2019 R&D Day

argenx

May 22, 2019 - New York

Forward-Looking Statements

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Agenda

8:30 AM:	**Introduction and Agenda** *Beth DelGiacco, VP Investor Relations*
8:30 – 8:45 AM:	**Creating Innovative Antibodies** *Tim Van Hauwermeiren, CEO*
8:45 – 10:00 AM:	**ARGX-117: Renaissance in Complement Targeting C2 & Therapeutic Potential** *Eric Hack, M.D, Ph.D., Prof. Immunology at UCM Utrecht* *Karen Silence, Project leader* **KOL Panel** *Ludo van der Pol, M.D., Ph.D., Associate Prof. of Neurology at UMC Utrecht* *Rafael Villicana, M.D., Associate Prof. of Mecidine at Loma Linda University Medical Center*
10:00 – 10:20 AM:	Q&A & coffee break
10:20 – 11:05 AM:	**ARGX-118: Immunology Breakthrough for Charcot-Leyden Crystal Crystallopathies** *Bart Lambrecht, M.D., Ph.D., Prof. Pulmonary Medicine at VIB, Ghent University*
11:05– 11:15 AM:	**Cusatuzumab Development Plan** *Wim Parys, CMO*
11:15 – 11:30 AM:	**argenx 2021: Global Commercial Vision** *Keith Woods, COO*
11:30 – 11:55 AM:	Q&A - Lunch

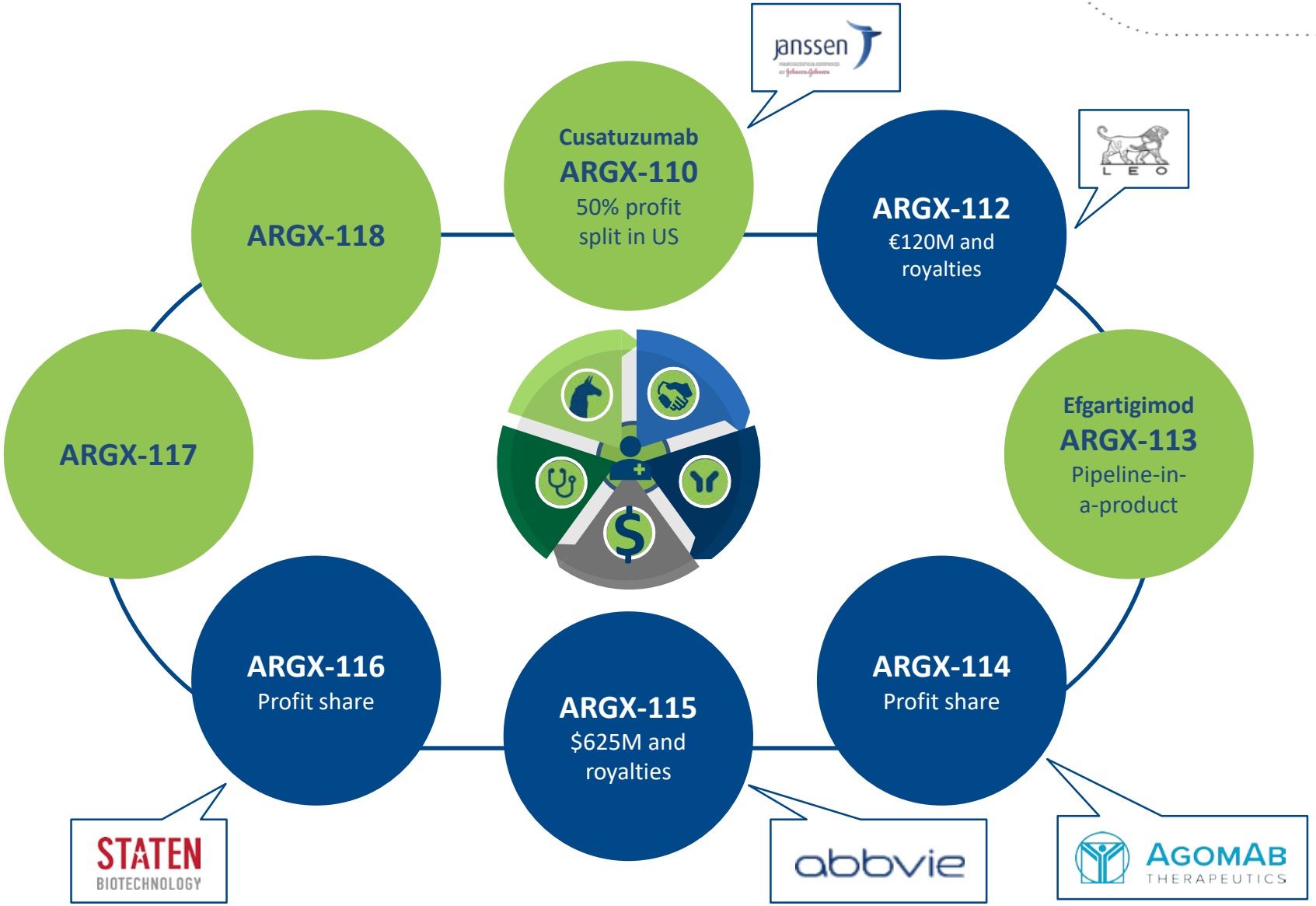
Creating Innovative Antibodies

Tim Van Hauwermeiren | Chief Executive Officer

argenx Today: Building Immunology Leadership

Late-stage immunology company	Two Phase 3 trials by end of 2019
Wholly-owned pipeline-in-a-product asset	Potential across multiple high-value indications
Proof-of-concept in two indications	Success in beachhead indications de-risks concept
Validating oncology collaborations	Maintaining 50% commercial rights with cusatuzumab
Proven engine to grow pipeline	Innovative Access Program in action

Serial Value Creation From Novel Targets



Deep Pipeline of Wholly-Owned Candidates for Orphan Indications

Product Candidate	Target	Indication	Preclinical	Phase 1	Phase 2	Phase 3	BLA	Next Milestone / Commentary
ARGX-113 Efgartigimod	FcRn	Myasthenia Gravis (MG)					adapt myasthenia gravis study	3Q18: Phase 3 initiated
		Immune Thrombocytopenia (ITP)						2H19: Phase 3 Program initiation (IV/SC)
		Pemphigus Vulgaris (PV)						1H19: Cohort 3 initiation
		Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)						2H19: Phase 2 initiation
		ENHANZE®SC						3Q19: Phase 1 initiation
ARGX-110 Cusatuzumab	CD70	Acute Myeloid Leukemia (AML)				janssen		$500 million upfront Eligible for up to $1.3 billion in milestones; tiered royalties
ARGX-117	C2	Severe Autoimmune IV/ENHANZE®SC						Complementary to ARGX-113 Option exercised for C2
ARGX-118	Galectin-10	Airway Inflammation						

Momentum Into Multiple Milestones

2019

- Phase 2 3rd cohort PV
- ARGX-118 Option Exercise
- SC/Enhanze® Phase 1 HV Data
- Phase 3 ITP IV/SC Start
- Phase 2 CIDP Start
- Phase 2 AML Start
- ARGX-117 CTA filing

2020

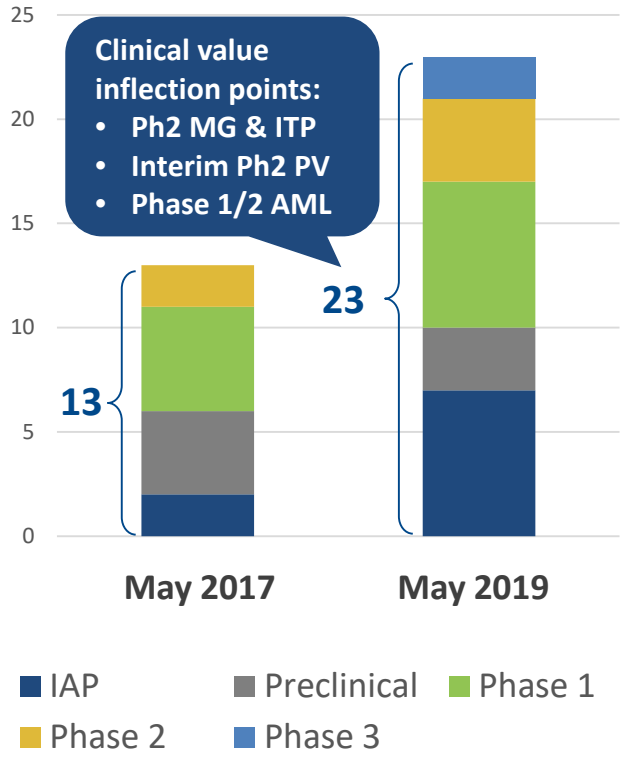
- Phase 2 PV Data
- Phase 3 ADAPT MG Data
- 5th Indication
- Development Update
- ARGX-119

Efgartigimod | Cusatuzumab | New Assets

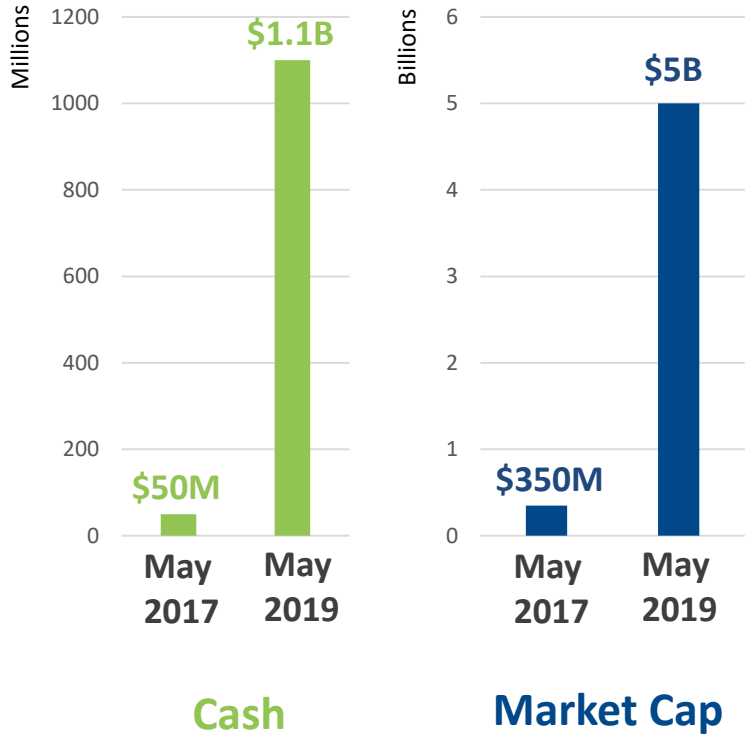
$1.1B in Cash; Funded Through 2021

Accelerated Expansion of Product Pipeline Drives Financial Strength

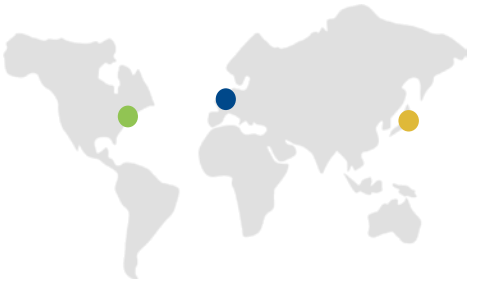
Accelerating & expanding development programs



Well-capitalized to advance to the next level



Global Expansion



- Ghent

Since 2019

- Boston
- Tokyo

Innovative Access Program (IAP): How We Build Value

Antibody discovery & development expertise – Translating basic science into meaningful clinical candidates

