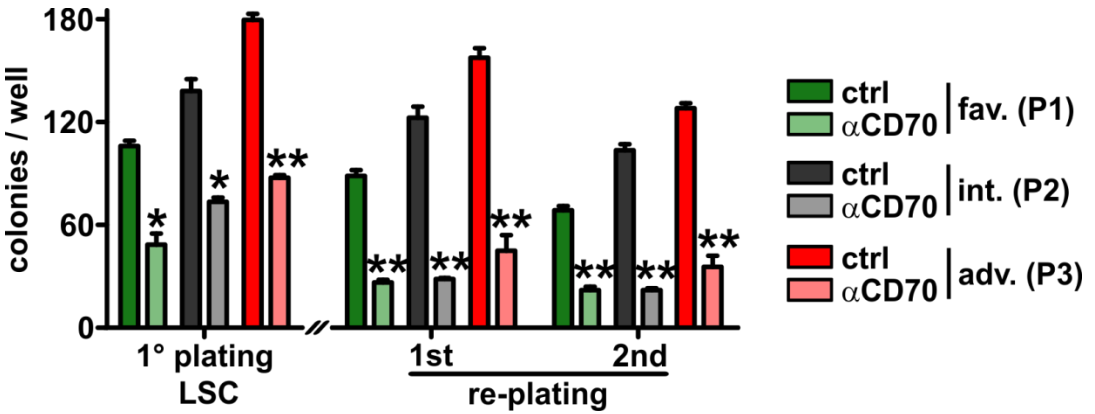
Riether et al, Journal of Experimental Medicine, 2016

ARGX-110: Leukemic stem cell function ex vivo

Long-term effects *ex vivo*



αCD70 reduces LSC colony formation

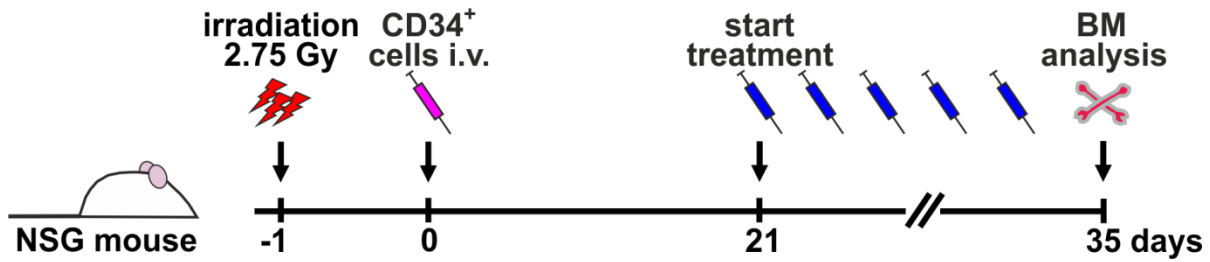


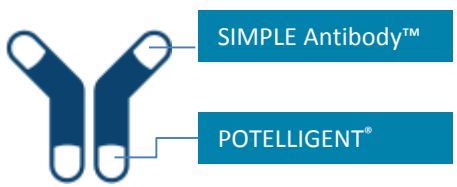
- αCD70 Ab reduces colony formation of LSC
- αCD70 Ab reduces LSC numbers as determined in serial re-plating experiments

