# Developing Highly Differentiated Antibody Therapeutics

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# Company Highlights

## Differentiated therapeutic antibodies pioneering in severe autoimmune diseases & cancer

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### Novel concept in autoimmunity

- **ARGX-113**: first-in-class FcRn antagonist targeting array of IgG mediated AI diseases
  - Phase 1: favorable safety profile; IgG reduction up to 85%
  - Phase 2: ongoing in myasthenia gravis, immune thrombocytopenia and pemphigus vulgaris

### Deep pipeline with multiple shots on goal

- **ARGX-110:** first-in-class CD70 antagonist in Phase 1/2 in CTCL and AML
- 4 clinical stage programs; 3 preclinical programs; Innovative Access Program

### Powerful technology suite

- **SIMPLE Antibody™:** Human V-regions sourced from llama unlock **novel & complex targets**
- **NHance®, ABDEG™, POTELLIGENT®:** Fc engineering to augment natural properties of antibodies

### Validating selective partnerships

- abbvie: **ARGX-115** (Immuno-oncology-focused novel target GARP)
  - $40mm upfront and up to $625mm in potential milestone payments
- Additional partnerships designed to maximize value of platform in non-core areas

Shire
LEO
STATEN BIOTECHNOLOGY

### Well financed to execute plan

- **Strong cash position:** €162mm Sept 30, 2017
- Blue chip investor base: more than 60% U.S. Shareholders
- 26.9 mio shares outstanding

# Recent Progress

## Pipeline

- ARGX-113 Phase 2 study in MG patients: 100% recruited (Oct '17)
- ARGX-113 for MG: Orphan drug designation by FDA (Sept '17)
- ARGX-113 Phase 2 study in ITP patients: 50% recruited (Sept '17)
- ARGX-113 Phase 2 study initiation in PV patients (Sept '17)
- ARGX-113 Phase 1 study initiation in healthy volunteers with subcutaneous formulation (Oct '17)

## Partnerships

- ARGX-115: 1st $10mm preclinical milestone payment received from AbbVie (May '17)
- ARGX-112: 2nd undisclosed preclinical milestone payment received from LEO Pharma (June '17)

## Financing

- Upsized $115mm IPO on Nasdaq (ticker: ARGX)(May '17)
- U.S. shareholding expanded above 60%
- Expanded U.S. analyst coverage
- Use of proceeds
  - Clinical development of ARGX-113 for the treatment of autoimmune diseases
  - Expand applications of ARGX-113 to develop a subQ formulation & explore additional indications
  - Clinical development of ARGX-110 for the treatment of hematological malignancies
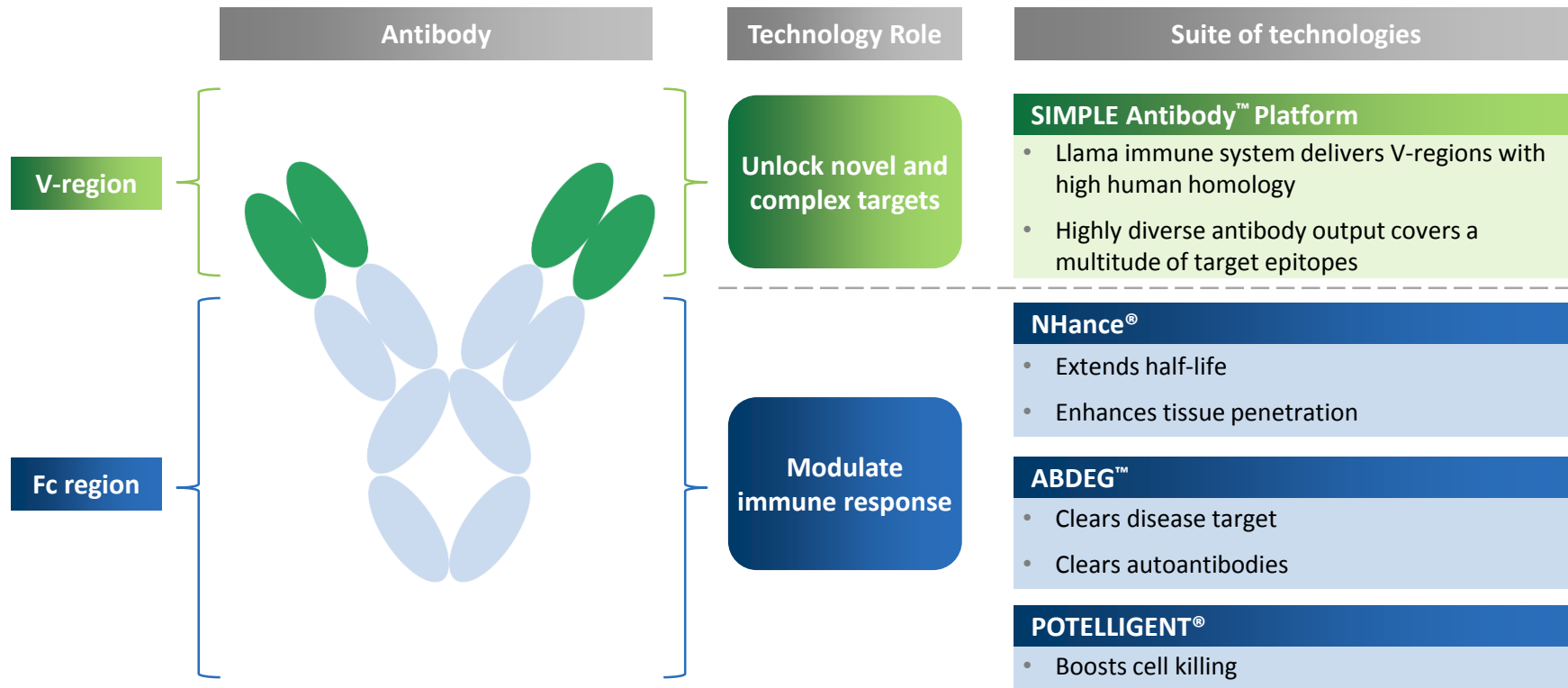
# Disciplined Business Model

Maximizes value of our suite of technologies and capabilities

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## Generating differentiated antibody candidates...

Novel Targets **+** argenx Technology Suite **=** Differentiated mAbs

## ...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** |
| Shire ✓ | ARGX-109 Bird Rock Bio ✓ | ARGX-115 abbvie ✓ | ARGX-113 ☐ |
| BAYER ✓ | ARGX-112 LEO ✓ | ARGX-111 ☐ | ARGX-110 ☐ |
| 💡 ✓ | ARGX-116 STATEN BIOTECHNOLOGY ✓ | | |

**Value inflection point**

# Augmenting Intrinsic Therapeutic Properties Of Antibodies

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| Antibody | Technology Role | Suite of technologies |
|---|---|---|

**V-region**

**Fc region**

**Unlock novel and complex targets**

**SIMPLE Antibody™ Platform**
- Llama immune system delivers V-regions with high human homology
- Highly diverse antibody output covers a multitude of target epitopes

**Modulate immune response**

**NHance®**
- Extends half-life
- Enhances tissue penetration

**ABDEG™**
- Clears disease target
- Clears autoantibodies

**POTELLIGENT®**
- Boosts cell killing

**We apply our unique suite of technologies to create differentiated product candidates against novel targets**

Klarenbeek et al. 2015, mAbs
Basilico et al. 2014, J Clin Inv.

# Deep Pipeline In Severe Autoimmune Diseases and Cancer

| Product Candidate | Target | Indication | Preclinical | Phase 1 | Phase 2 | Phase 3 | Next Milestone / Commentary |
|---|---|---|---|---|---|---|---|
| **Wholly-Owned Product Candidates** | | | | | | | |
| ARGX-113 (efgartigimod) | FcRn | Myasthenia Gravis | | | | | 1Q18: Phase 2 topline results |
| | | Immune Thrombocytopenia | | | | | 2H18: Phase 2 topline results |
| | | Pemphigus Vulgaris | | | | | 2H18: Phase 2 interim data |
| | | Chronic Autoimmune Diseases | | SubQ Formulation | | | 2H18: Phase 1 interim data |
| ARGX-110 (cusatuzumab) | CD70 | T-Cell Lymphoma | | Phase 1/2 | | | 2H18: Phase 2 topline results CTCL |
| | | Acute Myeloid Leukemia | | Phase 1/2 | | | YE17: Interim update Phase 2 CTCL and Phase 1 dose-escalation in AML/MDS |
| ARGX-111 | c-MET | Solid Tumors / Blood Cancer | | | | | Intend to partner |
| **Partnered Product Candidates** | | | | | | | |
| ARGX-109 (gerilimzumab) | IL-6 | Rheumatoid Arthritis | | | | | Eligible for up to €32.5mm in milestones, royalties & additional shares of Bird Rock stock |
| ARGX-112 | IL-22R | Skin Inflammation | | | | | Eligible for up to ~€100mm in milestones and tiered royalties |
| ARGX-115 (abbvie) | GARP | Cancer Immunotherapy | | | | | Received $50mm so far; eligible for up to $625mm milestones & tiered royalties |
| ARGX-116 (STATEN BIOTECHNOLOGY) | ApoC3 | Dyslipidemia | | | | | Eligible for double-digit royalties and exclusive option to license the program |

- We obtained the exclusive license option from **Broteio Pharma** for an antibody against a novel complement target
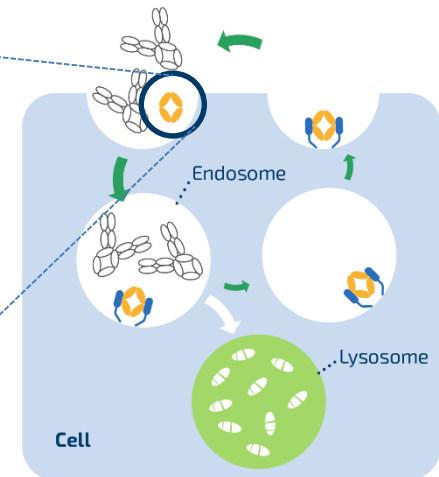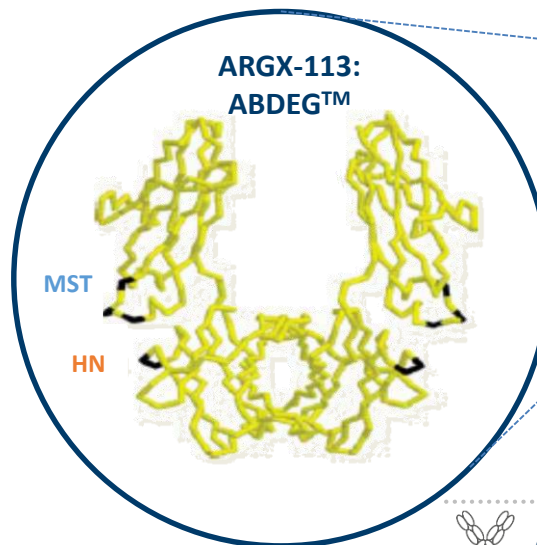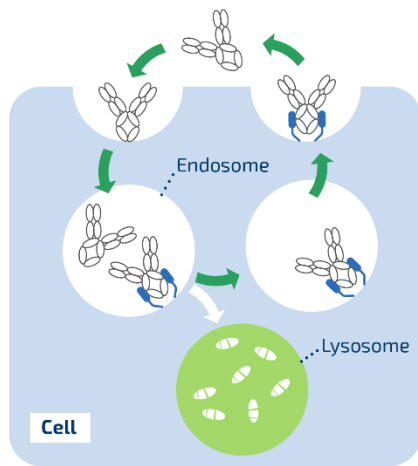- We have an antibody discovery alliance with *Shire* focused on multiple rare disease targets

# ARGX-113: A Pipeline-in-a-Product Opportunity

# ARGX-113: Lead Program Based On Novel Target FcRn

An innovative approach to eliminate IgG autoantibodies

**IgG antibodies recycle through FcRn[1]...**   **...ARGX-113 potently blocks FcRn...**   **...leading to IgG elimination**



Endosome

Lysosome

Cell

**ARGX-113: ABDEG™**

MST

HN

Endosome

Lysosome

Cell

Antibody      ARGX-113      FcRn

- ARGX-113 is a human IgG1 Fc-fragment that utilizes ABDEG™ Fc engineering technology[2][3]
- ARGX-113 targets and binds to FcRn blocking the recycling of IgG leading to an elimination of IgG antibodies
  - Demonstrated 50% to 85% reduction of circulating IgG antibody levels in Phase 1 trial
- Pathogenic IgG antibodies mediate multiple autoimmune diseases
  - 30% pathogenic IgG reduction believed to be clinically meaningful in MG
- Phase 2 focus on myasthenia gravis (MG) and immune thrombocytopenia (ITP), data est. 1Q2018/2H2018

(1) Roopenian et al. 2007, Nat Rev Immunol.
(2) Vaccaro et al. 2005, Nat Biotech.
(3) argenx data