Accessing Novel Targets Through Collaboration

argenx

Antibody expertise
- SIMPLE Antibody™, NHANCE®, ABDEG™, POTELLIGENT®

Top Academic Institutions

Disease Biology expertise
- Universities of Texas, Bern, Utrecht, Louvain, Penn, Columbia, Torino
- Institutes of Ludwig, de Duve, VIB, TAM

5-10 live programs at any given time

Co-creating first-in-class assets

WHOLLY OWNED

ARGX-113
ARGX-110 (Co-developed Janssen)
ARGX-117
ARGX-118

PARTNERED

ARGX-115 abbvie
ARGX-112 LEO
ARGX-116 STATEN
ARGX-114 AGOMAB THERAPEUTICS

From Immunology Breakthroughs to Impacting Patients' Lives

1

Novel Target Biology

- Academic collaboration
- First-in-class targets

2

Integrated Antibody Discovery Suite

- Meaningful differentiation
- Engineering excellence

5

Franchise Structure

- Neuromuscular and hematology
- Phase 3 studies ongoing in 2019

3

Rapid Pipeline Expansion

- Productive development engine
- One new pipeline asset per year

4

Maximum Value per Asset

- Pipeline-in-a-product strategy
- Driven by biological rationale

ARGX-117: Jumpstarting Product Development

1 Novel Target Biology

Complement component C2
UMC Utrecht: Erik Hack

2 Integrated Antibody Discovery Suite

Sweeping antibody

3 Rapid Pipeline Expansion

Exercised option to bring ARGX-117 in-house

Halozyme
Option exercised for C2 ENHANZE® SC technology

4 Maximum Value per Asset

Severe autoimmune diseases

5 Franchise Structure

CTA in 4Q 2019
Well-positioned within argenx franchises

ARGX-118: Building From Target Validation

1

Novel Target Biology

Galectin-10
VIB: Bart Lambrecht

2

Integrated Antibody Discovery Suite

Crystal-dissolving SIMPLE antibody

5

Preclinical Development

Lead optimization

3

Rapid Pipeline Expansion

Exercised option to bring ARGX-118 in-house

4

Maximum Value per Asset

Range of immunology indications

IAP Enables Full Spectrum of Antibody Creation: From Discovery to Development

Early Target Validation

Power of SIMPLE Antibody™ technology

→ *Charcot-Leyden Crystal dissolving antibodies*

Unravelling novel airway inflammation biology

→ *GAL-10 first novel airway inflammation target in decades*

ARGX-118

Jumpstart Product Development

Power of NHance™ technology and engineering know-how

→ *Turning unique mouse V-regions into highly differentiated product candidate*

Leveraging unique insights in complement disease biology

→ *Pipeline-in-product opportunity*

ARGX-117

ARGX-117: Renaissance in Complement Targeting C2 & Therapeutic Potential

Erik Hack | Prof. UMC Utrecht
Karen Silence | Project Leader argenx

Professor Erik Hack, M.D., Ph.D., UCM Utrecht

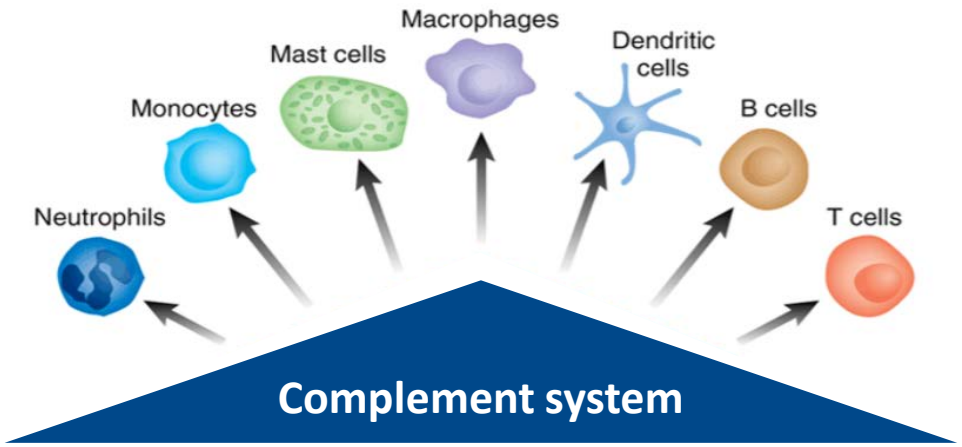
- Professor of Immunology at UMC Utrecht
- Sanquin, Head of Immunopathology
- Crucell, Head of the Protein Biologics Group
- Research interests: role of inflammation and coagulation in experimental and human diseases
- Lead development of Cinryze and Ruconest (C1-inhibitor in angioedema)
- Co-authored over 500 peer-reviewed papers; more than 23,000 citations

Therapeutic Renaissance in Complement

- Growing number of immune-mediated and inflammatory diseases that involve complement
- ‘07 — Eculizumab approval in 2007 validated concept of therapeutic complement intervention
- 20+ — 20+ clinical-stage drug candidates targeting various stages of complement cascade
- ↔ — No “one-size-fits all” – different complement driven diseases require different points of intervention

Complement: Cornerstone of Powerful Innate Defense System

Defense & Surveillance



Innate immunity	Disposal system	Adaptive immunity
• Opsonization • Lysis of pathogens • Chemotaxis • Inflammation • Cell activation	• Clearance of immune complexes and apoptotic cells	• Augmentation of antibody response • Promotion of T-cell response • Elimination of self-reactive B-cells • Enhancement of immunologic memory