Riether et al, Journal of Experimental Medicine, 2016

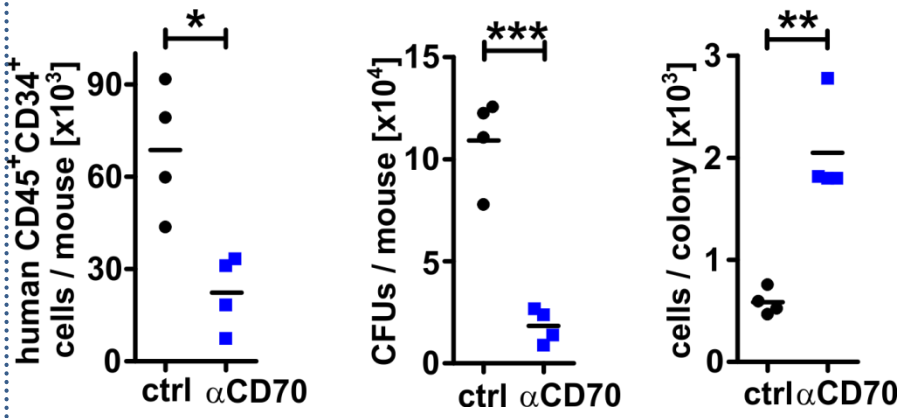
ARGX-110: Periodic treatment

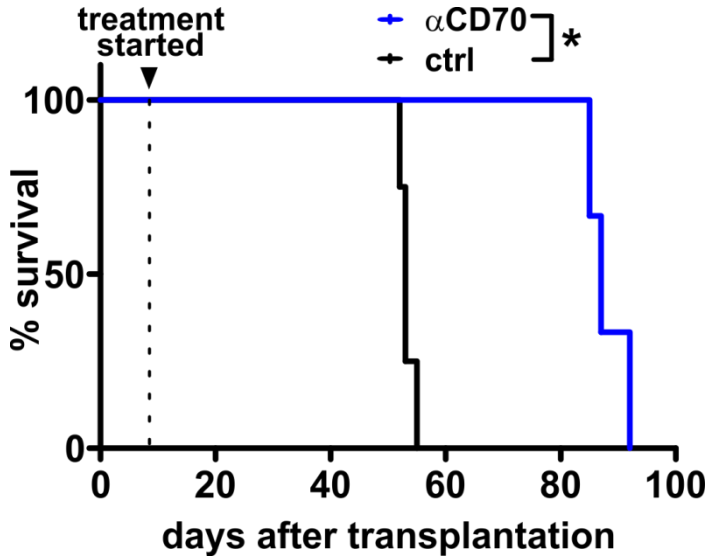
Reduction of LSCs cell numbers and function





αCD70 mAb treatment reduces LSCs cell function *in vivo* and prolongs survival

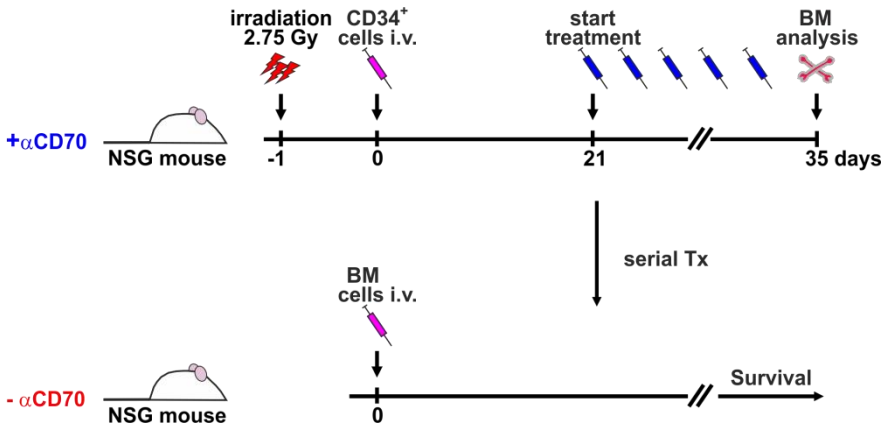




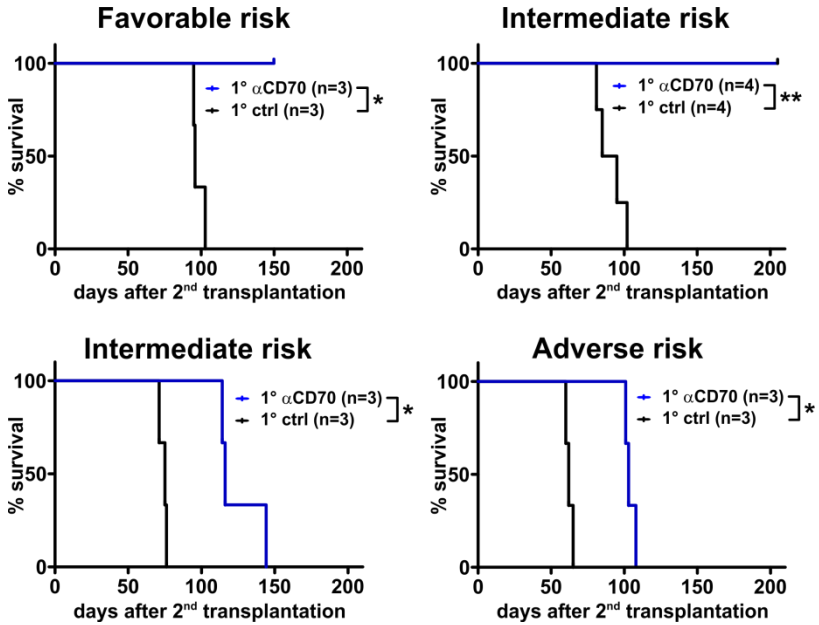
Riether et al, Journal of Experimental Medicine, 2016