## Prioritizing IgG autoantibody mediated diseases

**Landscape of IgG severe autoimmune diseases (selection)**

Immune Thrombocytopenia

Scleroderma

Lupus

Epidermolysis Bullosa Acquisita

Myasthenia Gravis

Rheumatoid Arthritis

Multiple Sclerosis

Anca Vasculitis

Pemphigus

Bullous Pemphigoid

**Solid Biological Rationale**
**Disease proven to be predominantly mediated by pathogenic IgGs**

**Feasible for Biotech**
**Orphan potential, economically viable, efficient clinical & regulatory pathway**

**Proof of Concept Value**
**Spill-over effect into adjacent indications**
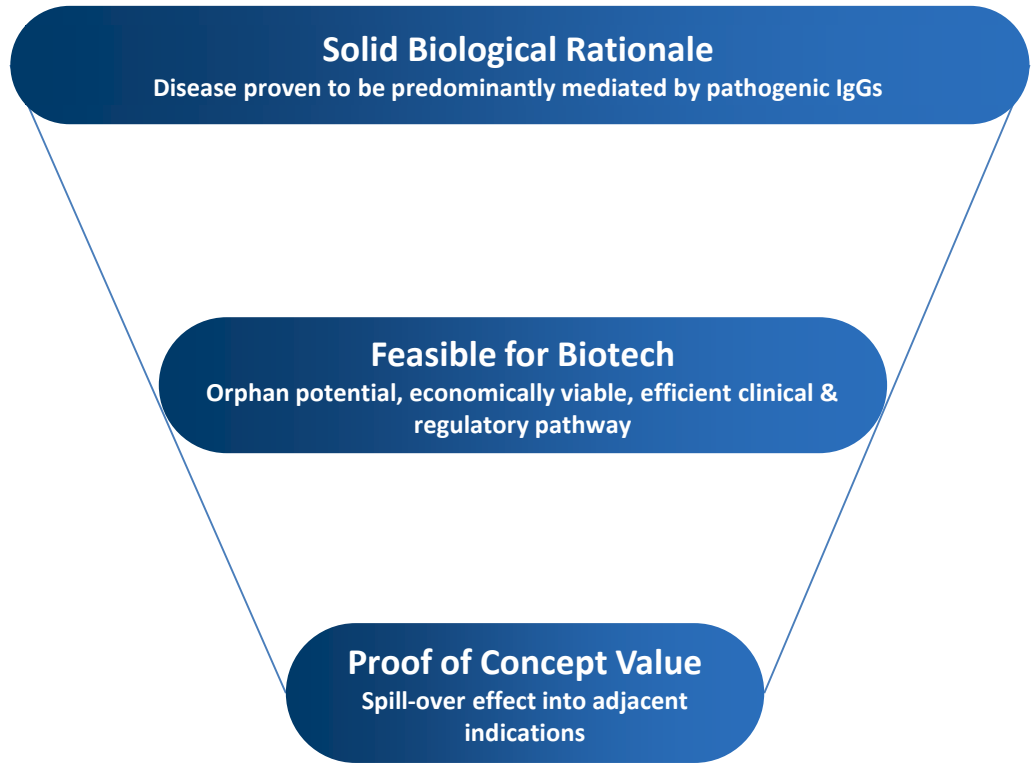
**Myasthenia Gravis**

**Immune Thrombocytopenia**

**Pemphigus vulgaris**

Beachhead neuromuscular diseases

Beachhead heme disorders

Beachhead blistering diseases

argenx data

# Myasthenia Gravis (MG) Overview

## What is Myasthenia Gravis?

- Rare autoimmune disorder; 64,000[1] patients in U.S., 55,000[2] with generalized MG, affecting all ages and both genders

- MG associated with muscle weakness; can be life threatening if respiratory muscles affected

- Symptoms include: Life-threatening choking; muscle dislocation; eyelid fatigue; pain; problems with vision, speech, mobility, fatigue

## Limited current treatment options

- Limited treatment options

  - Cholinesterase inhibitors
  - Corticosteroids
  - Immunosuppressants
  - IVIg or Plasmapheresis (exacerbations or rescue)
  - Thymectomy (minority of patients)

- Severe side effects of current treatment options: Injury, liver malignancy, osteopenia, osteoporosis, cataracts, depression, hypertension, hematologic suppression, headache, disfigurement, infection, thrombosis

- IVIg and Plasmapheresis place a heavy cost burden on healthcare systems in the acute setting (~$79,000[3] and ~$101,000[3] respectively)

## Myasthenia Gravis Cause

Autoantibodies (IgG type) destroy neuromuscular junctions:

- Blocking of Acetylcholine Receptors (AChRs)

- Cross-linking + internalization of AChRs

- Complement recruitment



- Myelin sheath
- Axon
- Acetylcholine
- Auto-antibodies
- Acetylcholine receptors
- Muscle
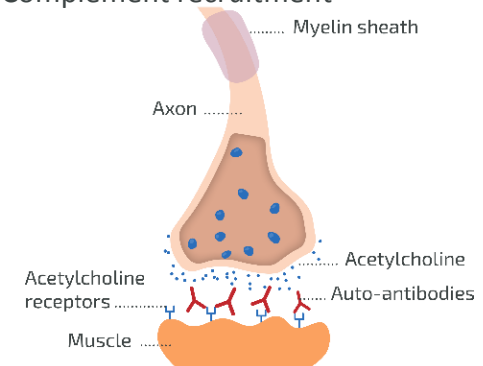
(1) Philips et al. 2003, Ann N Y Acad Sci.
(2) Drachman et al. 1993, New Eng J Med.
(3) Heatwole et al. 2011, J Clin Neuromuscul Dis.

# Autoantibody Levels (IgGs) Correlate With MG Disease Score

>30% autoantibody reduction clinically meaningful

| Treatment* | Plasmapheresis | Immuno-adsorption | IVIg |
|---|---|---|---|
| Decrease in autoantibody levels (%) after treatment | 62.6 ± 0.9 | 55.1 ± 3.2 | 28.9 ± 3.8 |
| Decrease in disease score (%) after treatment | 60.8 ± 3.5 | 42.4 ± 4.2 | 23.8 ± 3.7 |
| Clinical efficacy rate after 14 days** | 12/15 | 7/10 | 6/15 |
| Duration of hospital stay (days) | 12.80 ± 0.28 | 13.50 ± 0.50 | 16.00 ± 0.50 |

* Comparison between 3 cycles of Plasmapheresis/Immunoadsorption every 24h-48h and 5 cycles of IVIg every 24h
** Clinically effective if disease score has improved by >50% 14 days after treatment

**Degree of autoantibody reduction correlates with clinical improvement and reduced hospital stay**

Liu et al. 2010, Ther Apher Dial.

# Immune Thrombocytopenia (ITP) Overview

## What is Immune Thrombocytopenia?

- Rare bleeding disease; estimated 72,000[1] patients in US, more frequent in females and patients over 60

- Symptoms range from mild bruising to severe bleeding

- Symptoms include: Fatigue, emotional strain, impact on work, fear of bleeding, impact on social activities, bruising

## Limited current treatment options

- Limited treatment options

  - Multiple iterations on corticosteroids & IVIg

  - Immunomodulatory agents

  - TPO mimetics & splenectomy

- Severe side effects from current treatments:
  Anaphylaxis, anorexia, backache, cancer, cataracts, depression, diabetes, fatal hemolysis, hepatitis, hypertension, infections, infusion-related reactions, leukoencephalopathy, nausea, osteoporosis, psychosis, sweating, neutropenia, thrombosis, vomiting, weakness

- Romiplostim and Eltrombopag, last-line therapies for ITP and have generated global revenues of $584 million[2] and $635 million[3] in 2016
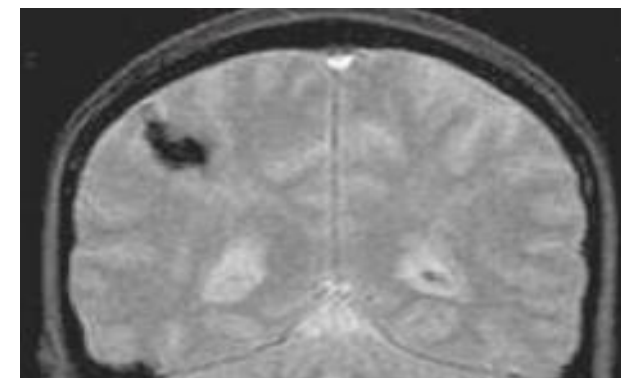
## Immune Thrombocytopenia Cause

Autoantibodies (IgG type) destroy blood platelets:

- Increased platelet removal

- Reduced platelet production



Platelets

Megakaryocytes

Bone narrow
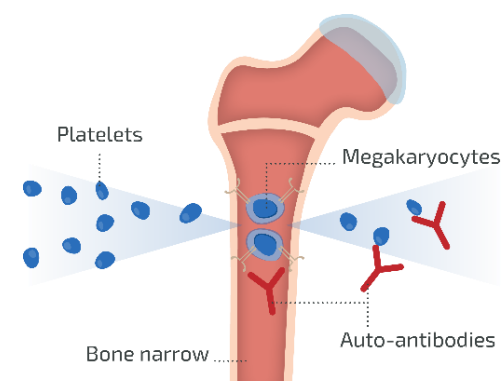
Auto-antibodies

(1) Saleh et al. 2015, Curr Med Res Opin.; Terell et al. 2012, Am J Hematol.; Grace et al. 2012, Pediatr Blood Cancer.
(2) Amgen Inc. 2016, Form 10-K.
(3) Novartis Annual Report 2016

Platelet levels during IVIg treatment in Adult Immune Thrombocytopenia

**Low bleeding risk**

**High bleeding risk**
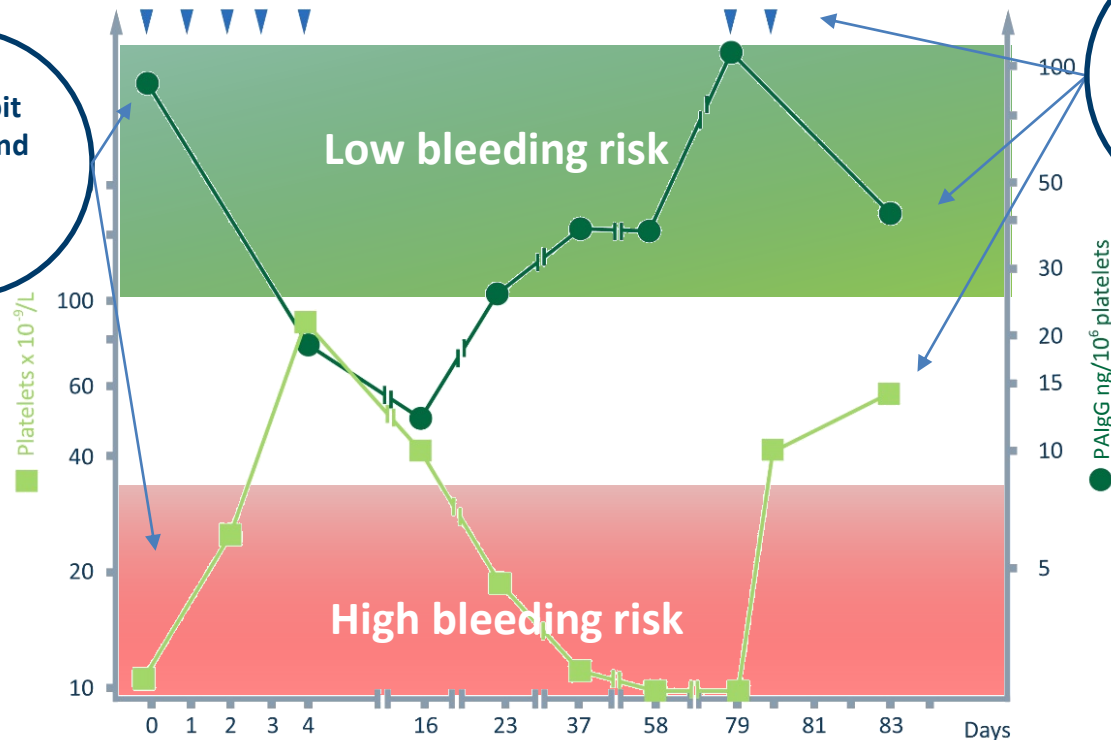
Autoantibodies inhibit platelet production and accelerate platelet destruction

Therapy aimed at reducing autoantibodies like IVIg (shown), plasmapheresis and immunoadsorption results in platelet increase

= IVIg treatment    = Autoantibody level    = Platelet counts

Winiarski et al. 1983, Scand J Haematol.