Source: Katie Ris-Vicari

Clinical Complications

1 **Excessive activation**

↓

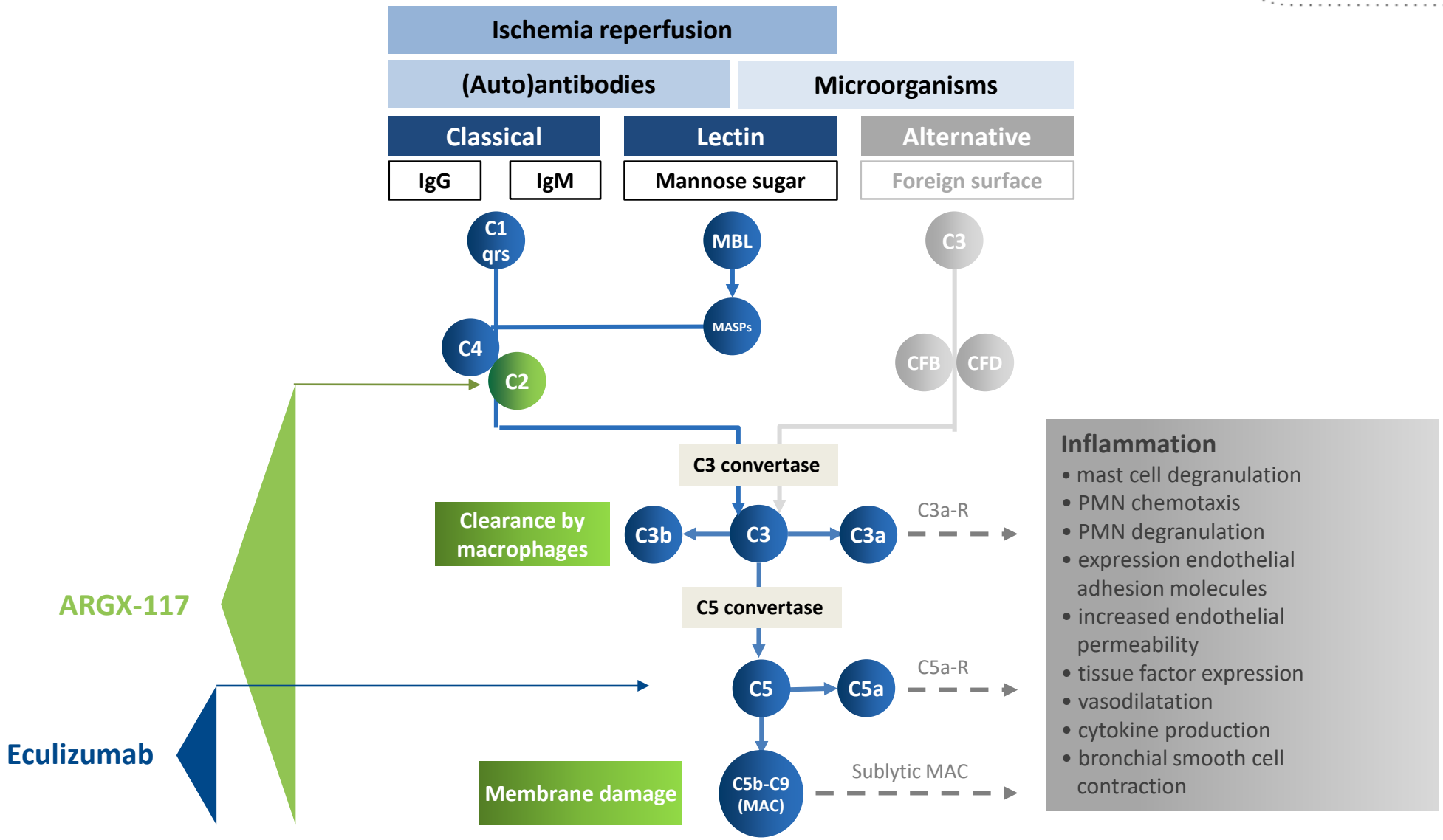
inflammation

2 **Too little activation**

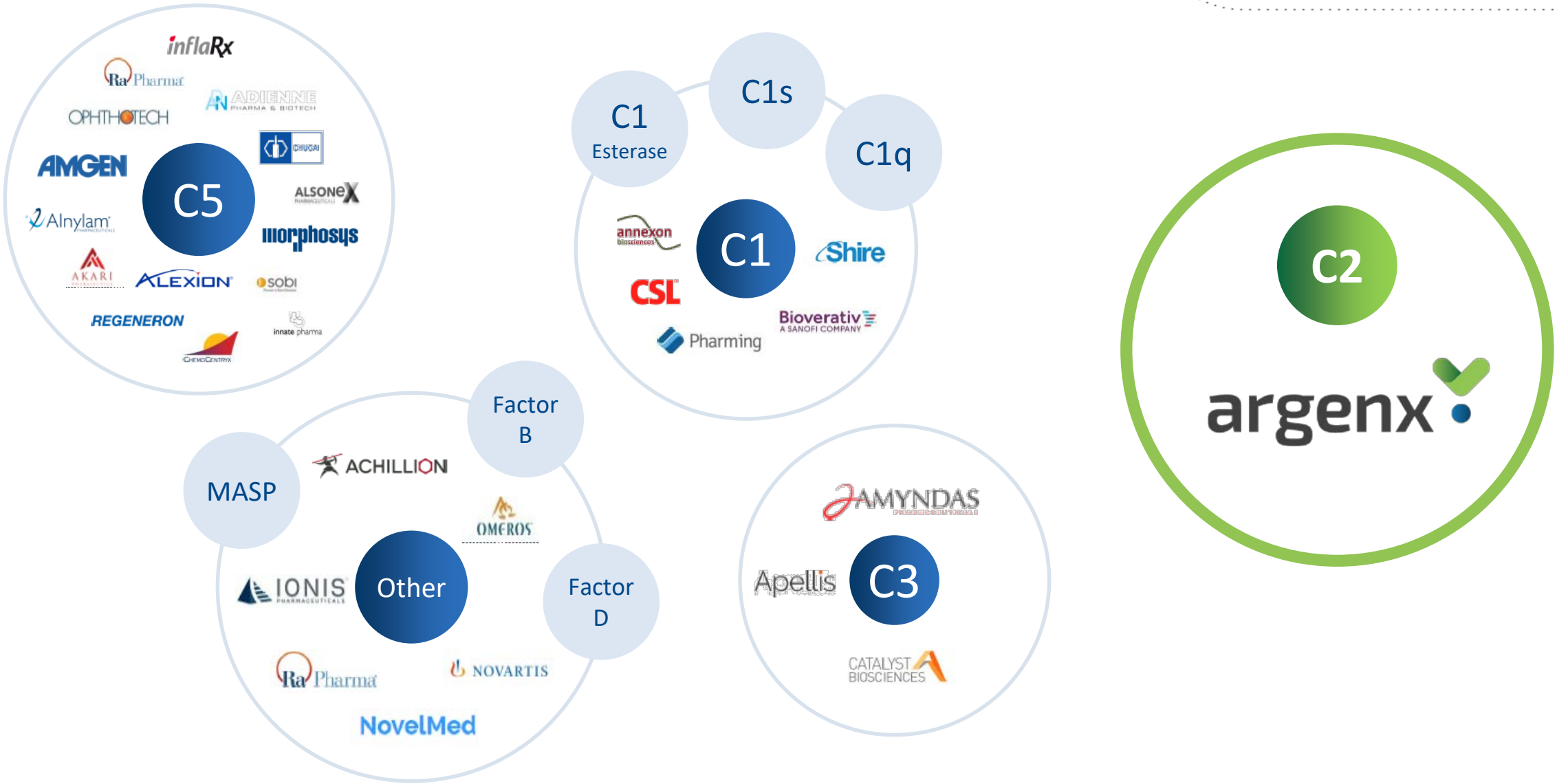
↓

risk for infections and for lupus

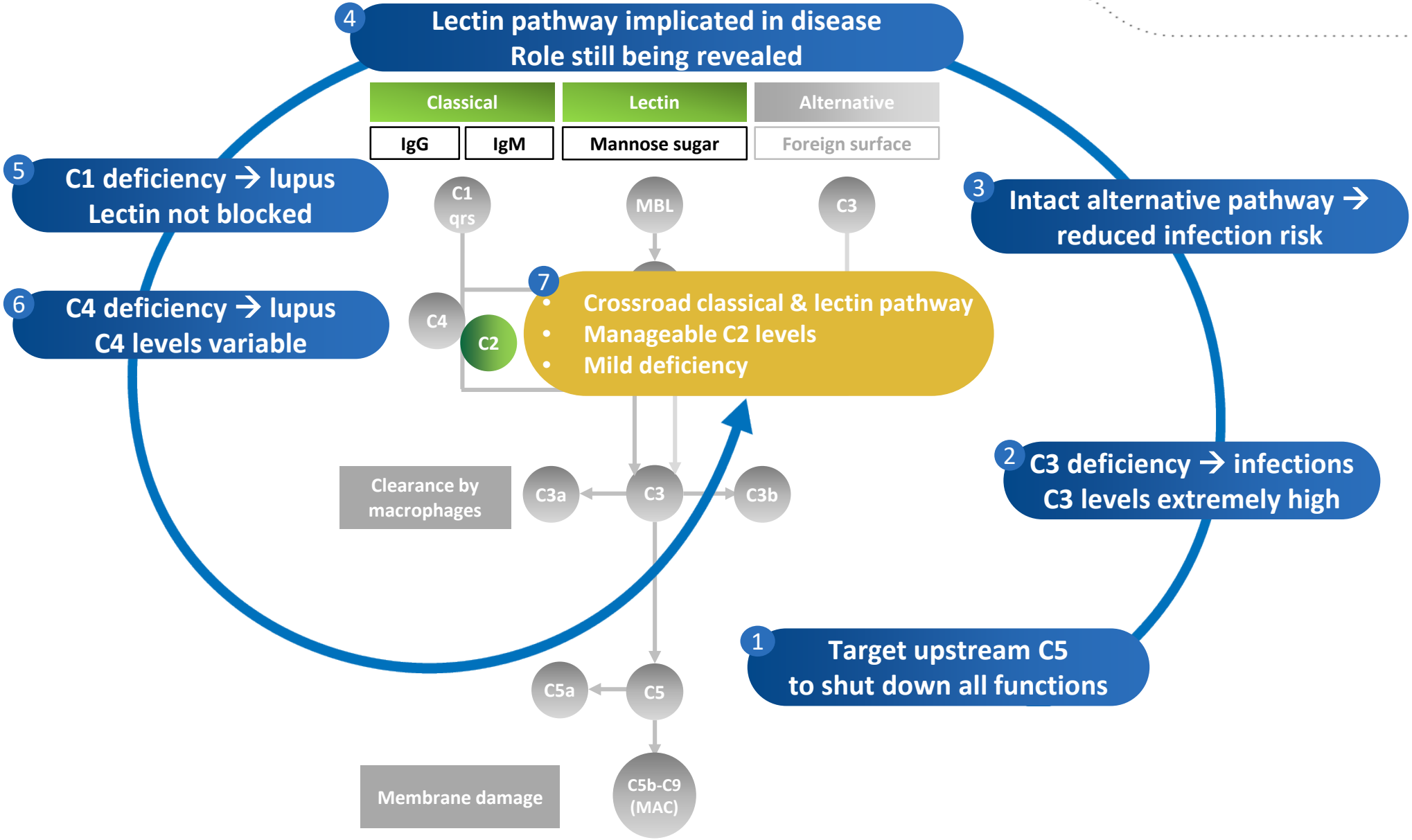
ARGX-117 Targets C2 Shutting Down Effector Functions Upstream of C5



Uniquely Positioned In Complement Space

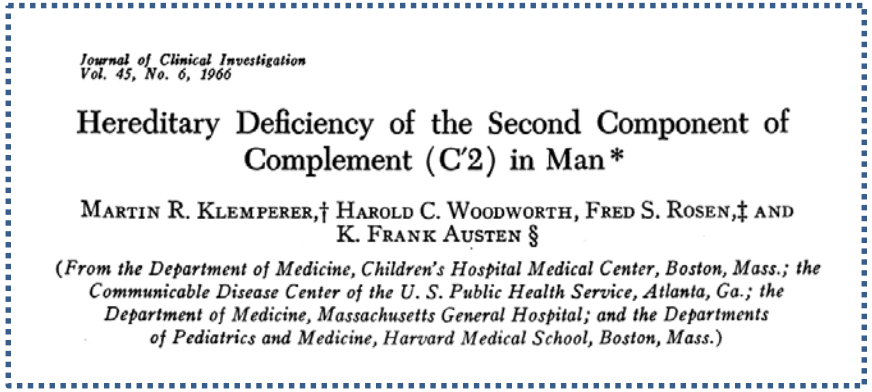


ARGX-117 Targets C2 Preserving Key Complement Functionality



Potential Best-in-Class Tolerability Profile

C2 deficiency observed in healthy people



Journal of Clinical Investigation
Vol. 45, No. 6, 1966

Hereditary Deficiency of the Second Component of Complement (C'2) in Man*

MARTIN R. KLEMPERER,† HAROLD C. WOODWORTH, FRED S. ROSEN,‡ AND K. FRANK AUSTEN §

(From the Department of Medicine, Children's Hospital Medical Center, Boston, Mass.; the Communicable Disease Center of the U. S. Public Health Service, Atlanta, Ga.; the Department of Medicine, Massachusetts General Hospital; and the Departments of Pediatrics and Medicine, Harvard Medical School, Boston, Mass.)

C2 deficiency has mildest phenotype among classical pathway deficiencies:

- No symptoms in 50% of cases
- Recurrent infections, particularly in childhood
- SLE/SLE-like condition in 10-30%

Prevalence of homozygous C2-deficiency: 1 in 10-20,000 persons (Caucasians)

Longstanding acquired C2 deficiency in hereditary angioedema (HAE) not associated with increased infection risk

Innovative Access in Action

argenx | **Broteio Pharma | UMC Utrecht**

Antibody expertise | Disease Biology expertise

- Antibody optimization: longer half-life and sweeping
- Focus on the science: good science leads to good development
- Open communication; fair economics; aligned goals

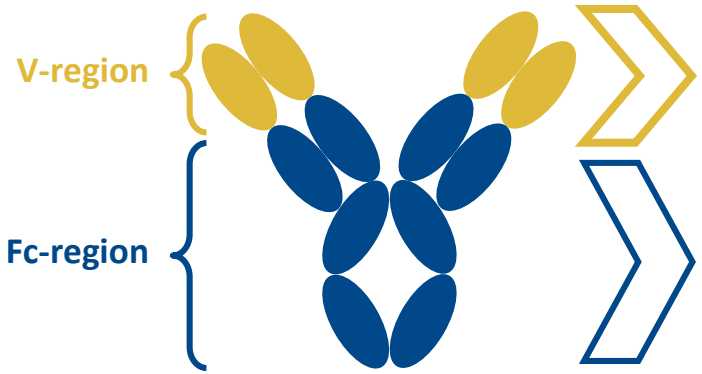
Next-generation complement therapeutics require **careful target selection**, patient population selection, **improved PK properties** (high plasma levels and rapid turnover of complement proteins) and **safety considerations**

Karen Silence, Ph.D., Project Leader argenx

- **Ph.D. at Centre for Molecular and Vascular Biology, University of Leuven, Belgium (Désiré Collen, M.D., Ph.D.)**
  - Preclinical development of Staphylokinase – fibrinolytic drug
- **Post doc at VIB (Belgium)**
  - Establishment of Ablynx NV
- **First employee at Ablynx (now Sanofi)**
  - Project leader caplacizumab - approved for acquired thrombotic thrombocytopenia purpura (aTTP)
  - Director pharmacology
- **One of the first employees at argenx**
  - Project leader cusatuzumab – partnered with Janssen Cilag
  - Project leader for ARGX-117

Innovative Access in Action: Stronger through Collaboration

ARGX-117



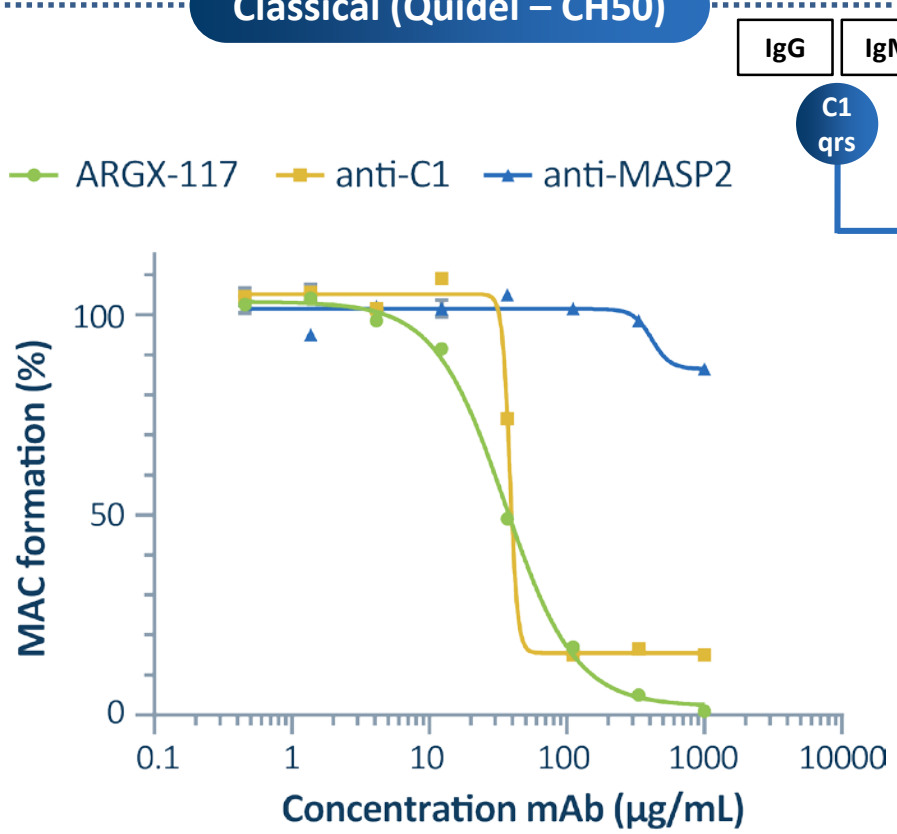
argenx — Antibody expertise

Broteio Pharma | UMC Utrecht — Disease Biology expertise

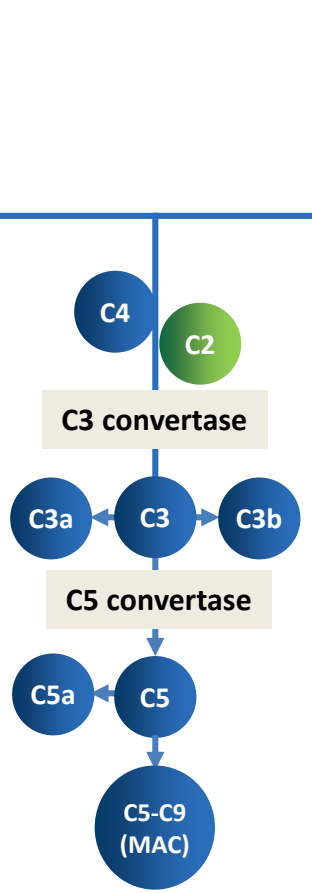
- BRO-2 antibody was optimized for better sweeping potency *in vivo*
- Generate strong translational data in disease through existing network in UMC Utrecht
- Only through true collaboration do we get to end product