ARGX-110: Periodic treatment

Long-term effects *in vivo*



BM of αCD70-treated contain fewer cells that transmit the disease (LSCs) in vivo

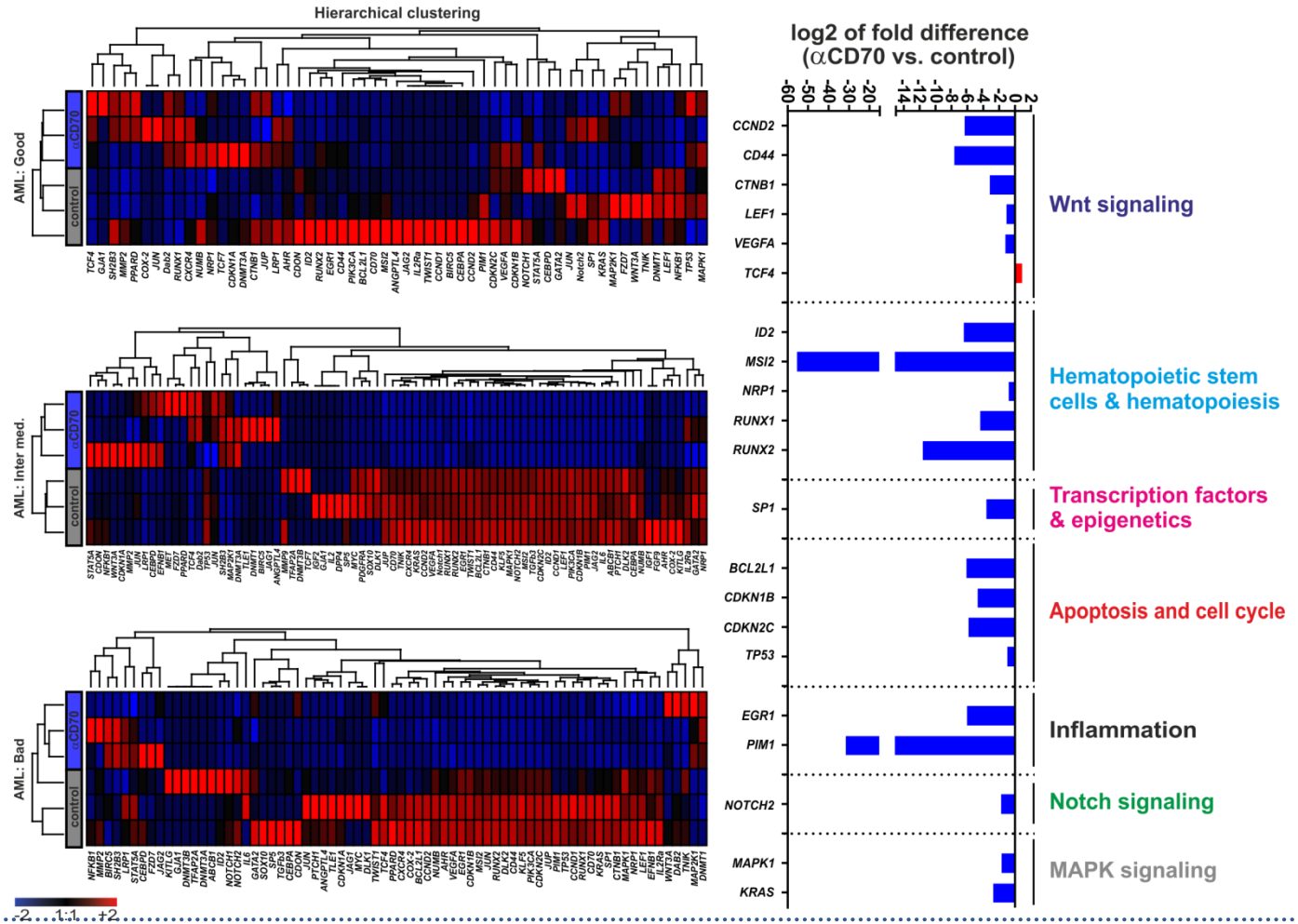


- Increased survival after secondary transplantation of AML BM cells from primary recipients transiently treated with αCD70 Ab