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# Pemphigus Vulgaris: Overview

## What is Pemphigus Vulgaris?

- Chronic, severe – potentially life-threatening – auto-immune disease

- ~ 17,000 people treated (US)[1]

- Mucosal and skin blisters leading to pain, difficult swallowing, skin infection

- Disease severity directly correlates to pathogenic IgG levels against desmoglein-1 (skin involvement) and desmoglein-3 (mucosal involvement)[2]

- Patients cycle through periods of remission and relapse for extended periods

## Limited current treatment options

- Current disease management comes with significant side effects and impacts QoL

    - High dose of corticosteroids and chronic immunosuppression (AZA, MFM)
    - Rituximab, IVIg, immunoadsorption and plasma exchange used for severe or refractory patients (10%), but not perceived as curative

- Treating physicians require new effective therapies with rapid onset of action that are safe

- Rituximab therapy shows slow onset of action, risk of developing serious adverse events and significant relapse rate [2] [3] [4]



### Pemphigus Vulgaris Cause

Diagnosis based on presence of pathogenic autoantibodies targeting desmoglein-1 and -3 in the skin
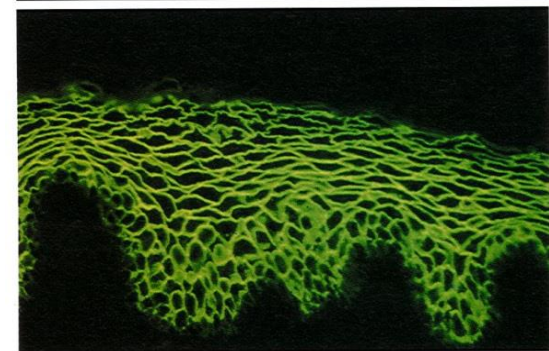


Auto-antibodies (predominantly IgG4 type) sterically hinder desmosomal adhesion and assembly – no complement involvement or immune effector activation[2]

(1) Collective Acumen  study (2) Kasperkiewicz et al. 2017, Nature Reviews
(3) Colliou et al. 2013, Autoimmunity (4) Joly et al. 2017, Lancet

# ARGX-113: Favorable Safety & Tolerability Profile

Phase 1 design: Double-blind, placebo-controlled trial in healthy volunteers

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

(mg/kg)

**SAD:** 50, 25, 10, 2, 0.2

4:2 → active:placebo

**MAD:** 25, 10

6:2 → active:placebo
Up to 6 doses

**Phase 1 HV: Completed**

- **Complete safety profile**
- **Complete PK/PD profile**
- **Phase 2 dose selected**
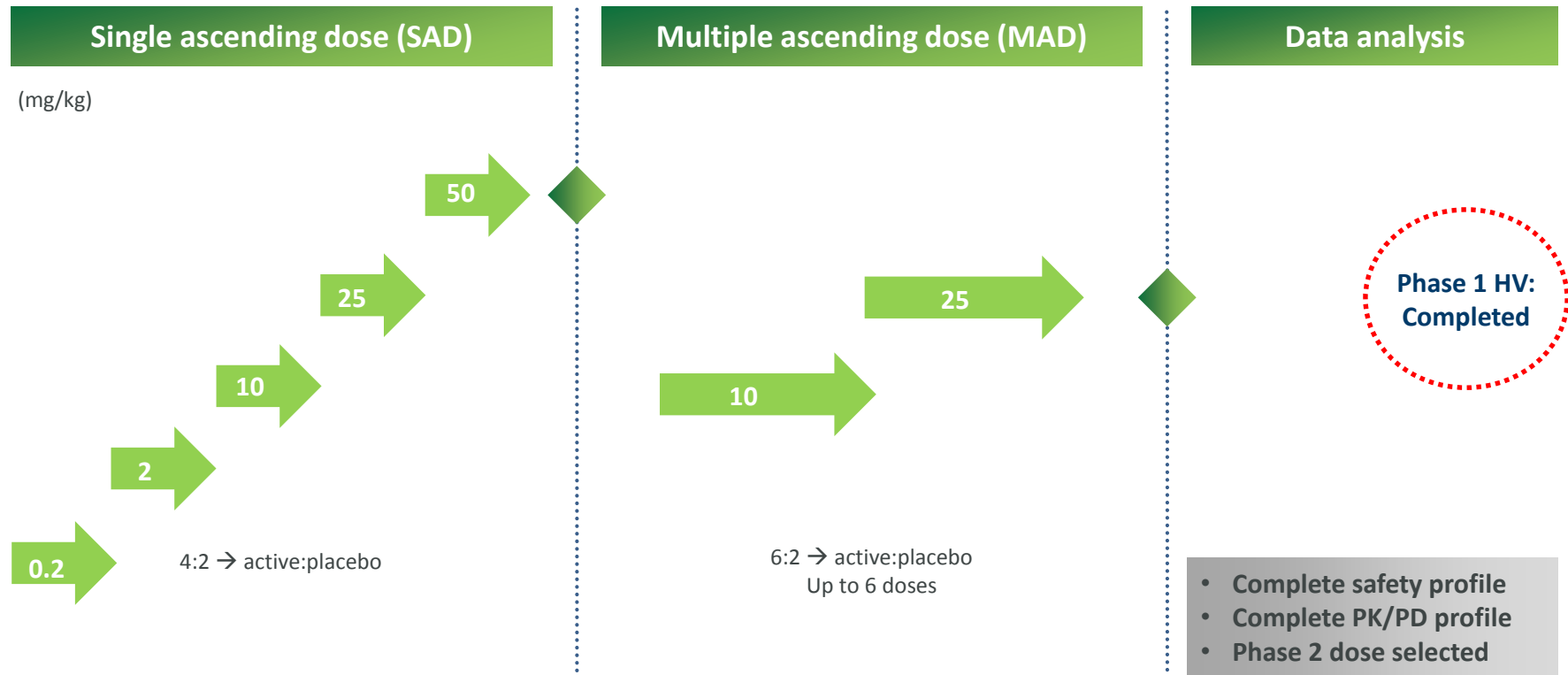
- SAD & MAD studies completed according to plan (62 healthy volunteers in total)

- Reported to be well tolerated in single and multiple doses of up to 25 mg/kg

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# ARGX-113: Selective IgG Reduction seen in Phase 1

Single ascending dose escalation study (SAD) in healthy volunteers (single 2hr infusion)



**Total IgG**

0.2 mg/kg
2 mg/kg
10 mg/kg
25 mg/kg
50 mg/kg

**Total IgM**

**Total IgA**
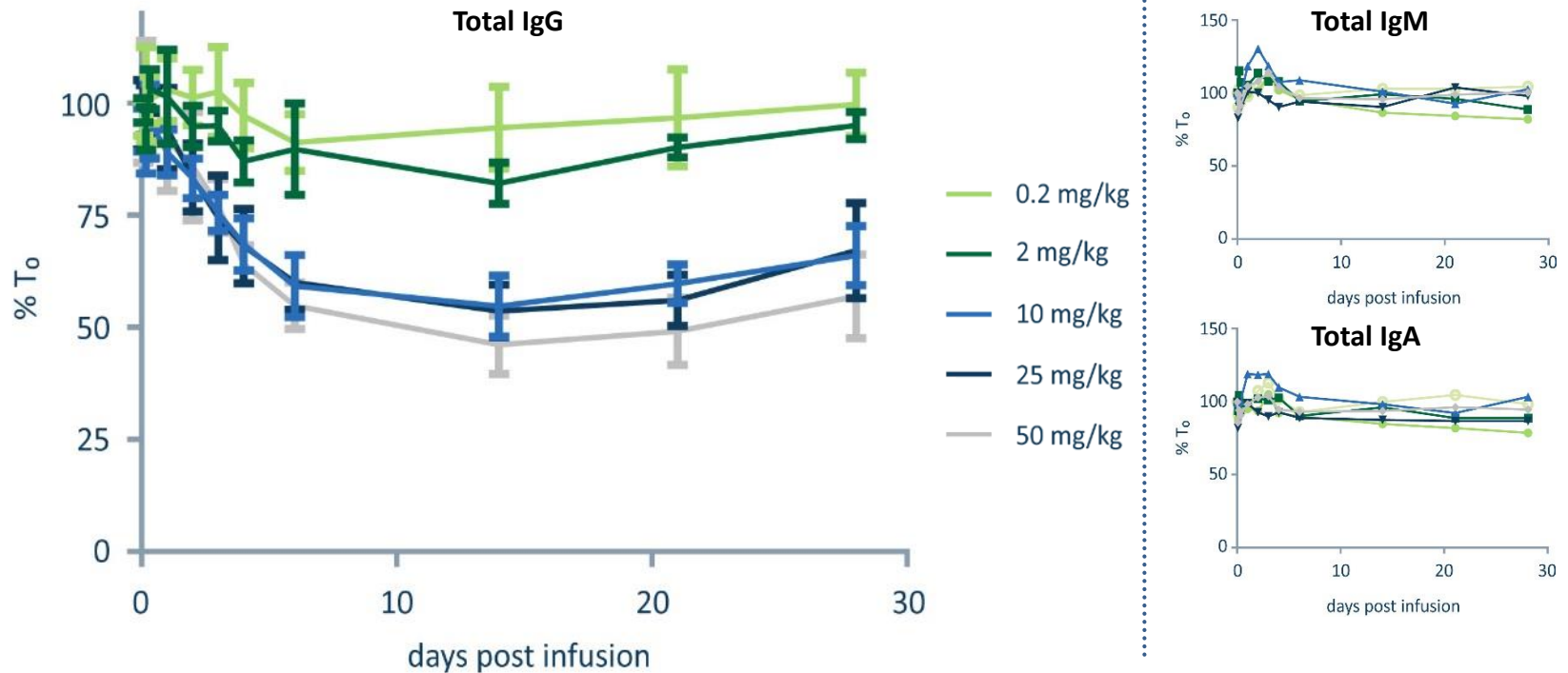
- ~50% IgG reduction (maximal PD effect) as of 6 days after infusion
- Selective IgG reduction, no significant reductions in IgM/IgA and albumin levels
- Low IgG levels maintained for more than four weeks after the last dose
- Saturation of PD effect observed at 10 mg/kg dose

argenx data

PD data multiple ascending dose (MAD) study in healthy volunteers

**Dosing 10 mg/kg; every 7 days**



**Total IgG**

▲ Moment of dosing (weekly dosing, 4x total, 10 mg/kg)
● active (n=6)
■ placebo (n=2)
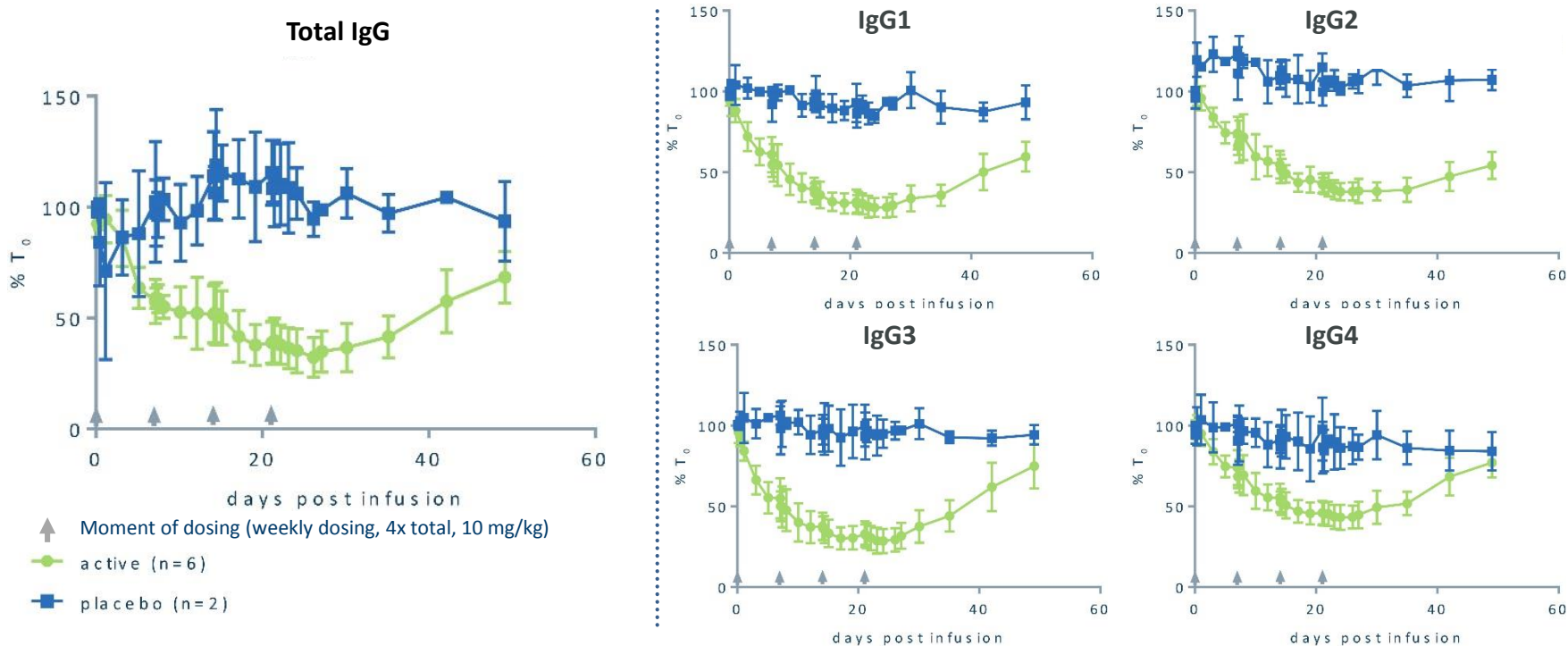
- Potent IgG reduction accross isotypes (AChR autoantibodies are IgG1/3; MuSK autoantibodies are IgG4)

- IgG reduction: 50% achieved in 1 week; up to 85% maximum reduction

- After last dose, IgG levels remain reduced by 50% or more for ~3 weeks, return to baseline after > 1 month

- Comparable data for 25 mg/kg, every 7 days (data not shown)

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# ARGX-113 in MG: Phase 2 Trial Design

**Study 100% recruited Oct 2017**

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| Screening/Randomization | Treatment Phase | Follow-up Phase |
|---|---|---|