ARGX-117: Potently Blocks Classical and Lectin Pathways

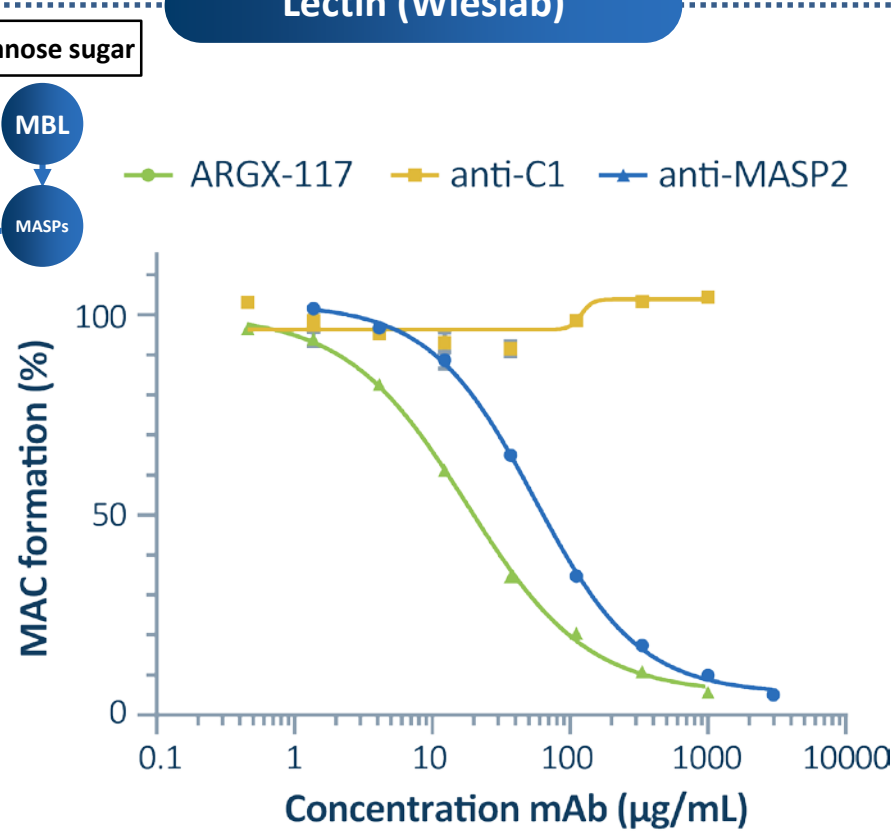
Classical (Quidel – CH50)



EC50 (µg/mL)		
ARGX-117	Anti-C1	Anti-MASP-2
36	~39	>1000



Lectin (Wieslab)



EC50 (µg/mL)		
ARGX-117	Anti-C1	Anti-MASP-2
55	>1000	18

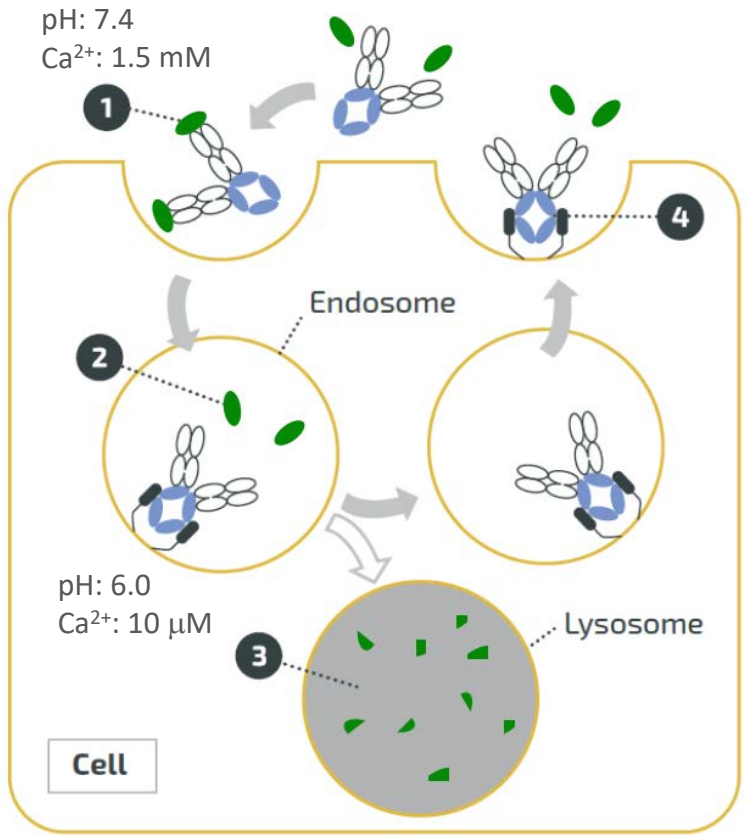
ARGX-117: V and Fc Regions Act in Concert to Sweep C2

1 **ARGX-117 binds C2 in circulation**

2 **ARGX-117/C2 complex taken up by pinocytosis entering the endosome**

3 **Affinity of ARGX-117 for C2 is low at pH 6.0 and 10 µM Ca^{2+} Target is released and degraded in lysosome**

4 **ARGX-117 remains bound going back into circulation to bind to new C2 because of NHance™ mutations**

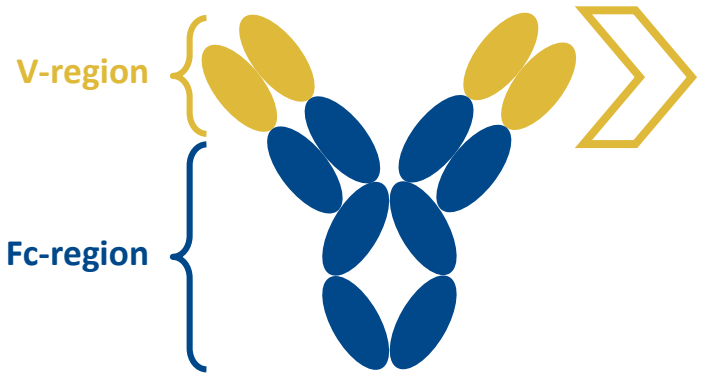


ARGX-117

C2

ARGX-117: Intrinsic pH Dependent Target Binding

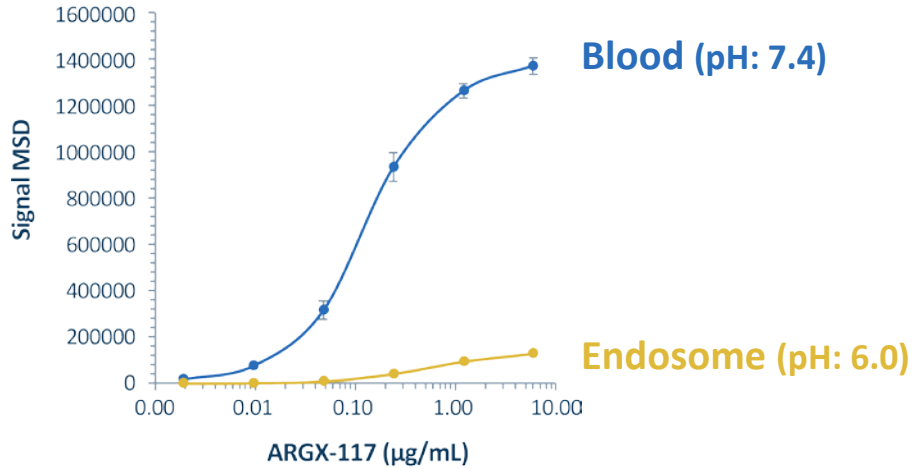
Differential binding in blood and endosome



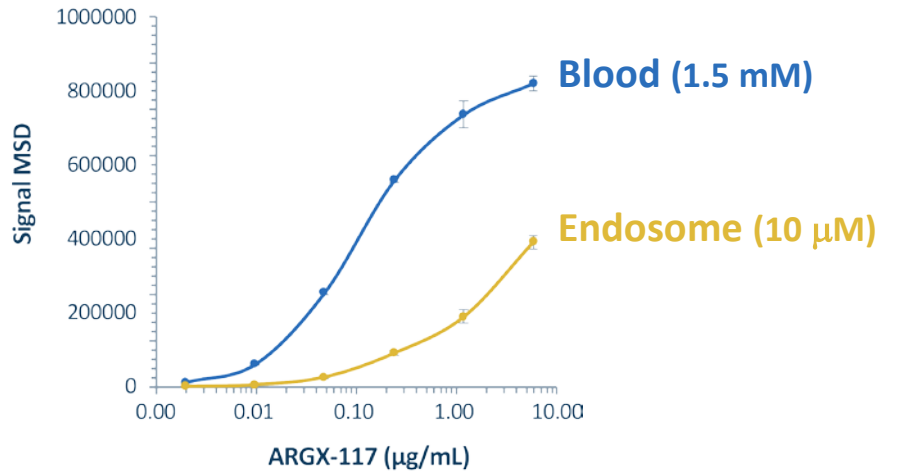
V-regions:

- 97% human identity
- Affinity for C2 in solution ~3 nM

pH dependent C2 binding

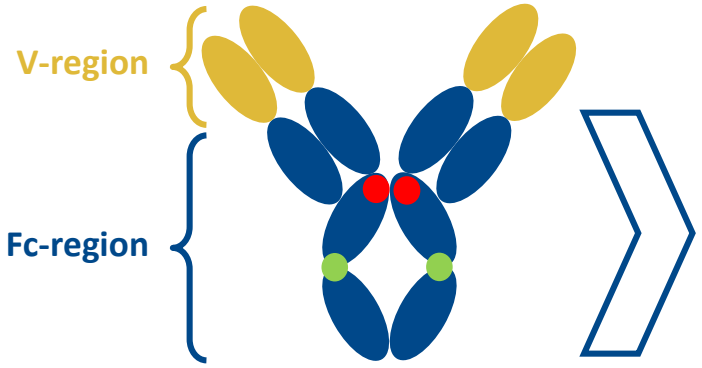


Calcium dependent C2 binding



ARGX-117: Fc Modulations Increase Endosomal FcRn Binding and Knockout

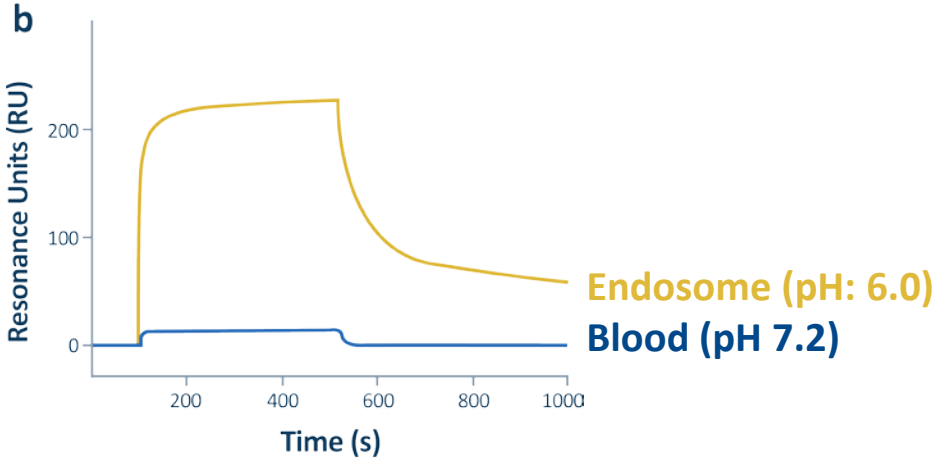
Effector Functions



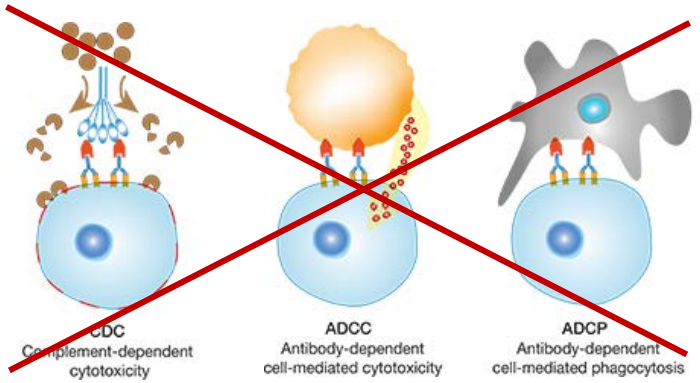
Fc-region:

- Human IgG1
- NHance™ modulates FcRn binding (●)
- LALA mutations knock out effector function (●)

NHance™ modulates FcRn binding



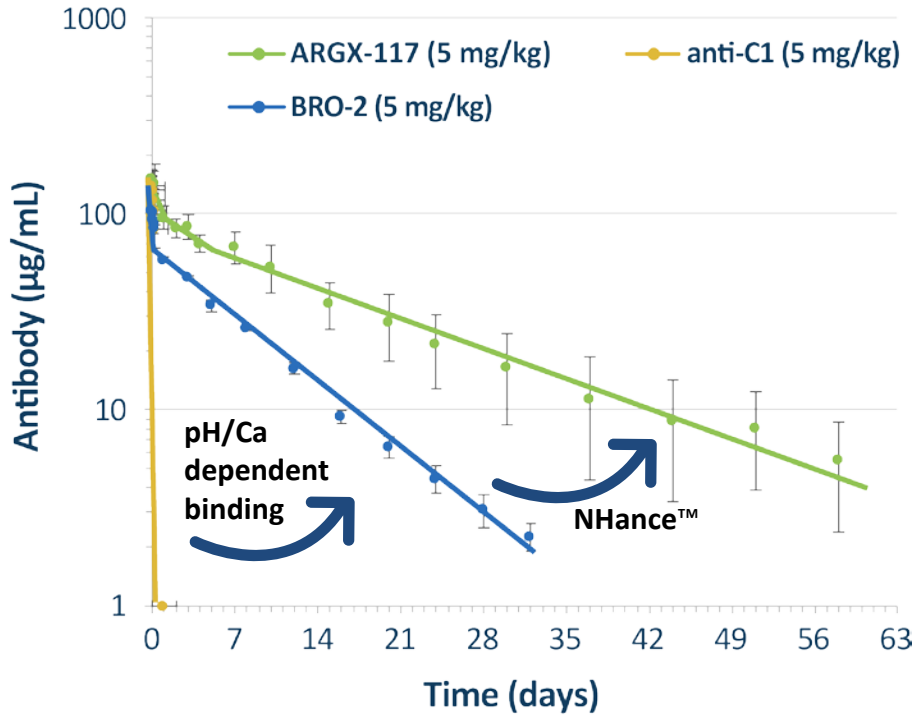
LALA mutations knock out effector functions



From Journal of Virology, 2001: 75: 12161–12168

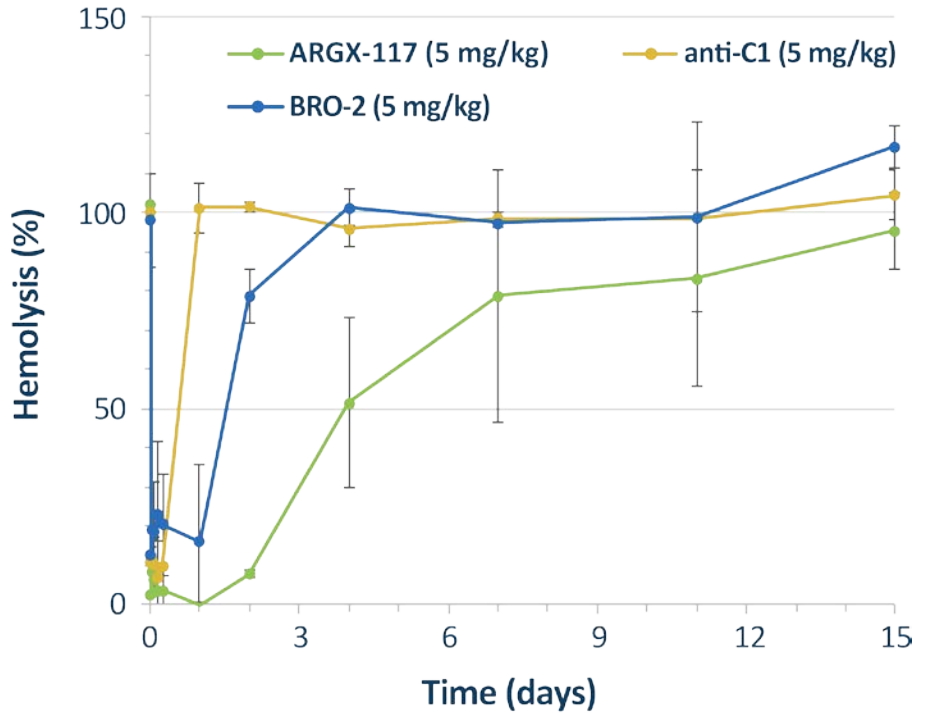
ARGX-117: Longer Half-life and Differentiated Pharmacodynamic Effect in Cyno