- Increased survival observed for AML blasts taken from all 3 AML risk categories

Riether et al, Journal of Experimental Medicine, 2016

Blocking CD70/CD27 signaling

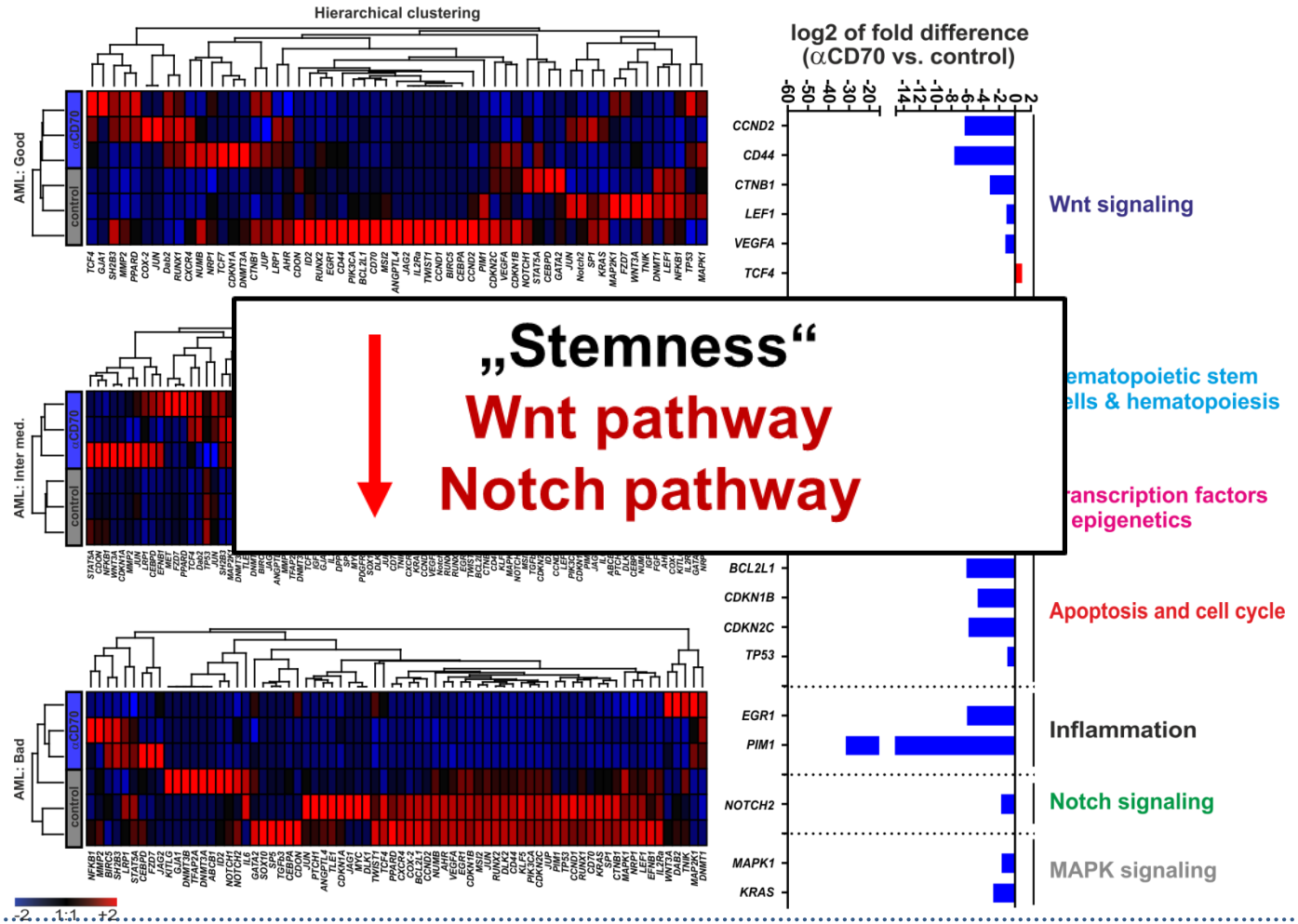
Reduction in stem cell characteristics – Transcriptome analysis