**Screening ≤2 weeks**

**Randomization**

SoC + ARGX-113 (10mg/kg)
N=12

SoC + Placebo
N=12

4 doses; N= up to 24

**≤2 weeks** | **3 weeks** | **8 weeks**
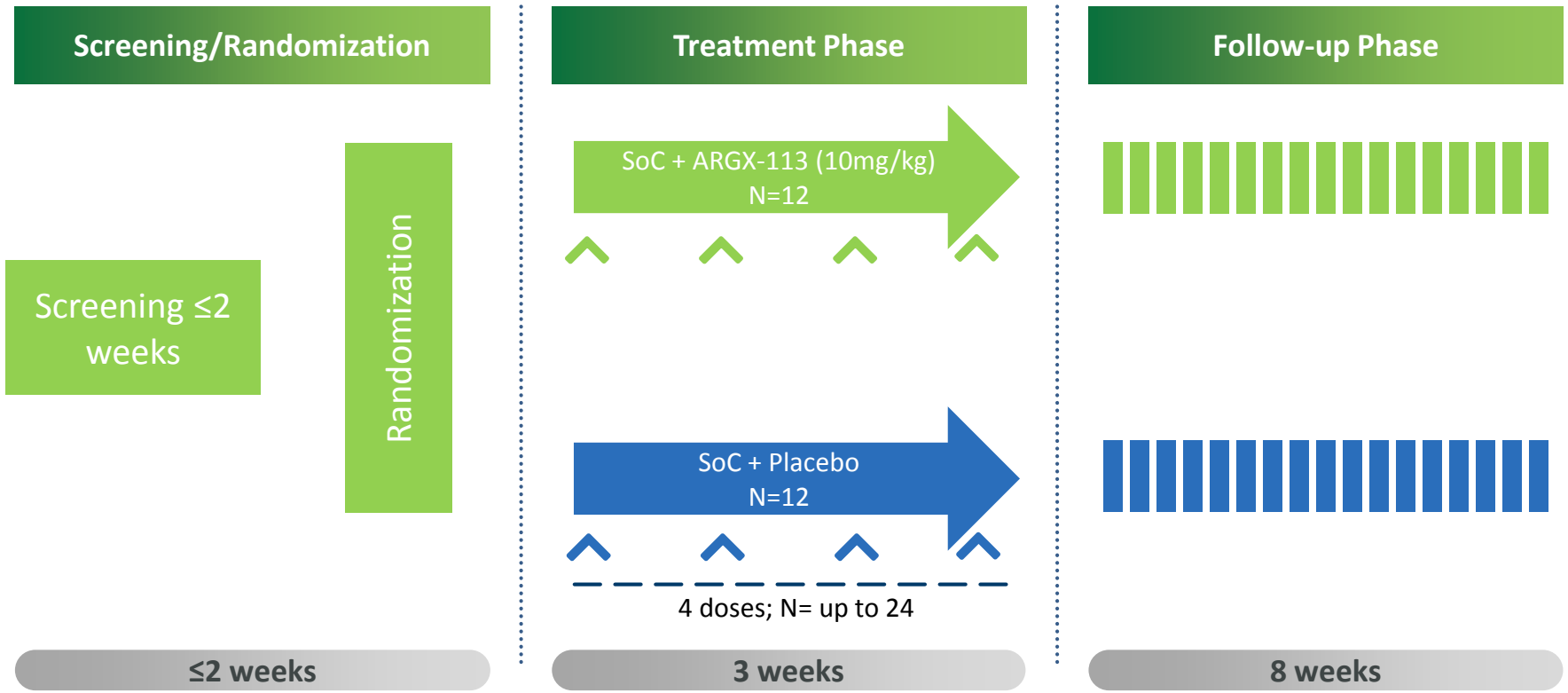
- Population: MG patients with generalized muscle weakness with total MG-ADL score ≥ 5*

- Primary Objectives: Evaluate safety and tolerability

- Secondary Objectives: (i) Evaluate efficacy, impact on quality of life and immunogenicity
  (ii) Assess pharmacokinetics (PK) and pharmacodynamics (PD) markers

argenx data, *> 50% of this score attributed to non-ocular items.

# ARGX-113 in ITP: Phase 2 Trial Design

| Screening/Randomization | Treatment Phase | Follow-up Phase |
|---|---|---|

Screening ≤2 weeks

Randomization

SoC + ARGX-113 (10mg/kg)
N=12

SoC + ARGX-113 (5mg/kg)
N=12

SoC + Placebo
N=12

4 doses; N= up to 36

| ≤2 weeks | 3 weeks | 8 weeks |
|---|---|---|
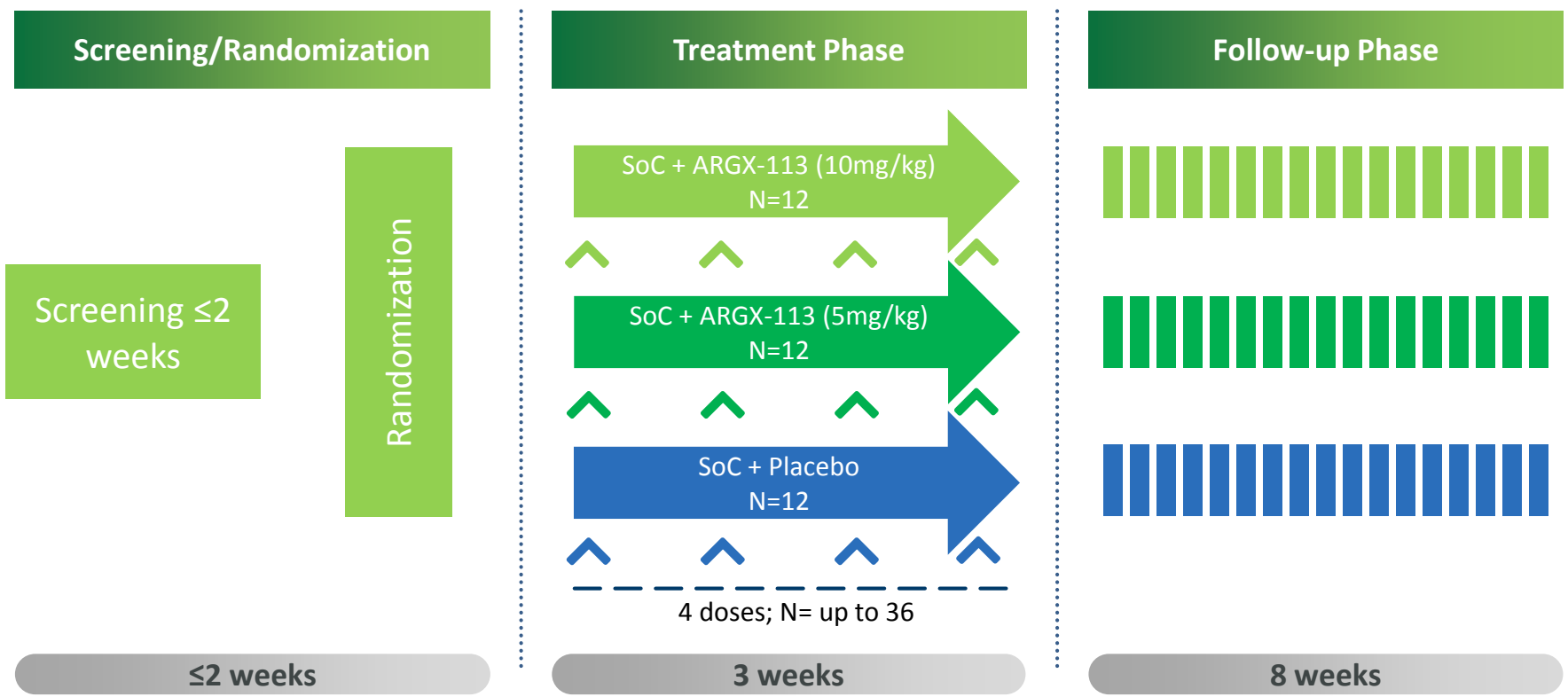
- Population: ITP patients with platelet levels < 30 X $10^9$/L

- Primary Objectives: Evaluate safety and tolerability

- Secondary Objectives:   (i) Evaluation of efficacy based on platelet counts, use of rescue treatment & bleeding events
(ii) Assess pharmacokinetics (PK) and pharmacodynamics (PD) effect
(iii) Evaluate immunogenicity

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# ARGX-113 Phase 2 study : IDMC-driven adaptive design

| Treatment Phase | Follow-up Phase |
|---|---|

| Induction | Maintenance | |
|---|---|---|
| **3 weeks** | **6 weeks** | **8 weeks** |

COHORT 1: N= 4

ARGX-113 (10mg/kg)

ARGX-113 (10mg/kg)

4 infusions (weekly)

2 infusions (w2, w6)

COHORT 2 & 3: N= 4 + 4

ARGX-113 (adjusted dose)

ARGX-113 (adjusted dose)

4 infusions (weekly)

adjusted frequency
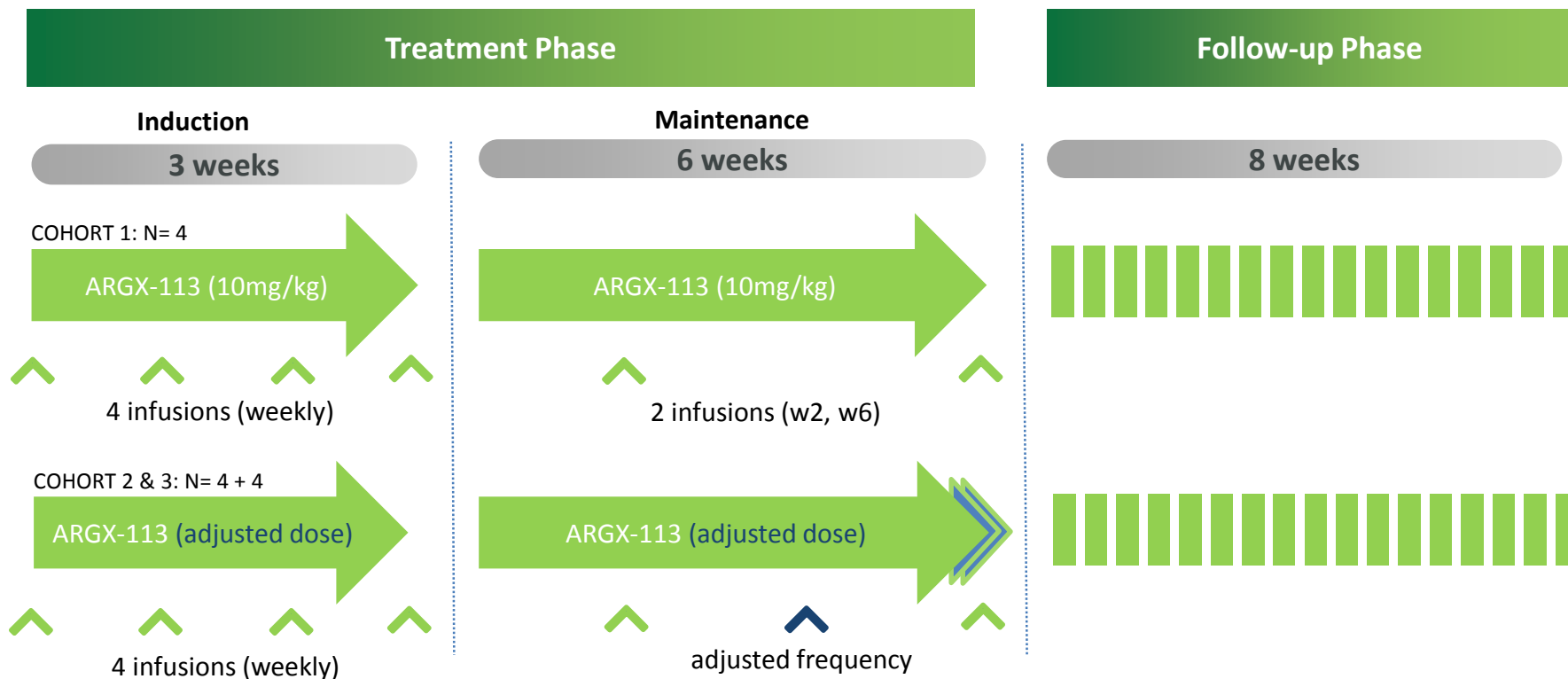
- Patients enrollment divided in 3 sequential cohorts
- IDMC recommendations for cohorts 2 & 3:
    - Change of dose (max dose of 25mg/kg)
    - Frequency of administration at maintenance (max 2 extra doses after each cohort)
    - Expansion of maintenance duration

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# ARGX-113: Feasibility of SubQ Dosing

Exploring SubQ formulations for larger patient populations (chronic, ex-hospital)

**PK single dose administration: IV vs SubQ (in cyno)**

**PD single dose administration: IV vs SubQ (in cyno)**

- ● 20mg/kg ARGX-113 i.v.
- ■ 20mg/kg ARGX-113 s.c.

- ● 20mg/kg ARGX-113 i.v.
- ■ 20mg/kg ARGX-113 s.c.