Pharmacokinetics



Prolonged half life…

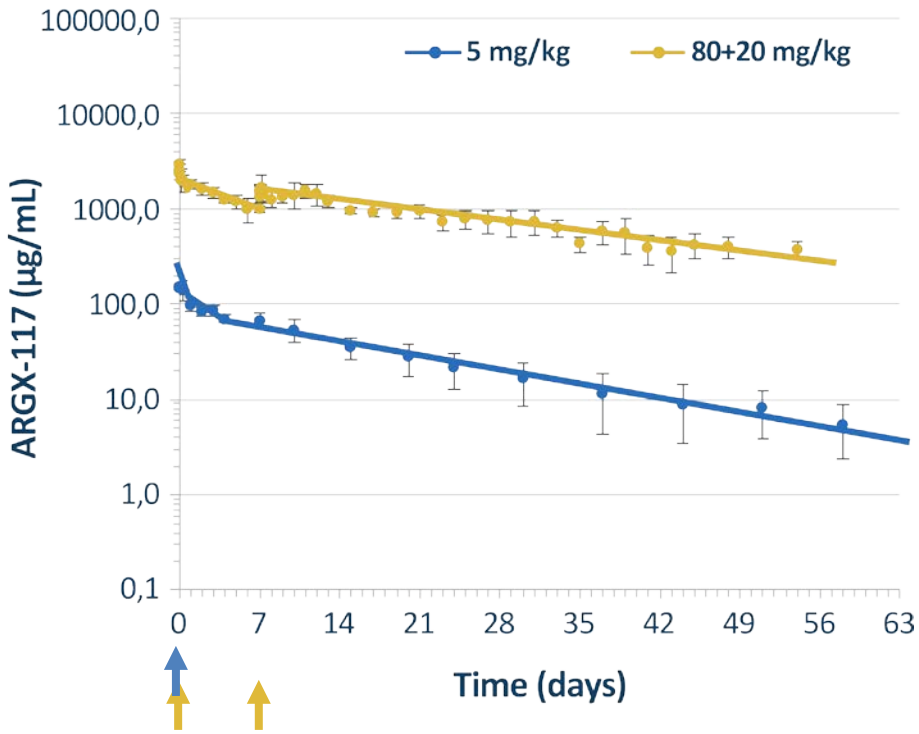
Pharmacodynamics



…results in extended PD profile

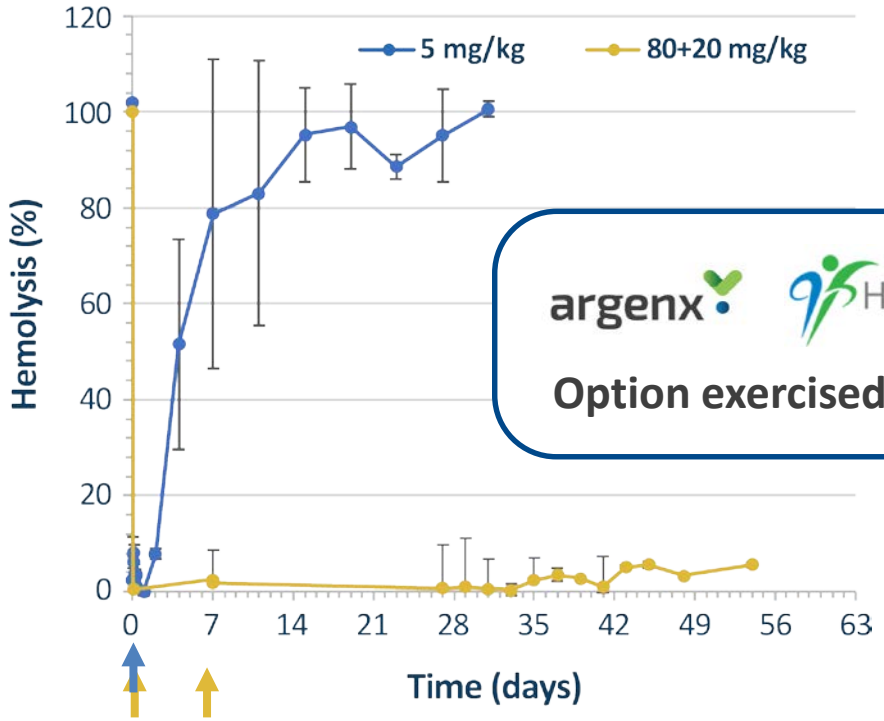
ARGX-117: Dosing Optionality in Cyno

Pharmacokinetics



Half life ARGX-117: 2-3 weeks

Pharmacodynamics



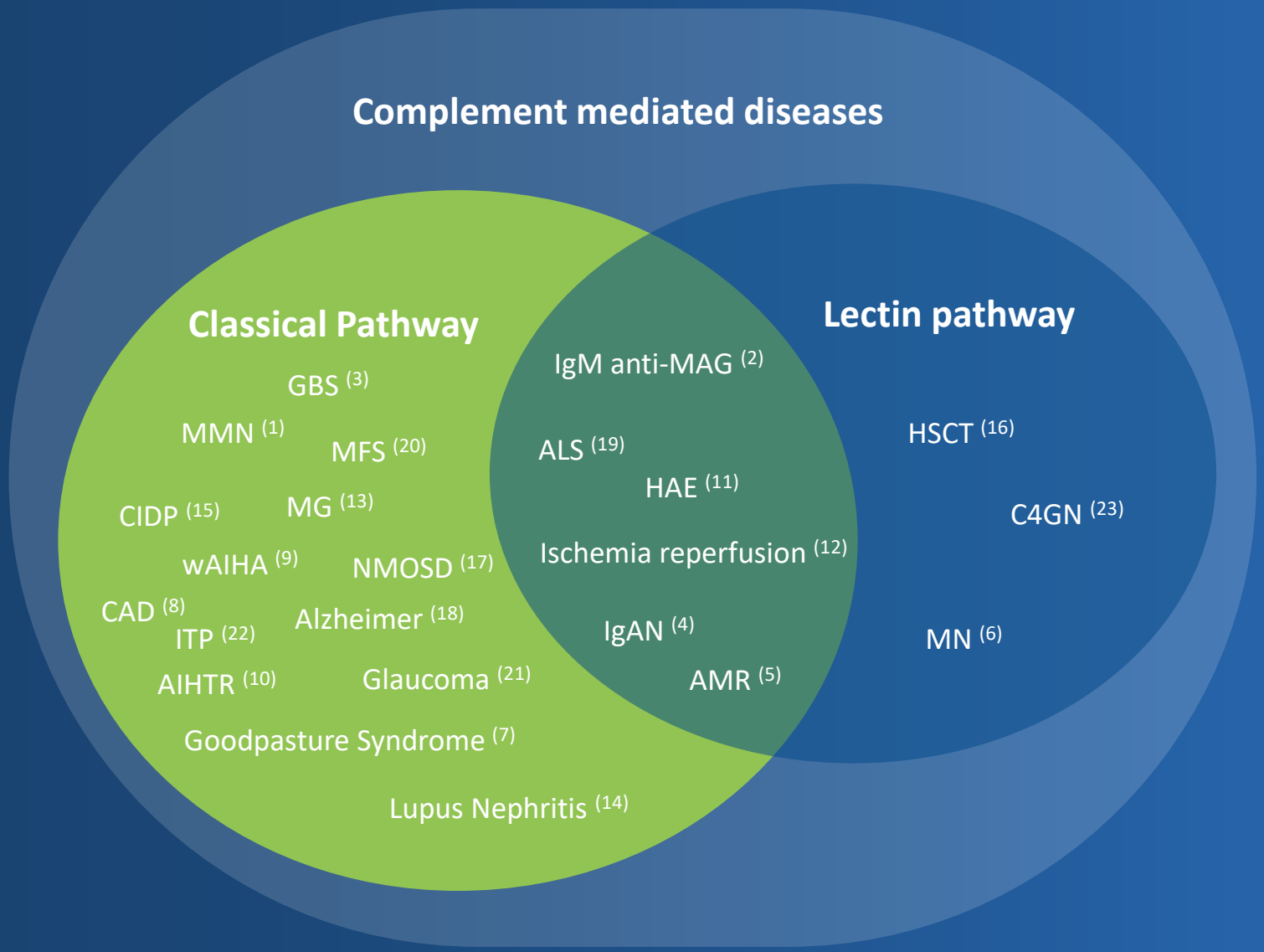
argenx Halozyme

Option exercised for C2

Blocking for 2 months after repeat dosing

C2 levels cynomolgus monkey = 4x human

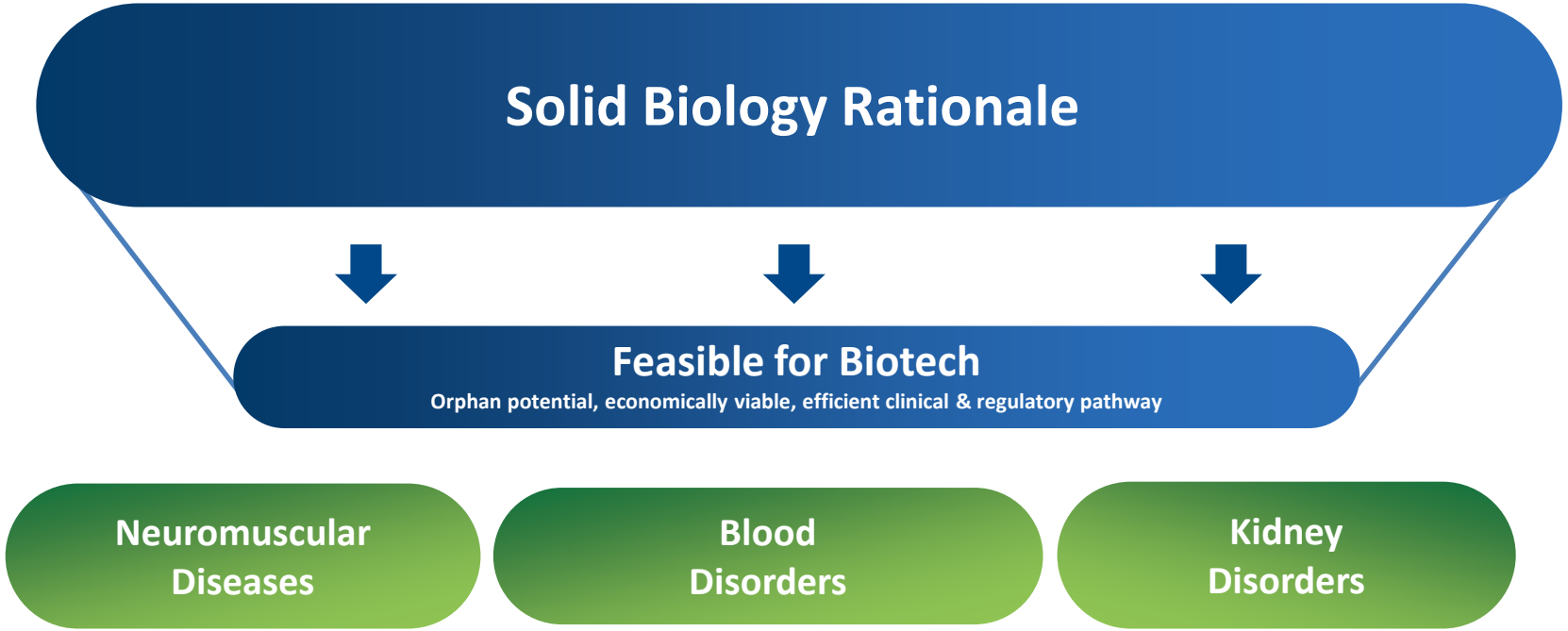
Classical and Lectin Pathways are Involved In Many Autoimmune Diseases



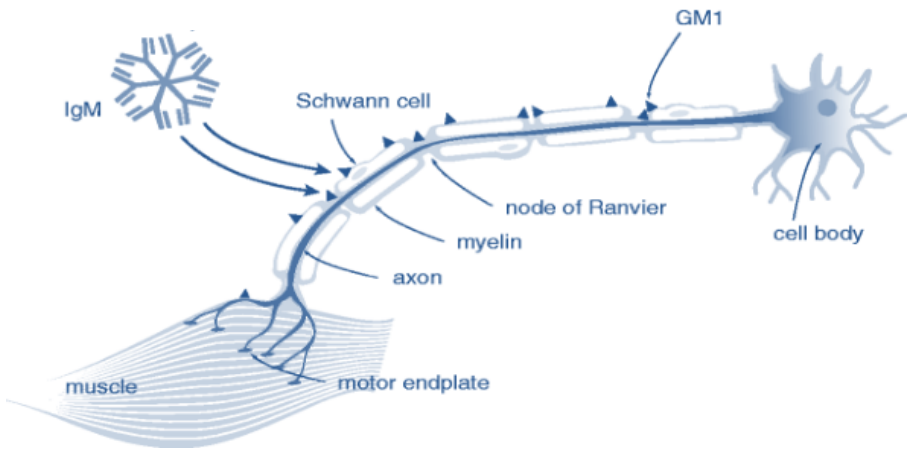
1. Vlam et al, 2015, Neurology
2. Stork et al, 2016, J of Neuroimmunol
3. Goodfellow et al, 2016, Nat Rev
4. Medjeral-Thomas et al, 2018, Kidney Int report
5. Montgomery et al, 2016, Am Soc of Transplant
6. Couser, 2017, Clin J Am Soc Nephrol
7. Greco et am, 2015, Autoimmun Rev
8. Jäger et al, 2018, Blood
9. Berentsen et al, 2015, Transfus Med Hemother
10. Sharp et al, 2014, Front in Immunol
11. Csuka et al, 2017, Mol Immunol
12. Gorsuch et al, 2012, Immunobiol
13. Howard, 2018, Ann NY Acad Sci
14. Bao et al, 2015, Kidney Dis
15. Querol et al, 2017, Scientific Reports
16. Swierzko et al, 2018, Front in ImmunolG
17. Yoshikura et al, 2017, J Neuroimmunol
18. Morgan, 2018? Semin Immunopathol
19. Kjaeldgaad et al., 2018, Mol Immunol
20. Lehmann et al., 2008, Brain
21. Williams e al., 2016, Mol. neurodegeneration
22. Peerschke et al., 2016, Br J Haematol
23. Sethi et al., 2016, Am J of Kidney Diseases

ARGX-117: Pipeline-in-a-Product Opportunity

Classical and Lectin Pathway-mediated Severe Autoimmune Diseases



Multifocal Motor Neuropathy (MMN): Model System for Indication Selection ARGX-117



- Monoclonal plasma cells produce **IgM** against **GM1**
- **Classical pathway** of complement activated
  - Demyelination/ disruption Schwann-cell-axolemma junctio
  - Displacement of ion-channel clustering
  - Disturbing membrane integrity
- Results is loss of strength

Classical (IgM Mediated) pathway activation

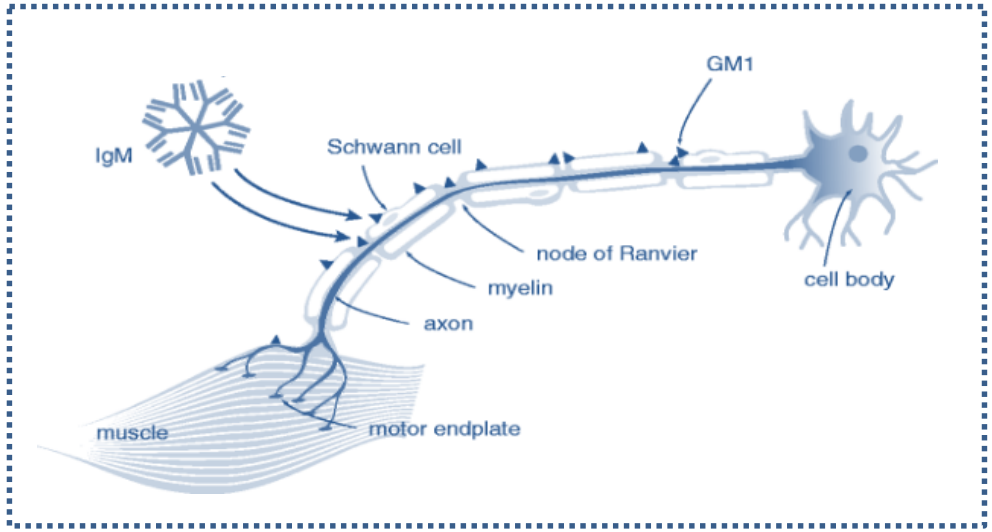
IVIg at high doses is effective

Eculizumab in MMN did not show benefit on top of IVIG

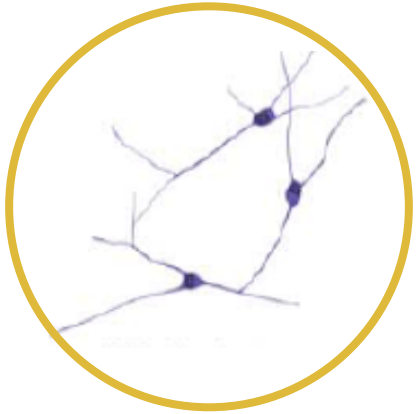
Hypothesis:
Other mechanisms must be in play which are not driven by MAC