Riether et al, Journal of Experimental Medicine, 2016

Blocking CD70/CD27 signaling

Reduction in stem cell characteristics

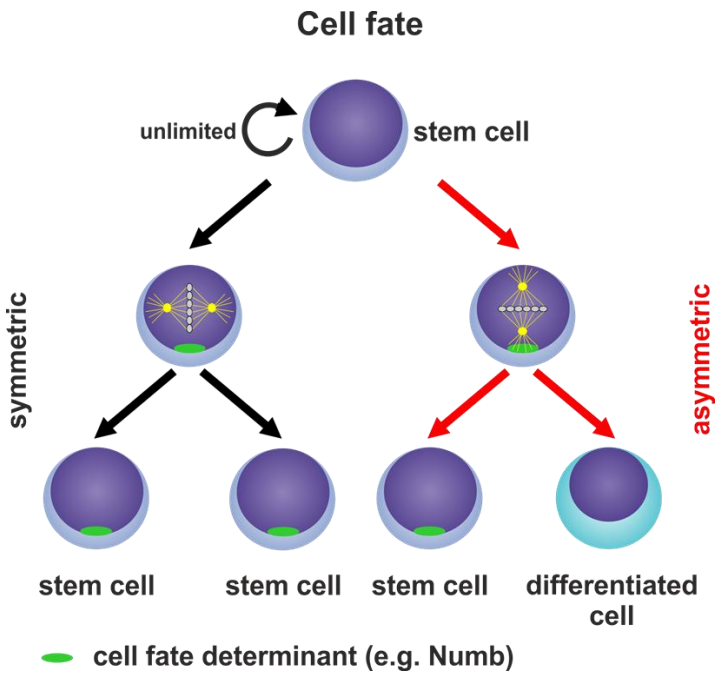


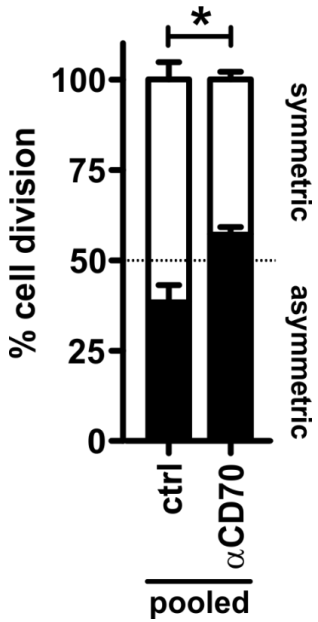
Riether et al, Journal of Experimental Medicine, 2016

Blocking CD70/CD27 signaling

Induction of asymmetric division

Cell division pattern: symmetric → asymmetric (differentiation)

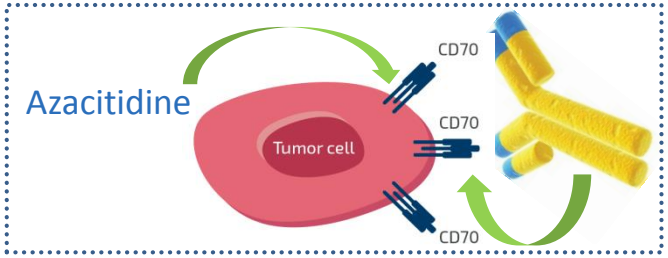




- Treatment of patient AML blasts with αCD70 Ab:
  - reduced symmetric division
  - increased myeloid differentiation

Riether et al, Journal of Experimental Medicine, 2016

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



Phase I – Dose escalation

Safety and tolerability

Vidaza = 75 mg/m2 (standard of care)