ARGX-113 (µg/ml)

Days post administration

cyno IgG % $T_0$

Days post administration
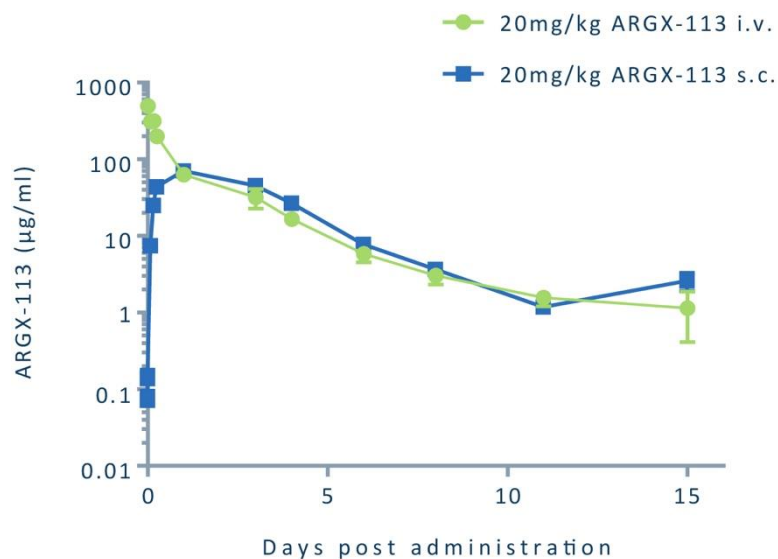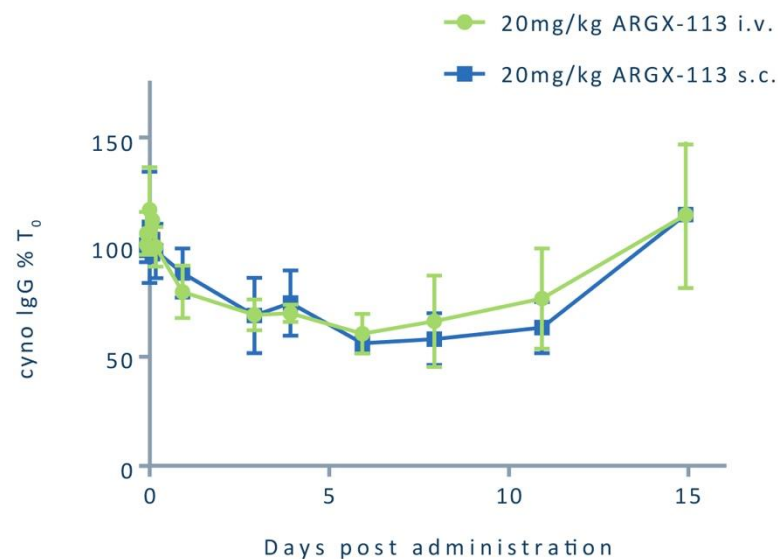
- Comparable PK and PD of IV versus SubQ dosing in preclinical studies demonstrated
  - Comparable half life
  - Favorable bio-availability of the compound in SubQ dosing (> 75%)
  - Comparable reduction of IgGs with single dose; up to 50%

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# ARGX-110: Phase 1 / 2 Mono & Combo Therapy

## Three distinct modes of action to target CD70+ tumor cells

**Activation of the pathway leads to release of sCD27**

**CD70/CD27 (receptor) signalling leads to proliferation and survival of tumor cells**

CD27    CD70

Tumor cell

Treg

CD70    CD27

CD70    CD27

CD70

**1** **Block tumor growth signal**

**2**

**3** **Restore immune surveillance**

**Kill tumor**
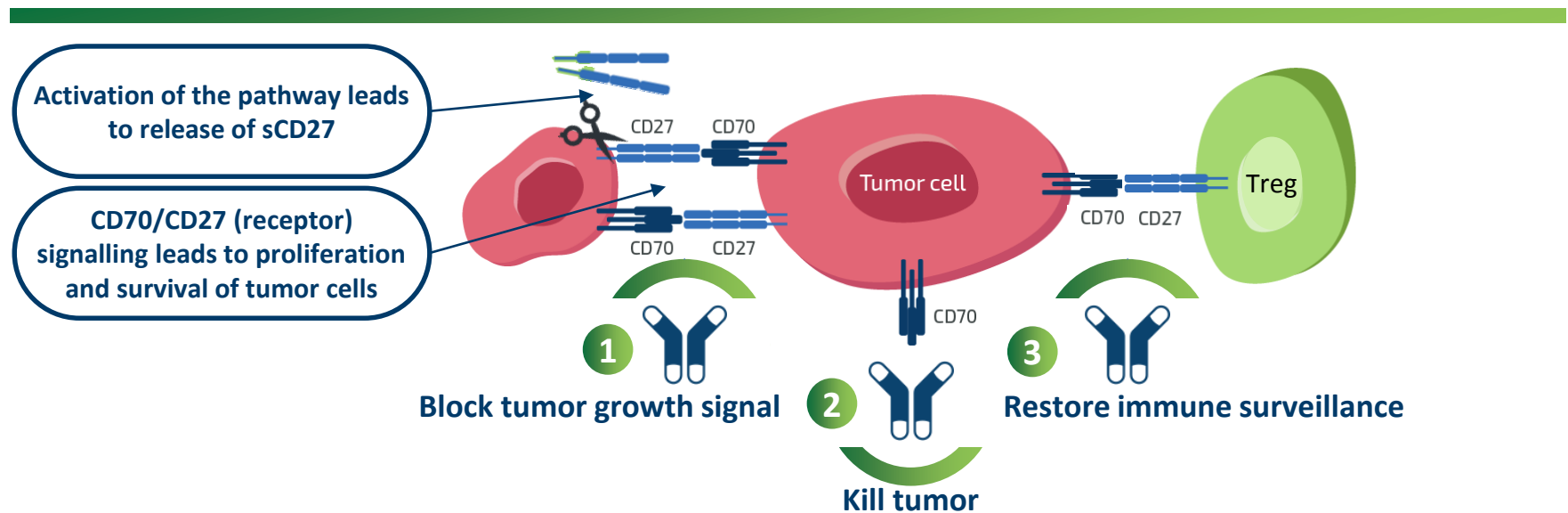
- ARGX-110 is a SIMPLE Antibody™, equipped with POTELLIGENT® Fc engineering technology
- ARGX-110 targets CD70 to block CD27 interaction, kill CD70 expressing cells and restore immune surveillance
- Soluble CD27 is a biomarker
- Phase 1: encouraging safety & tolerability profile and promising preliminary signs of efficacy in CTCL
- Focus on two rare & aggressive hematological tumors: CTCL and newly diagnosed AML / high-risk MDS
  - Interim results from dose escalation part of Phase 1/2 AML/MDS trial expected YE:2017
  - Interim POC data from Phase 2 CTCL trial expected YE:2017

# Cutaneous T-Cell Lymphoma: Fact sheet

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## What is Cutaneous T-Cell Lymphoma?

- Rare and incurable sub-type of T-cell lymphoma

- Prevalence (US & Canada): ~ 30,000 & Incidence (US): ~ 3,000[1]

- Patients typically diagnosed in their 60s

- Mycosis fungoides (50%), Sézary syndrome most common types [2]

- Symptoms include: severe rash, itching, tumor, skin Infections

- Skin infection often cause of death

## Limited current treatment options

- Initial treatment includes topical dermatology agents (corticosteroids, PUVA, e-beam therapy)

- Advanced stage patients treated with systemic oncology agents which are only moderately effective and not curative

  - Targretin bexarotene (oral) 1st line option – ease of administration

  - Istodax romidepsin (ORR: 34%, mDoR: 13-15 mos)[3] 2nd line – complicated dosing and myelosuppression

  - Antifolates (methotrexate, pralatrexate), Campath, chemo (Doxil, CHOP, etc)

- Heavily pre-treated, elderly patients are unfit for aggressive chemotherapy or stem cell transplantation

- Significant unmet need for effective, tolerable, long-lasting CTCL treatments



## Cutaneous T-Cell Lymphoma Cause

- Disease aetiology unknown

- Potentially caused by aberrant stimulation of CD4+ T-cells by Langerhans cells, specialized antigen presenting cells in skin

- Malignant T-cells become independent of stimulation by LCs and invade other tissues

- Sézary syndrome is a leukemic variant of CTCL
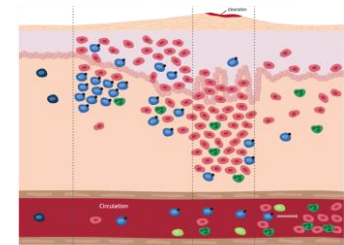
(1) Cutaneous Lymphoma Online Learning Center: http://www.clfoundation.org/online-learning-center/disease/faq/who-gets-cutaneous-lymphoma-how-many-people-have-it.
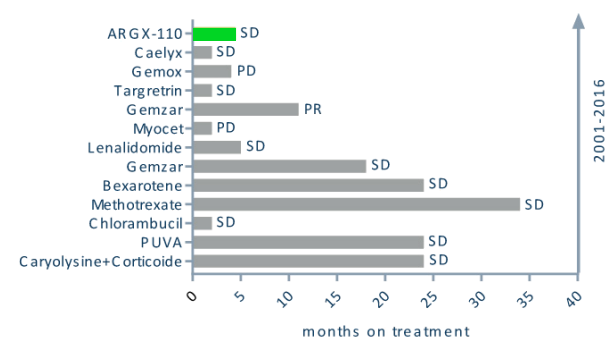(2) Lymphoma Research Foundation: http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300151
(3) http://www.istodax.com/hcp/ctcl/study-design/efficacy

## Phase 1-2: Typical patients are elderly and failing multiple lines of previous treatment



© argenx, based on Kim et al., 2005, J Clin Invest, argenx data –patient anecdotes – uncleaned.
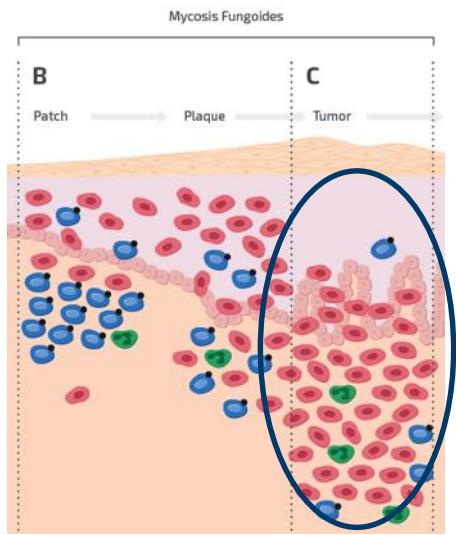
# ARGX-110: Effect On Malignant Cells In Skin

## Patient example 1: Cutaneous TCL – mycosis fungoides (MF)
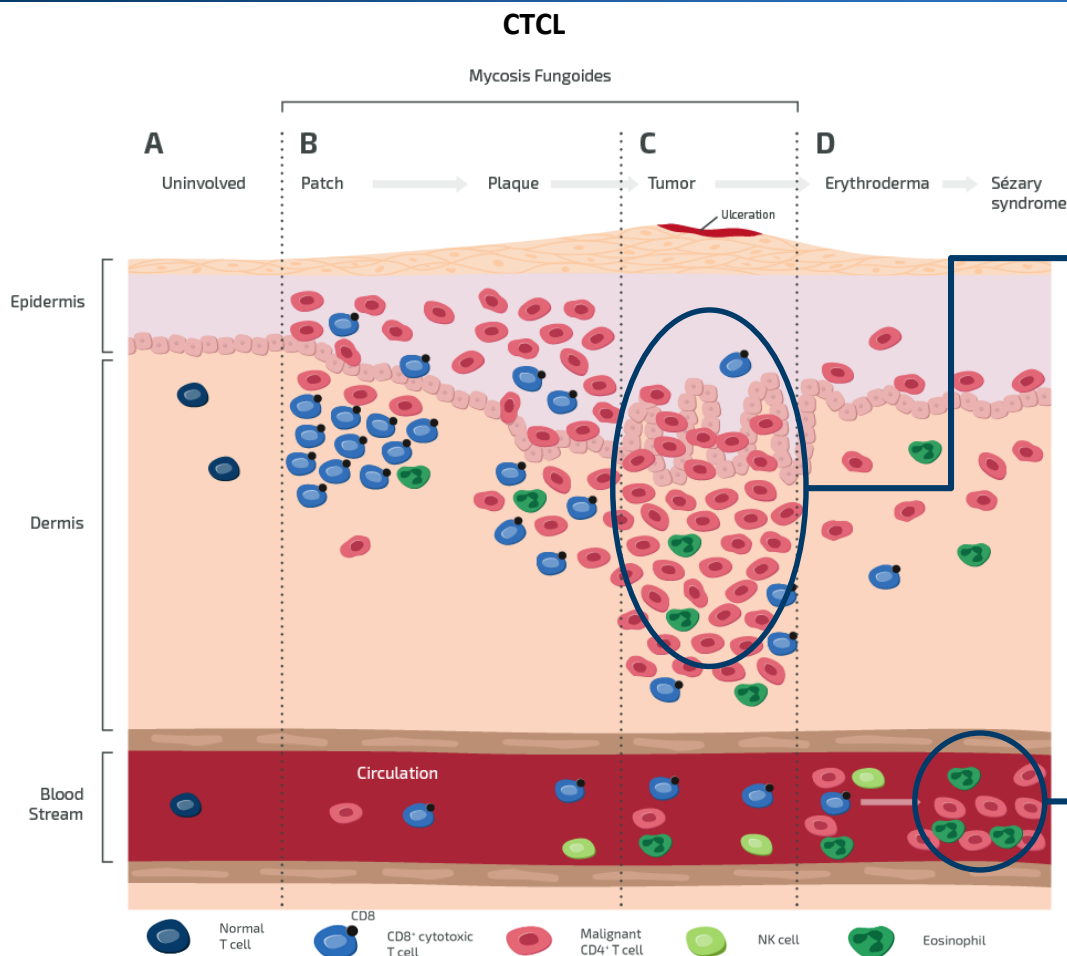


**Typical Mycosis fungoides (MF) patient**

| Patient | 67 year old male CTCL-MF, diagnosed 2001 |
|---------|------------------------------------------|
| Tumor | Skin T4, Nx, M0, B0 (Stage IIIA) |
| Doses | 6 |