J Clin Immunology, 2010: 30: 79–83
J Peripheral Nervous system, 2011: 16: 84-91

Multifocal Motor Neuropathy: Model System for Indication Selection ARGX-117



Motor neurons derived from pluripotent stem cells



Schwann cells

Complement activation using MMN patient derived IgM

IgM

Serum

Complement active serum

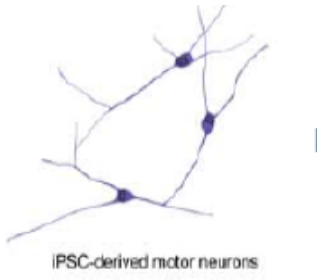
Ann Neurol, 2016: 80: 71-88

Biology Rationale: C2 is Critical for Complement Activation Induced by IgM in MMN

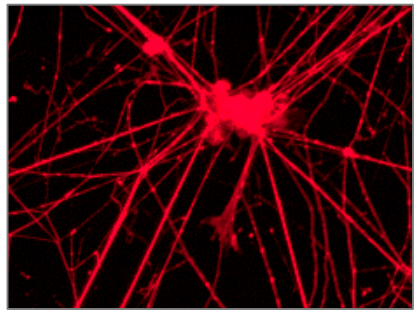
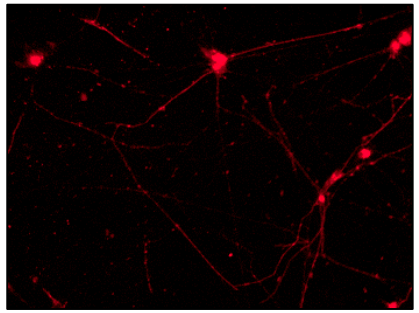
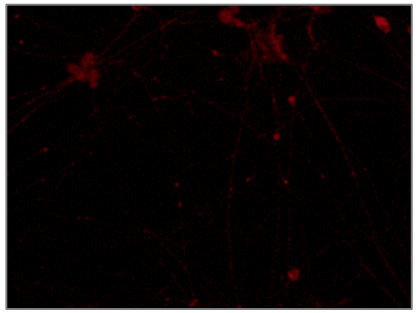
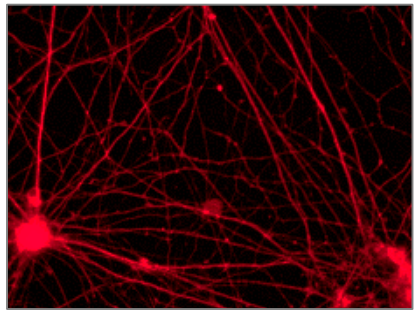
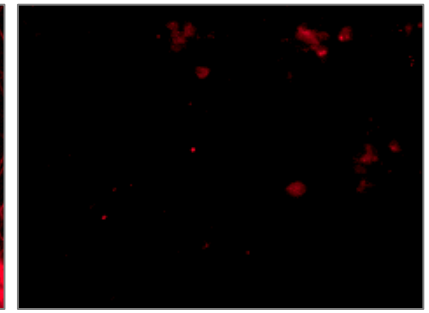
ARGX-117 blocks C3 deposition

Serum MMN patient

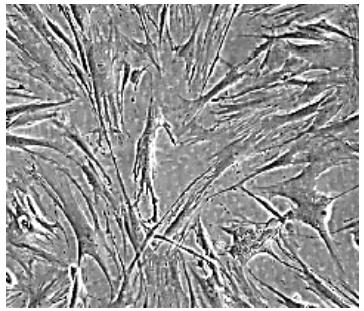
Motor neurons



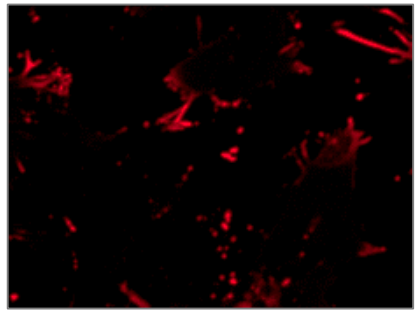
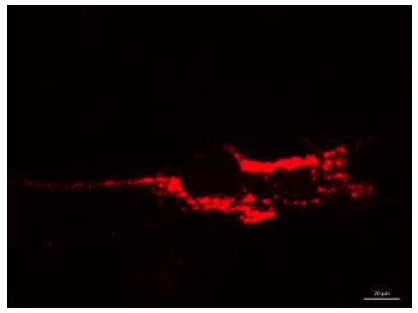
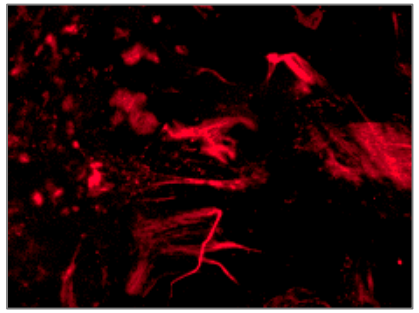
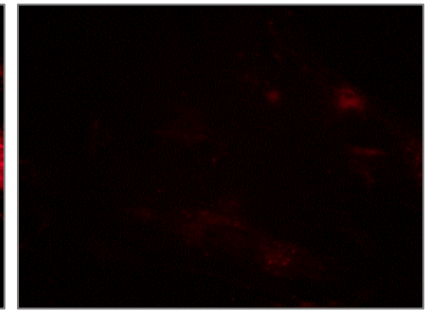
C3 deposition

Isotype control	IVIg	C2 depleted serum	C2 depleted serum + 100% C2	ARGX-117
				

Schwann cells

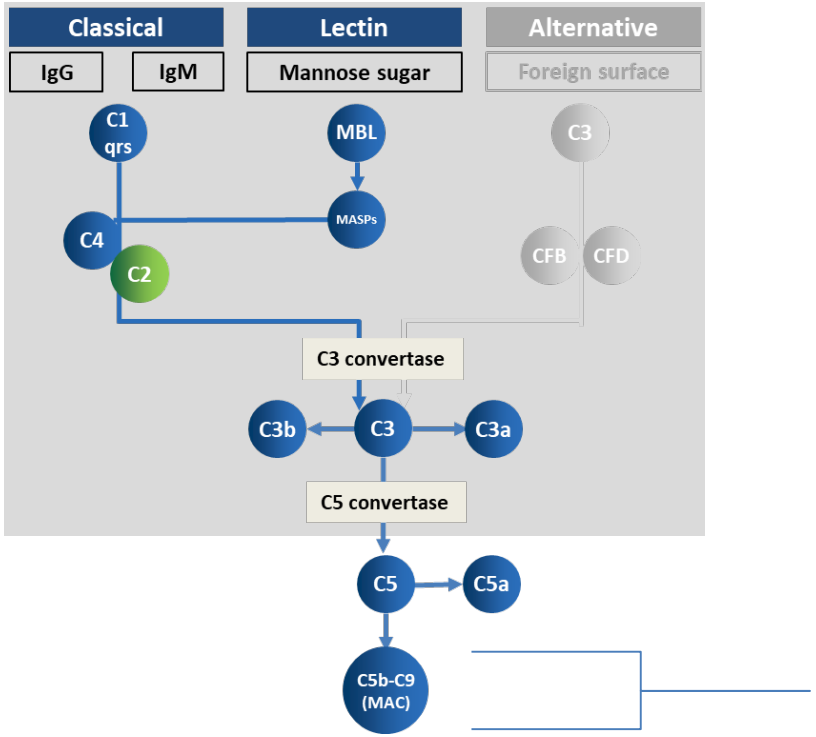


C3 deposition

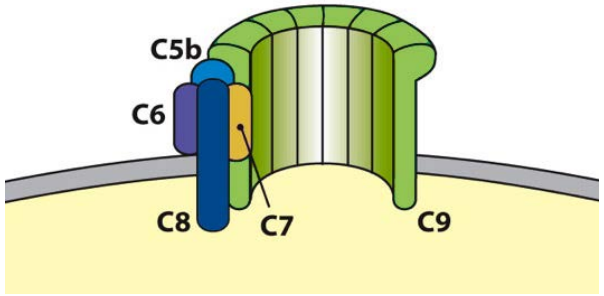
C3 Activation Confirmed Mode of Action of IgM in MMN

No MAC formation due to high CD59 expression - Complement activation upstream of C5

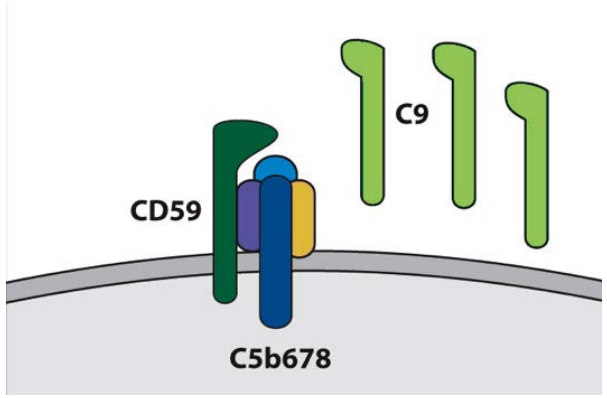


High CD59 expression inhibits MAC formation

C5-C9 activation: Assembly of MAC complex



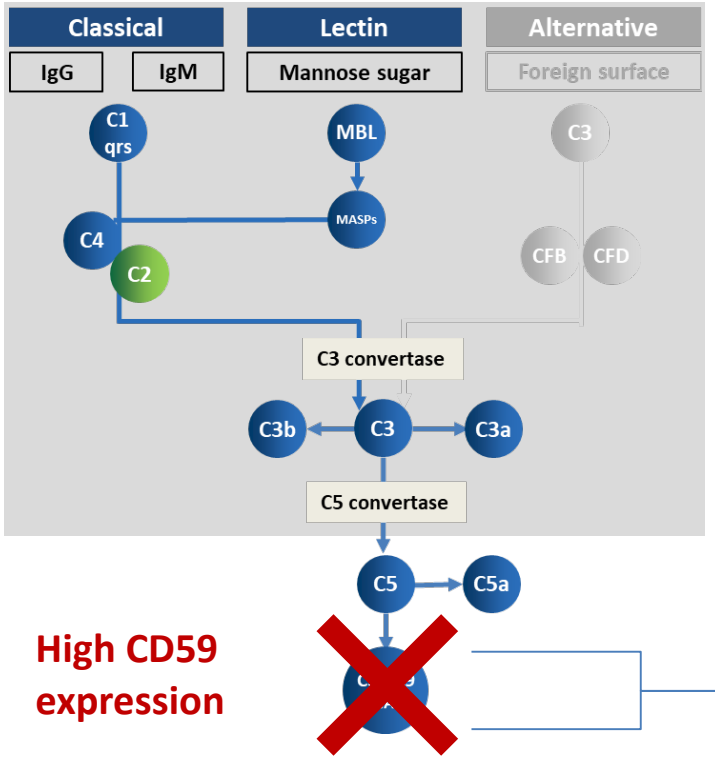
CD59 prevents recruitment of C9 – No MAC formation