10mg/kg

N = 3+3

3mg/kg

N = 3+3

1mg/kg

N = 3+3

N = up to 18

Phase II – Proof of concept

Efficacy

selected ARGX-110 dose

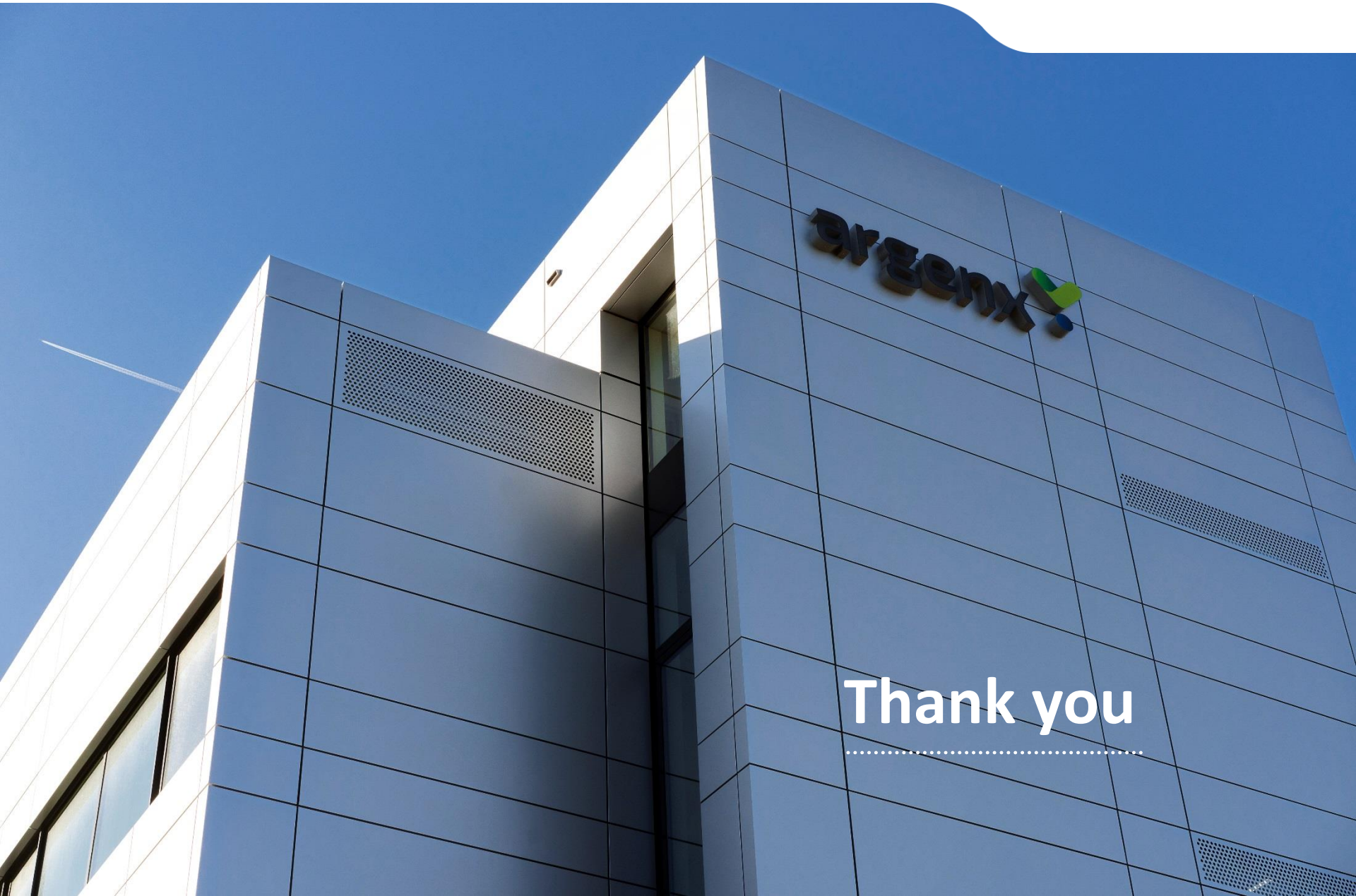
N = 15

selected ARGX-110 dose

N = 9 – (3-6 from Ph I)

N = up to 24

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


Thank you