**Decrease of CD4+ malignant T-cells**

CD4+

**Depletion of CD70+ malignant T-cells**

CD70

**Infiltration of CD8+ T-cells**

CD8+

Pre-treatment

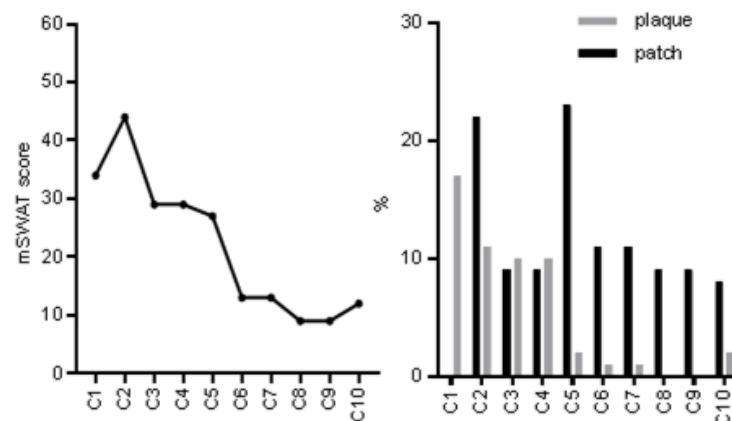post (Cycle 2)

# ARGX-110: Improved mSWAT & Skin Lesions

## Patient example 2: Cutaneous TCL – mycosis fungoides (MF)



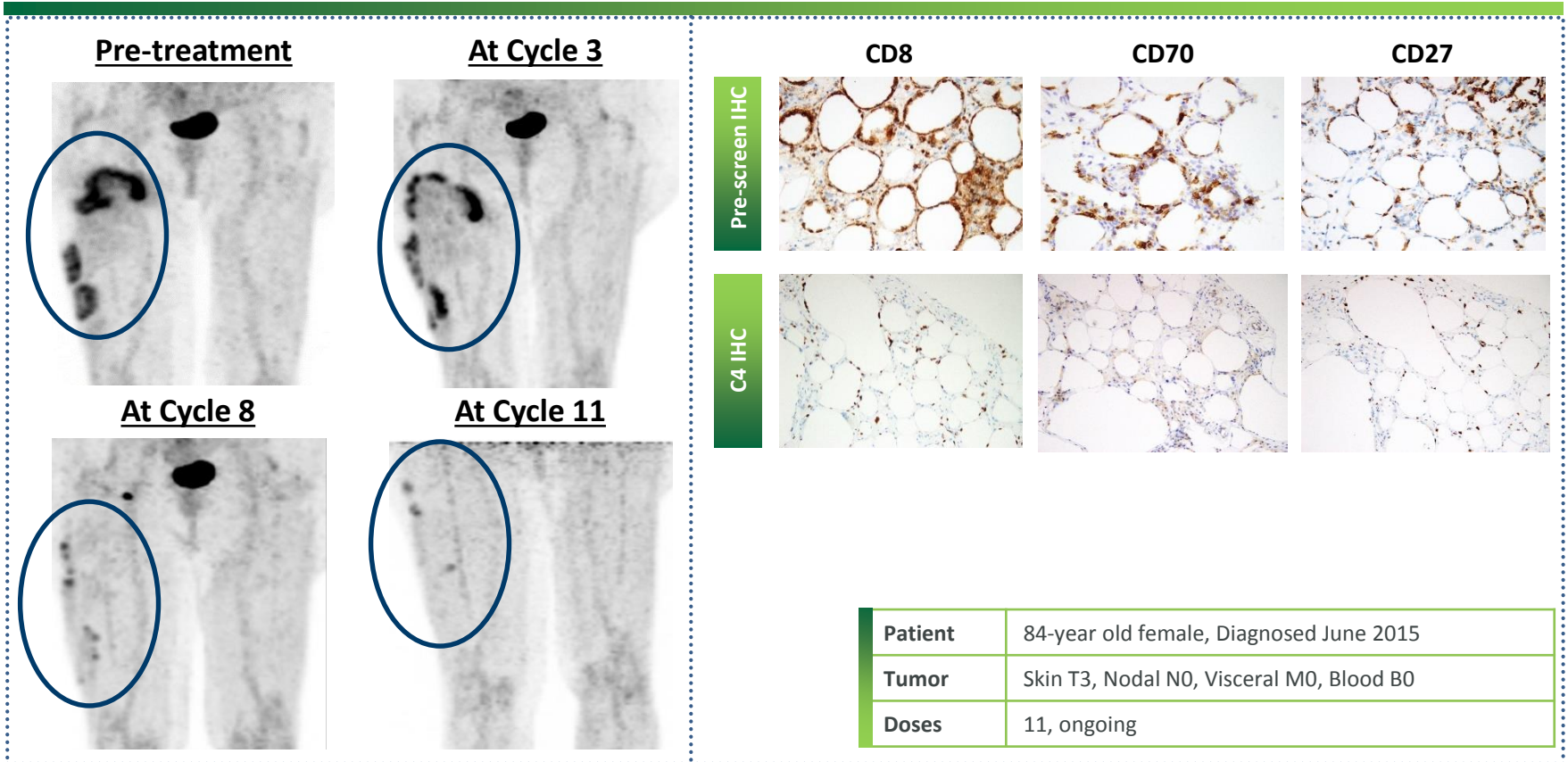**Pre treatment**     **At cycle 6**

- 60% reduction of mSWAT score constitutes a partial response (PR)
- Decrease in surface area of cutaneous tumor lesions
- Lesions improve from plaques to patches
- Some lesions completely resolved

| Patient | 79 year old female with CTCL-MF, diagnosed 2007 |
|---------|------------------------------------------------|
| Tumor | Skin T2, N0, M0, B0 (stage IB) |
| Doses | 16, 1 mg/kg q3w |

argenx data –patient anecdotes – uncleaned. Pictures kindly provided by investigator.

## Patient example 3: CTCL (panniculitis like TCL type)



| Patient | 84-year old female, Diagnosed June 2015 |
|---------|------------------------------------------|
| Tumor | Skin T3, Nodal N0, Visceral M0, Blood B0 |
| Doses | 11, ongoing |

- Partial Response after 5 doses (dose 1 mg/kg)
- Further improvement through cycle 8 to 11 cycles (dose increased to 5 mg/kg)
- Patient now on maintenance dose of 5 mg/kg q6wk

# ARGX-110 Shows Activity Across CTCL Types & Disease Stages

## Interim Phase 1b data in CTCL

June 1, 2017

| Indication[1] | Stage | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8 | C9 | C10 | C11 | C12 | C13 | C14 | C15 | C16 | C17 | C18 | C19 | C20 | Best Response[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CTCL with circ clone | Not known | ■ | ■ | ■ | ■ | ■ | ■ | | | | | | | | | | | | | | | Stable Disease |
| CTCL TFH like | Not known | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | Stable Disease |
| CTCL-SS | Not known | ■ | | | | | | | | | | | | | | | | | | | | Progressive disease |
| CTCL TFH like | T2, N0, M0, B0 | ■ | | | | | | | | | | | | | | | | | | | | Progressive Disease |
| **CTCL panniculitis type*** | T3, N0, M0, B0 | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | | | | | | | Partial Response |
| CTCL-MF/SS (+PTCL-NOS[3]) | T4, N3, M0, B0 | ■ | | | | | | | | | | | | | | | | | | | | Progressive disease |
| CTCL-MF | T4, N0, M0, B0 | ■ | ■ | ■ | ■ | ■ | | | | | | | | | | | | | | | | Stable Disease |
| CTCL-MF | T4, Nx, M0, B0 | ■ | ■ | ■ | ■ | ■ | ■ | | | | | | | | | | | | | | | Stable Disease |
| CTCL-MF | T2, N0, M0, B0 | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | | | | | | Partial Response |
| CTCL-MF | T4, Nx, M0, B0 | ■ | | | | | | | | | | | | | | | | | | | | Progressive Disease |
| CTCL-SS | T4, N3, M0, B1 | ■ | | | | | | | | | | | | | | | | | | | | Progressive Disease |
| CTCL-SS | T4, Nx, M0, B2 | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | ■ | | | | | | | | Partial Response |
| CTCL-SS | T2, Nx, M0, B2 | ■ | | | | | | | | | | | | | | | | | | | | Progressive Disease |
| CTCL-MF | T3, N0, M0, B1 | ■ | ■ | ■ | ■ | ■ | ■ | | | | | | | | | | | | | | | Stable Disease |
| CTCL-MF* | T1, Nx, M0, B0 | ■ | ■ | ■ | ■ | ■ | | | | | | | | | | | | | | | | Stable Disease |
| CTCL-MF | T3, Nx, M0, B0 | ■ | ■ | ■ | | | | | | | | | | | | | | | | | | Stable Disease |

- Encouraging signs of clinical activity
- Heavily pre-treated patients on study dosed up to 16 cycles
- Itching often disappears after first cycle(s)

*Number of cycles on study, one cycle = 3 weeks, 17 cycles = ~1 year*

■ 1 mg/kg   ■ 5 mg/kg

argenx data (uncleaned)
* Still on study as of June1, 2017
(1) CTCL = cutaneous T-cell lymphoma; MF = mycosis fungoides; SS = Sézary syndrome.
(2) Based on modified Severity Weighted Assessment Tool (mSWAT) scoring, a common method of scoring skin lesions in CTCL; assess number and severity of lesions as and total body surface area affected. Stable disease = mSWAT score does not increase by >25%; partial response = at least 50% reduction in mSWAT score; complete response = 100% reduction in mSWAT score.
(3) NOS: not other specified. PTCL-NOS is the most common TCL subtype.

# Acute Myeloid Leukemia (AML) Overview
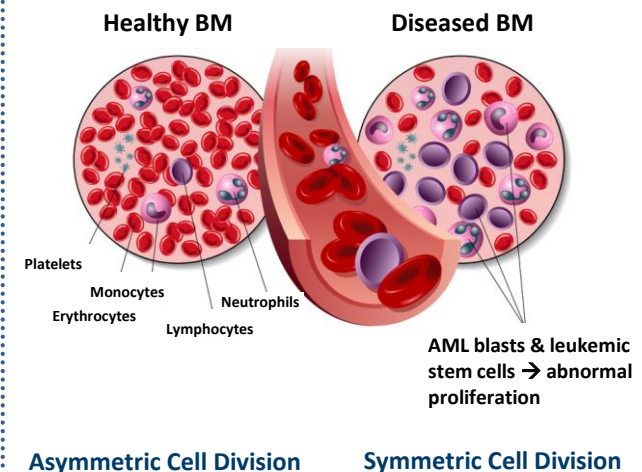
## What is Acute Myeloid Leukemia?

- Rare hematologic cancer characterized by **excessive proliferation of myeloid stem cells** and their **failure to properly differentiate into mature white blood cells**

- Symptoms include: weight loss, fatigue, fever, night sweats, loss of appetite, shortness of breath, easy bruising, infections, bleeding

- Disease progresses very rapidly and is fatal if left untreated

- ~22,000[1] new cases per year in the U.S. — **2nd most common leukemia subtype** in adults

- Generally a **disease of the elderly** — 60% of diagnosed patients are older than 60

## Limited current treatment options

- **Elderly, frail patients** are typically unfit for high dose chemotherapy — **receive palliative treatment with hypomethylating agents**

  - Median survival of 7 – 10 months

  - 5 year survival rate of ~6%[2] for patients over 65

- Younger patients (<45yr) typically get aggressive chemotherapy ("7+3" regimen) to induce remission followed by stem cell transplant

  - 5 year survival rate of ~57%[2] for patients under 45

- **Significant need for safer and more effective treatment options**



### Effects of AML on Bone Marrow

Healthy BM — Diseased BM

Platelets
Monocytes
Erythrocytes
Neutrophils
Lymphocytes

AML blasts & leukemic stem cells → abnormal proliferation
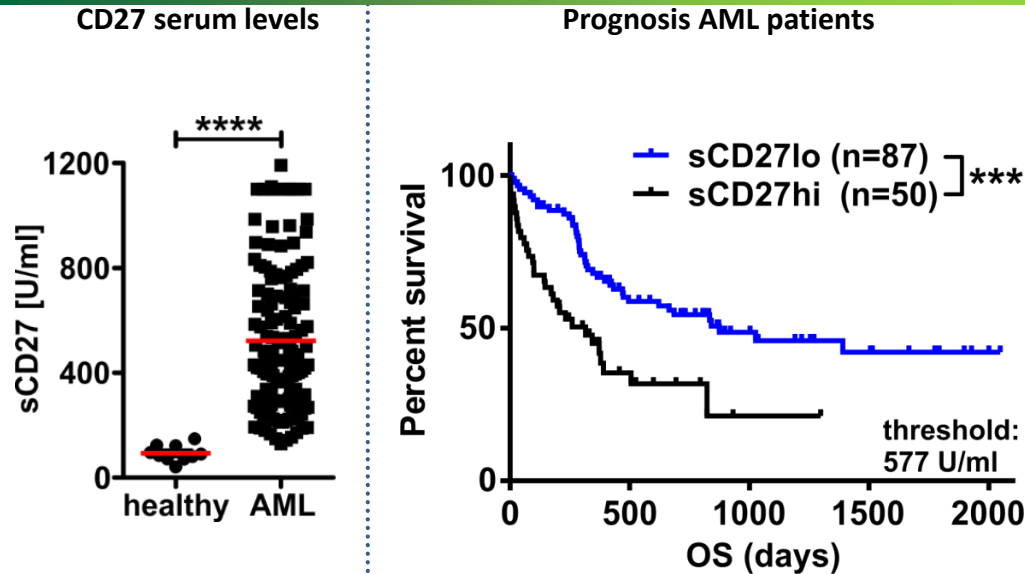
Asymmetric Cell Division — Symmetric Cell Division

(1) American Cancer Society: http://www.cancer.org/cancer/leukemia-acutemyeloidaml/detailedguide/leukemia-acute-myeloid-myelogenous-key-statistics .
(2) National Cancer Institute: Howlader et al. (eds). SEER Cancer Statistics Review, 1975-2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER web site, April 2016. Table 13.16
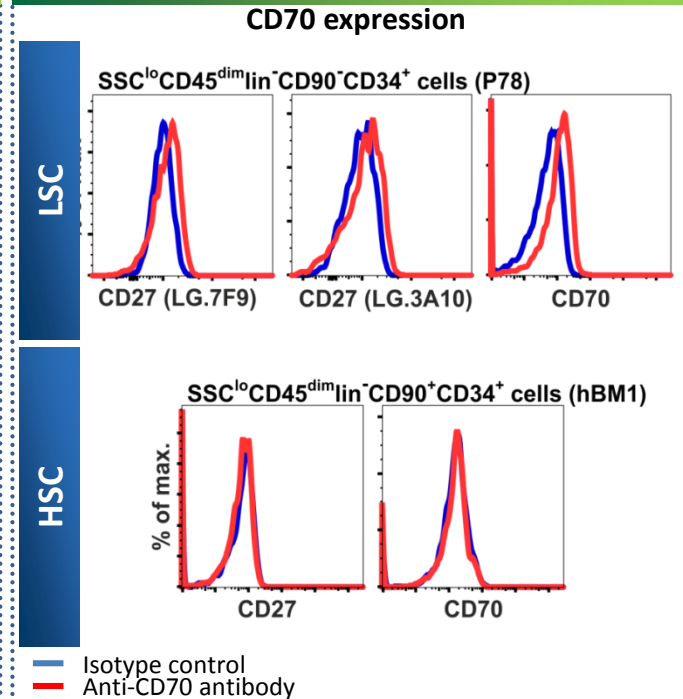
Potential to selectively target leukemic stem cells in AML patients



**Elevated sCD27 serum levels correlate with poor prognosis**

CD27 serum levels

Prognosis AML patients

sCD27lo (n=87)
sCD27hi (n=50) ***

threshold: 577 U/ml

**CD70 is selectively overexpressed on LSCs**

CD70 expression

LSC

$SSC^{lo}CD45^{dim}lin^-CD90^-CD34^+$ cells (P78)

CD27 (LG.7F9)   CD27 (LG.3A10)   CD70

HSC

$SSC^{lo}CD45^{dim}lin^-CD90^+CD34^+$ cells (hBM1)

CD27   CD70

— Isotype control
— Anti-CD70 antibody

- Elevated sCD27 serum levels in all newly diagnosed AML patients, **regardless of risk or age categories**
- sCD27 levels are an independent **negative prognostic marker in all newly diagnosed AML patients**
- **CD70 expressed on ~100% of AML blasts**, majority of malignant cells are CD70/CD27 double-positive
- **CD70/CD27 selectively overexpressed on Leukemic Stem Cells (LSCs)**, not on Hematopoietic Stem Cells (HSCs)

Riether et al. 2017, J Exp Med.

## Long-term effects *ex vivo*
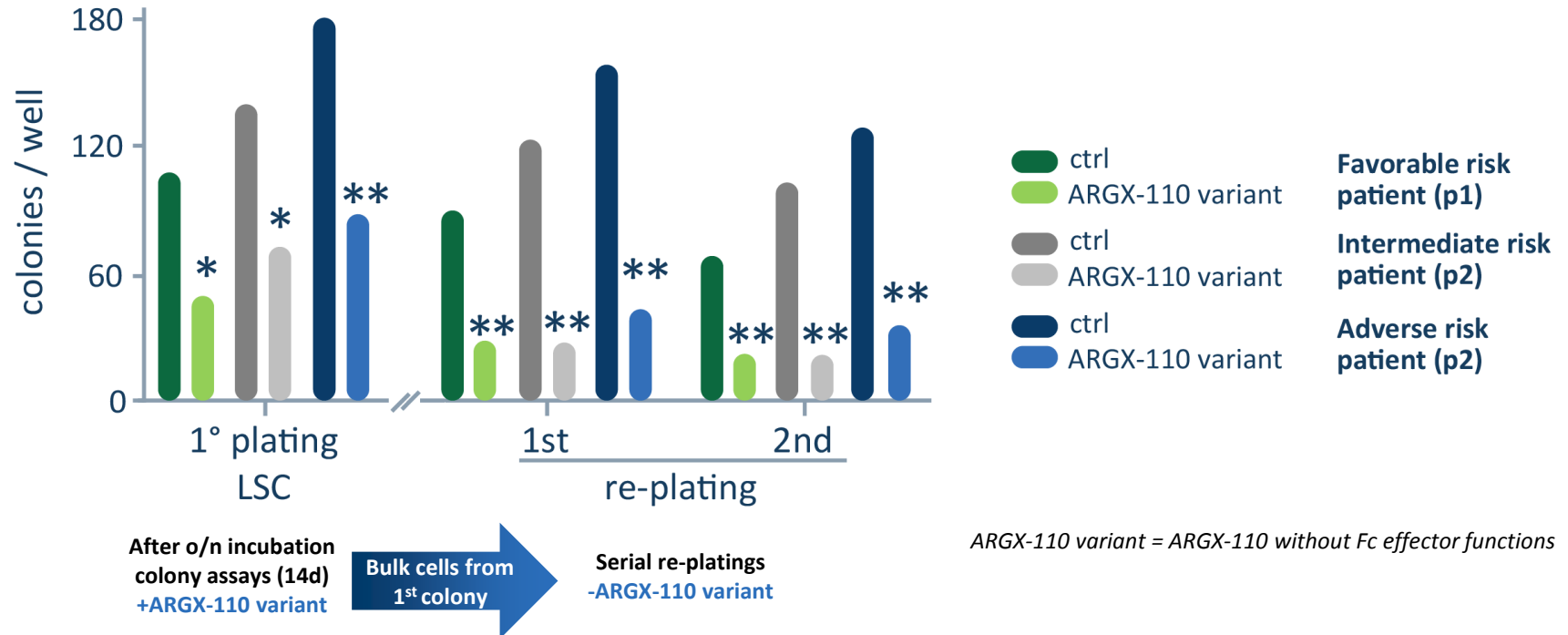


- Reduces LSC colony formation across patient risk categories (favorable/intermediate/adverse risk)
- Reduces LSC numbers as determined in serial re-plating experiments
- Blocking CD70 results in: (1) lasting down-regulation of stem cell genes (2) **increasing myeloid differentiation**

Riether et al. 2017, J Exp Med.

# ARGX-110: Curative Potential Of Monotherapy In Mouse Model

## Shown to reduce LSCs, increasing survival in AML model
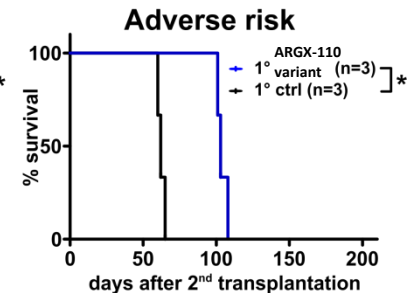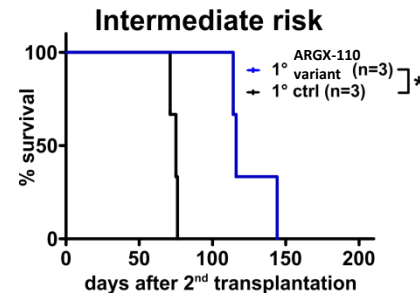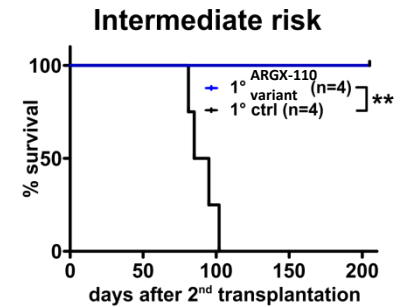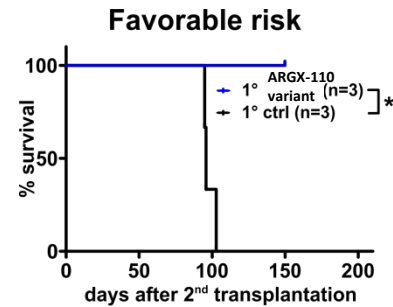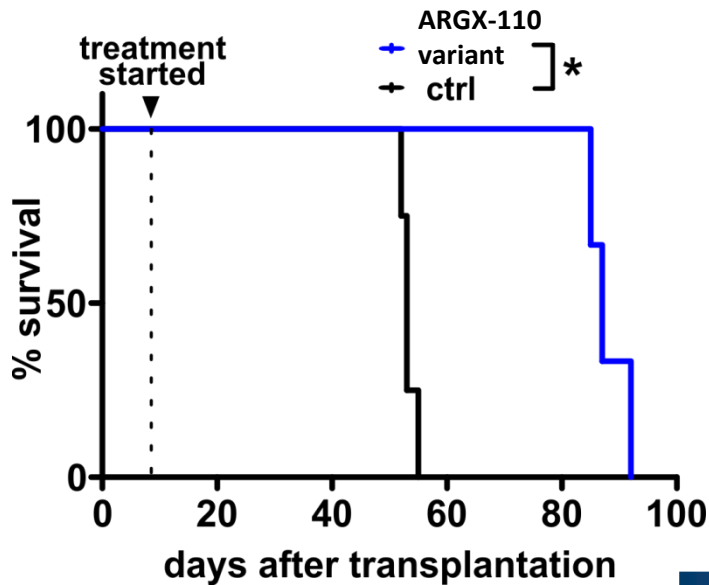


**Initial in vivo treatment**
**+ARGX-110 variant**

**Grafting Whole Bone Marrow cells from treated into new mice (14d after start of treatment)**

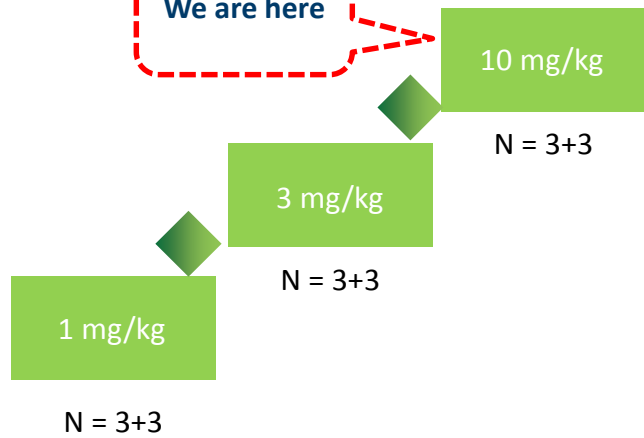**Transplant, evaluation**
**-ARGX-110 variant**

- Increased survival after secondary transplantation of AML BM cells from primary recipients transiently treated with ARGX-110 variant

- Increased survival observed for AML blasts taken from all 3 AML risk categories (fav/int/adv)

Riether et al. 2017, J Exp Med.

# ARGX-110 & Azacitidine For AML/MDS: Phase 1 / 2 Combo

## Phase 1 – Dose escalation

Safety and tolerability

Vidaza = 75 mg/m$^2$ (standard of care)

**We are here**

10 mg/kg

N = 3+3

3 mg/kg

N = 3+3

1 mg/kg

N = 3+3

N = up to 18

## Phase 2 – Proof-of-Concept

Efficacy

selected ARGX-110 dose

N = 15

selected ARGX-110 dose

N = 9 – (3-6 from Ph 1)
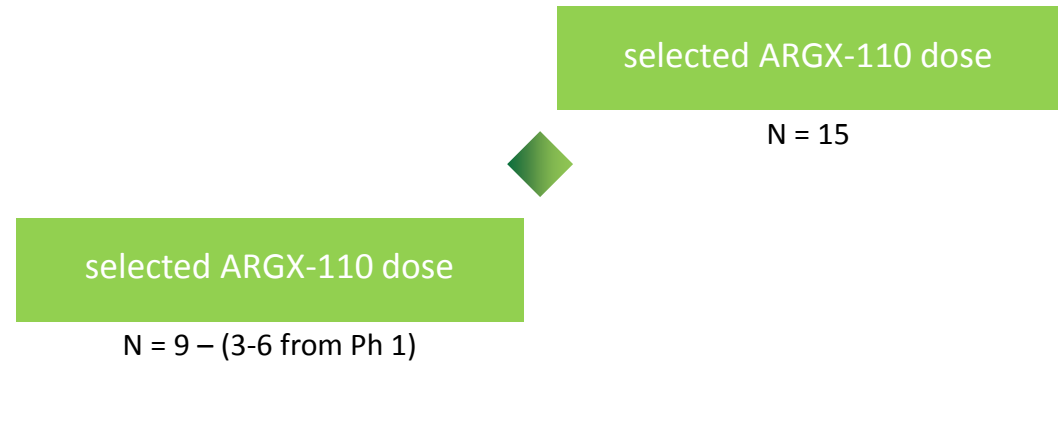
N = up to 21

- Hypomethylation agents such as Azacitidine increase CD70 expression[1]

- Population: untreated AML & high risk of myelodysplastic syndrome (MDS)*, eligible for AZA

- Design: open-label, non-controlled, non-randomized

*Some Myelodysplastic Syndrome (MDS) patients are at high risk of developing AML; MDS affects bone marrow cells, reducing their ability to produce red & white blood cells
(1) Zhou et al. 2011, Lupus.

# Business
# development & financials

# AbbVie Partnership for Novel Target GARP

## Strategic Antibody Collaboration Details

- **GARP** is a protein specifically present on the surface of activated regulatory T-cells (Tregs)
- **AbbVie** has option to
  - obtain exclusive, worldwide license to develop and commercialize ARGX-115
  - fund further GARP-related research by argenx beyond ARGX-115
- **argenx** conducts and funds all R&D through completion of IND-enabling studies
- **argenx** retains rights to combine ARGX-115 with its pipeline programs

## Financial Highlights

- **$40mm upfront payment**
- **Received** first of two **$10mm** preclinical milestones
- **$625mm in potential** development, regulatory and commercial **milestones**
- **Tiered royalties** on sales at percentages ranging from **mid-single digits to low teens**
- **Co-promotional** rights for ARGX-115-based products in the **European Economic Area and Switzerland**

# Additional Strategic Collaborations

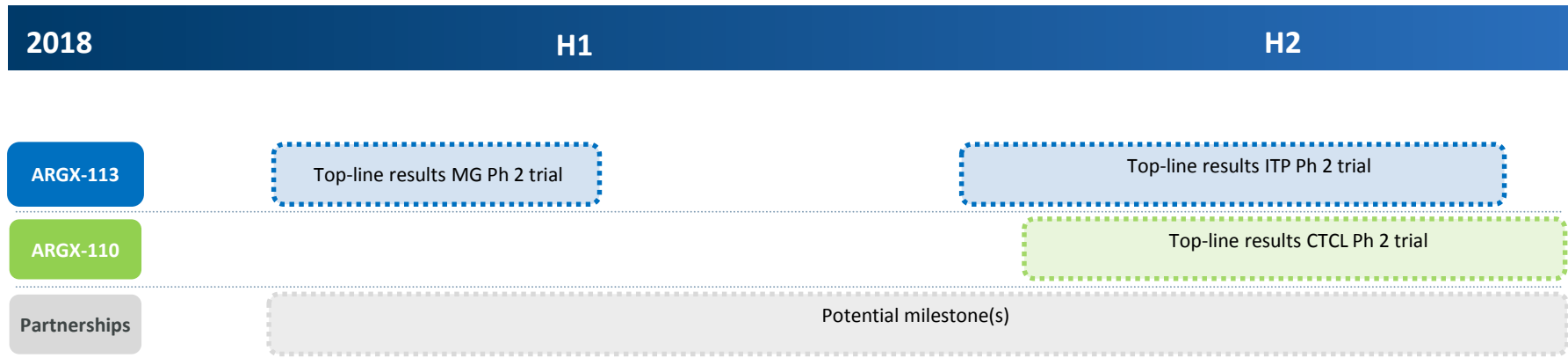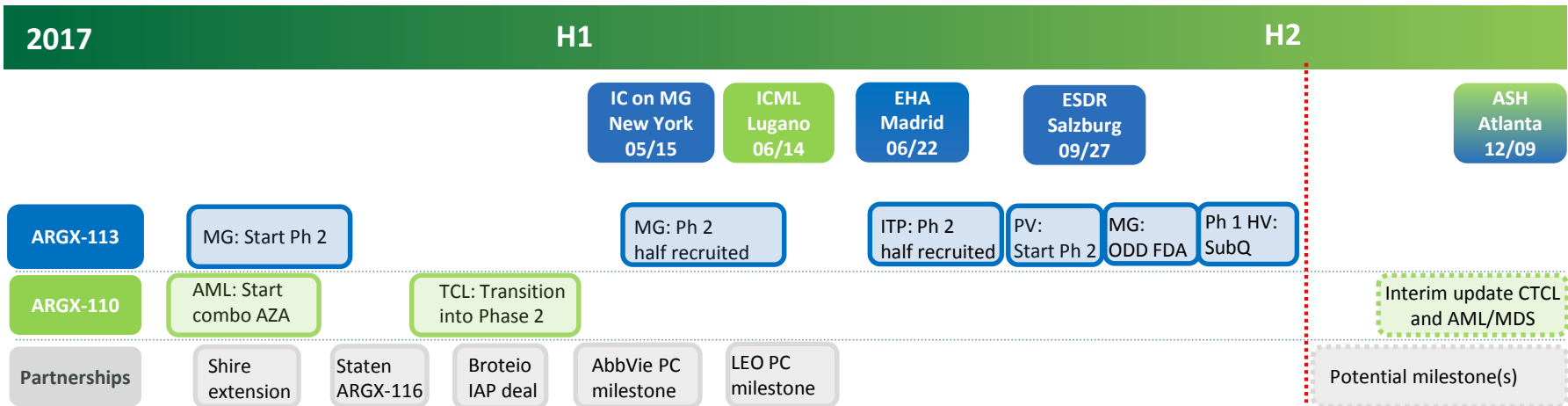| Partner | Asset | Key commentary |
|---------|-------|----------------|
| BIRD ROCK BIO | **ARGX-109** (Gerilimzumab) | • Focused on developing an anti-IL-6 antibody for **Rheumatoid Arthritis** <br> • Bird Rock responsible for all costs incurred in R&D and commercialization |
| LEO | **ARGX-112** | • Focused on **inflammation-based dermatological indications** <br> • LEO Pharma funds >50% of all development costs up to CTA approval and all development post-approval of first Phase 1 trial in Europe <br> • argenx is eligible for ~€100mm in aggregate milestone payments + tiered royalties |
| STATEN BIOTECHNOLOGY | **ARGX-116** | • Focused on developing an anti-ApoC3 antibody for **dyslipidemia** <br> • Jointly responsible for conducting dyslipidemia research — Staten responsible for additional clinical development <br> • argenx eligible for royalties in the low twenties |
| **Broteio Pharma** | **Undisclosed** | • Focused on developing a differentiated antibody against a novel complement target <br> • Potential to act synergistically with ARGX-113 <br> • Jointly responsible for development expenses until preclinical POC — argenx granted exclusive option to license program after achieving preclinical POC |
| **Shire** | **Discovery Programs** | • Focused on **novel rare disease targets** <br> • Provides Shire access to SIMPLE Antibody™ platform + Fc engineering technologies <br> • argenx has received $12mm in aggregate upfront and milestone payments and R&D fees over the course of the collaboration <br> • Shire purchased €12mm of argenx ordinary shares through participation in July 2014 IPO |

# Key Upcoming Milestones & Communications

**argenx**

## 2017

| | H1 | | H2 |
|---|---|---|---|

**Events:**
- IC on MG New York 05/15
- ICML Lugano 06/14
- EHA Madrid 06/22
- ESDR Salzburg 09/27
- ASH Atlanta 12/09

**ARGX-113**
- MG: Start Ph 2
- MG: Ph 2 half recruited
- ITP: Ph 2 half recruited
- PV: Start Ph 2
- MG: ODD FDA
- Ph 1 HV: SubQ

**ARGX-110**
- AML: Start combo AZA
- TCL: Transition into Phase 2
- Interim update CTCL and AML/MDS

**Partnerships**
- Shire extension
- Staten ARGX-116
- Broteio IAP deal
- AbbVie PC milestone
- LEO PC milestone
- Potential milestone(s)

## 2018

| | H1 | | H2 |
|---|---|---|---|

**ARGX-113**
- Top-line results MG Ph 2 trial
- Top-line results ITP Ph 2 trial

**ARGX-110**
- Top-line results CTCL Ph 2 trial

**Partnerships**
- Potential milestone(s)

# Appendix

argenx

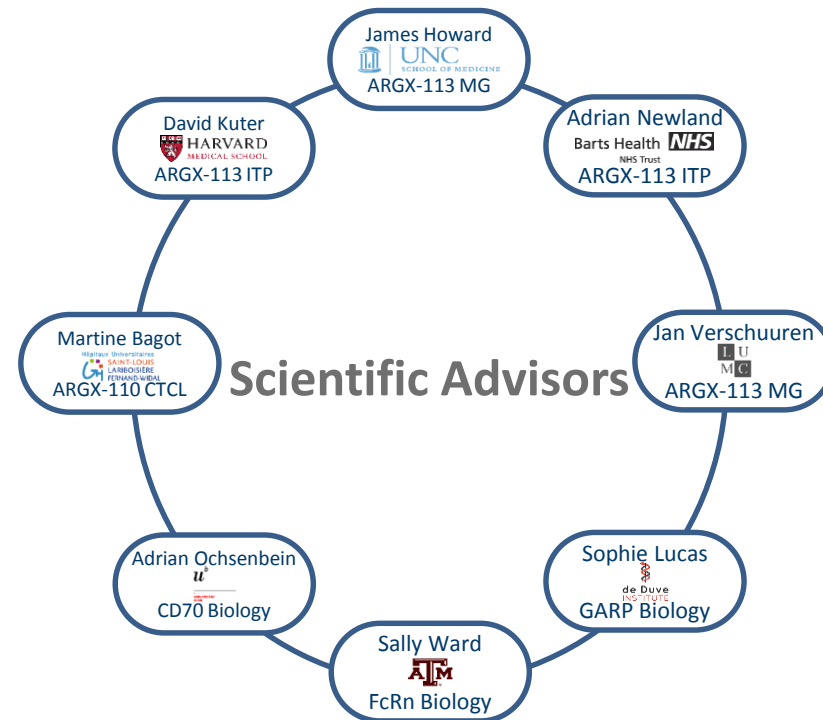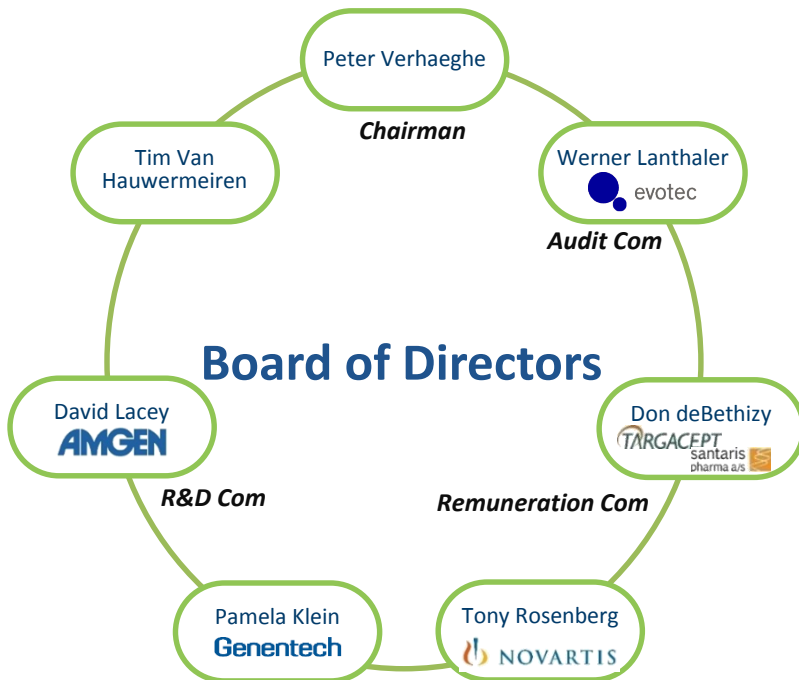## Management

| | | | | | | |
|---|---|---|---|---|---|---|
| **Tim Van Hauwermeiren** *Chief Executive Officer* | **Eric Castaldi** *Chief Financial Officer* | **Hans de Haard, Ph.D.** *Chief Scientific Officer* | **Torsten Dreier, Ph.D.** *Chief Development Officer* | **Nicolas Leupin, M.D.** *Chief Medical Officer* | **Debbie Allen, Ph.D.** *SVP, Business Development* | **Dirk Beeusaert** *General Counsel* |

## Board of Directors

Peter Verhaeghe
*Chairman*

Werner Lanthaler — evotec
*Audit Com*

Tim Van Hauwermeiren

David Lacey — AMGEN

*R&D Com*

Don deBethizy — TARGACEPT / santaris pharma a/s

*Remuneration Com*

Pamela Klein — Genentech

Tony Rosenberg — NOVARTIS

## Scientific Advisors

James Howard — UNC School of Medicine
ARGX-113 MG

David Kuter — HARVARD MEDICAL SCHOOL
ARGX-113 ITP

Adrian Newland — Barts Health NHS Trust
ARGX-113 ITP

Martine Bagot — Hôpitaux Universitaires SAINT-LOUIS LARIBOISIÈRE FERNAND-WIDAL
ARGX-110 CTCL

Jan Verschuuren — LUMC
ARGX-113 MG

Adrian Ochsenbein
CD70 Biology

Sally Ward — A&M
FcRn Biology

Sophie Lucas — de Duve INSTITUTE
GARP Biology

# argenx

## Please Join argenx for a Lunch and Discussion during the ASH Annual Meeting

### Advancing ARGX-110 to clinical proof-of-concept in acute myeloid leukemia (AML) & cutaneous t-cell lymphoma (CTCL)

**Monday, December 11, 2017**

12:00 PM – 1:30 PM

**Omni Atlanta Hotel**

South Tower Atrium Terrace

Birch Room

100 CNN Center NW

Atlanta, GA 30303

*Next to Convention Center*

**Please RSVP by Monday, December 4**

Rachel Frank

rachelf@sternir.com

212.362.1200

### Agenda

**Overview of AML**
Gail Roboz, MD
Weil Cornell Medicine, New York

**CD70: Novel AML Target**
Hans de Haard, PhD, argenx

**Phase 1/2 AML Trial: Proof-of-Biology Data**
Nicolas Leupin, MD, argenx

**Phase 1/2 CTCL Trial: Data Update**
Nicolas Leupin, MD, argenx

**Q&A**

### Guest Speaker

**Gail Roboz, MD**

*Professor of Medicine and Director of Clinical and Translational Leukemia Program*

Weill Medical College of Cornell University and New York Presbyterian Hospital

*Following the presentation, please join us and our colleagues from the University of Bern for an informal mix and mingle.*