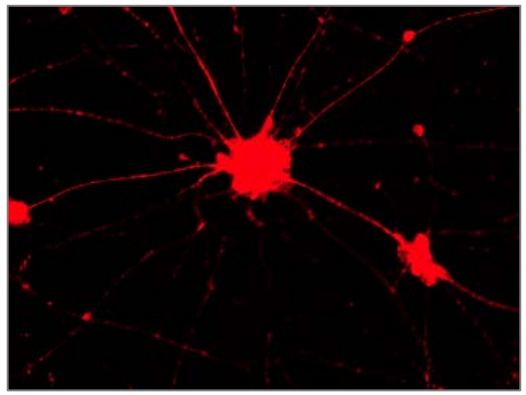
Hypothesis: Pathology of MMN is upstream of C5

C3 Activation Confirmed MOA of IgM in MMN

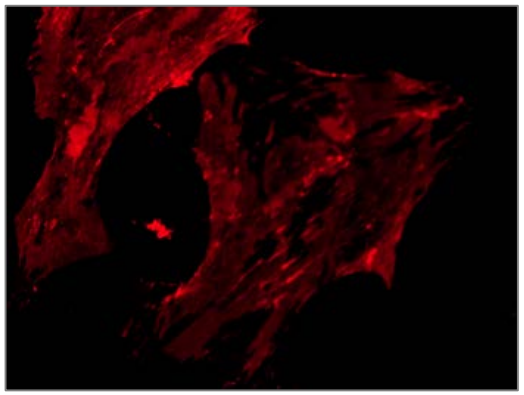
High expression of CD59 in Motor Neurons and Schwann cells



CD59 staining



Motor neurons

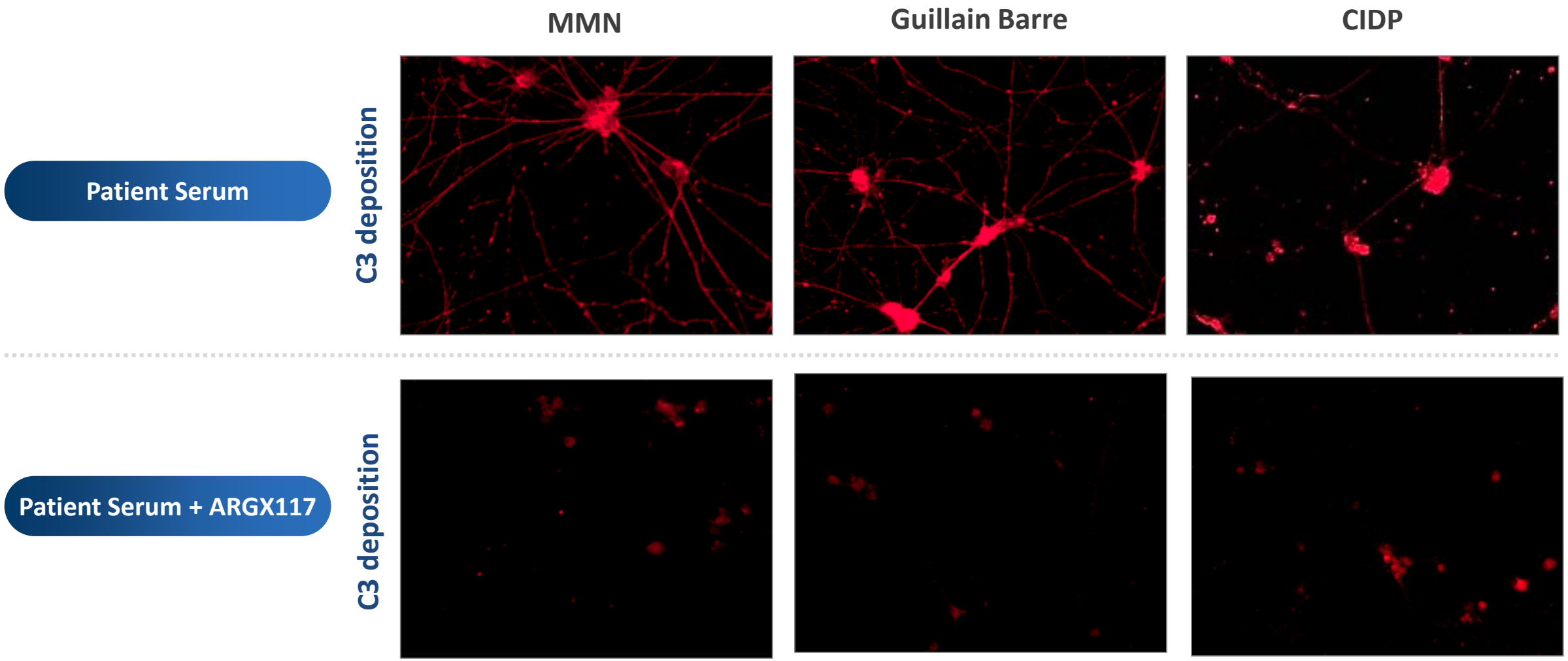


Schwann cells

	Normal	Stripped
CD59	High	Absent
C3	✓	✓
MAC	✗	✓
Cell lysis	✗	✓

C3 activation confirmed MOA in MMN

Unique Biology Insights Translate to Other Motor Neuron Diseases



Feasibility: Efficient Clinical and Regulatory Path

MMN indication has precedent clinical and regulatory pathway

Journal of the Peripheral Nervous System 18:321–330 (2013)

RESEARCH REPORT

A controlled trial of intravenous immunoglobulin in multifocal motor neuropathy

Angelika F. Hahn[1], Said R. Beydoun[2], Victoria Lawson[3], for The IVIG in MMN Study Team[†], MyungShin Oh[4], Victoria G. Empson[5], Heinz Leibl[6], Leock Y. Ngo[7], David Gelmont[7], and Carol L. Koski[8]

[1]*Department of Neurology, London Health Sciences Centre, London, Ontario, Canada;* [2]*Department of Neurology, University of Southern California, Los Angeles, CA, USA;* [3]*Department of Neurology, The Ohio State University, Columbus, OH, USA;* [4]*Clinical Biostatistics, Baxter Healthcare Corporation, Westlake Village, CA, USA;* [5]*Clinical Scientific Affairs and* [6]*Clinical Research, BioTherapeutics, Baxter Innovations GmbH, Vienna, Austria* [7]*Clinical Research, BioTherapeutics, Baxter Healthcare Corporation, Westlake Village, CA, USA and* [8]*Santa Fe, NM, USA*

Abstract Intravenous immunoglobulin (IVIG) has become the standard treatment for multifocal motor neuropathy (MMN) based on limited data. To critically assess the efficacy, safety, and tolerability of 10% liquid IVIG (IVIG), 44 adults with MMN were randomized

Feasibility: Orphan Potential & Economically Viable Indication

Unmet need for new therapies that slow down progression of disease and reduce reliance on IVIg

Prevalence

~13,000 patients in the US

Underdiagnosed

Predominantly men under 50

Multifocal Motor Neuropathy

MMN

Rare inflammatory neuropathy; ALS patient that didn't die

Slowly progressive

Asymmetric distal limb weakness mainly affecting upper limbs

Patients become dependent

Diagnosis / Metrics

Anti-GM1 IgM antibody presence

Nerve conduction block

Defined clinical endpoints (i.e. 9-HPT, grip strength, Guy's neurological disability score)

Treatment

First line therapy is frequent, high dose of IVIg over 2-5 days

Patients unhappy with short duration of effect, disease progression despite strict adherence, side effects of IVIg

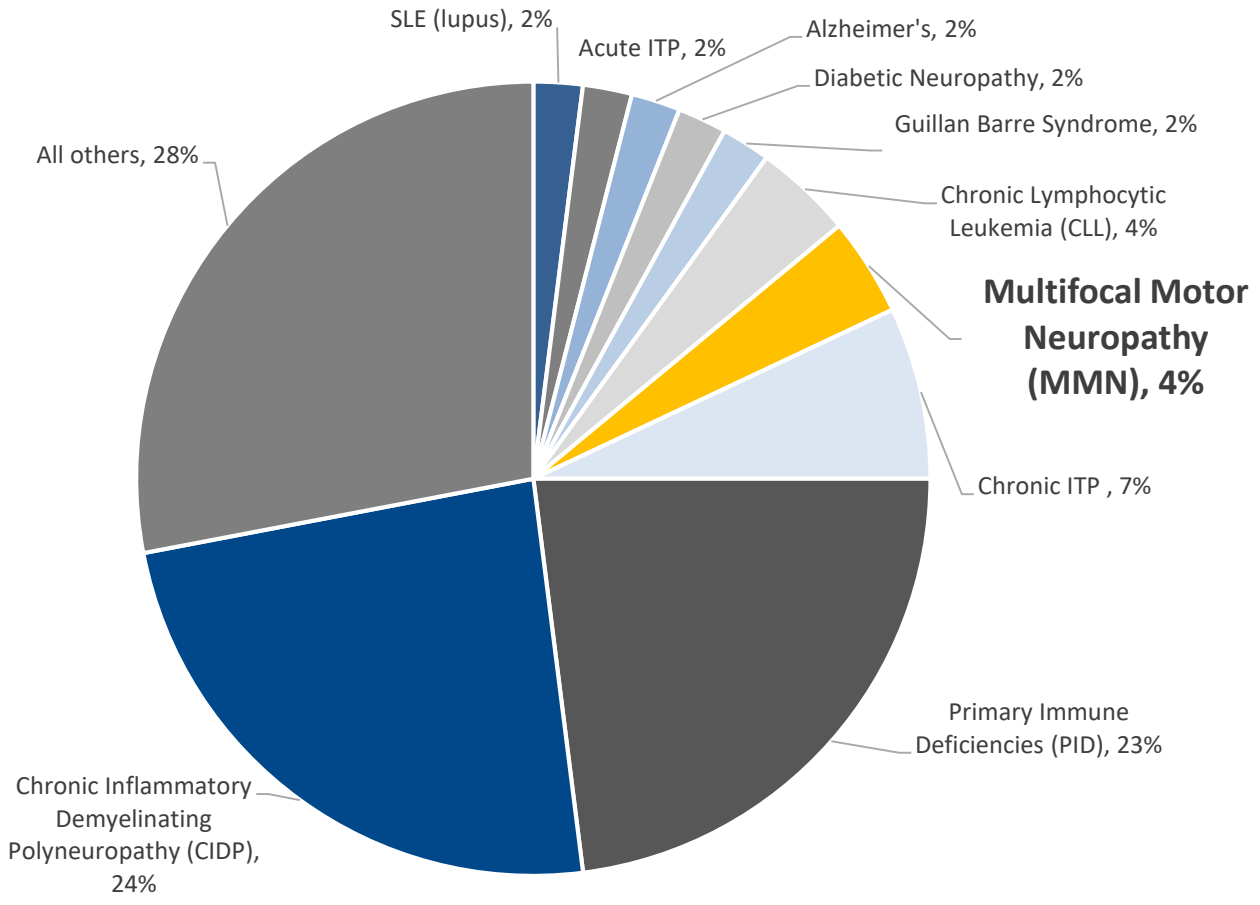
Payors aligned in need for new therapies

Vlam et al., Nat. Rev.Neurol, 2012

Feasibility: Economically Viable Indication

MMN Represents 4% of Total IVIg Market by Volume

Total IVIg consumption (US)



Global IVIg market

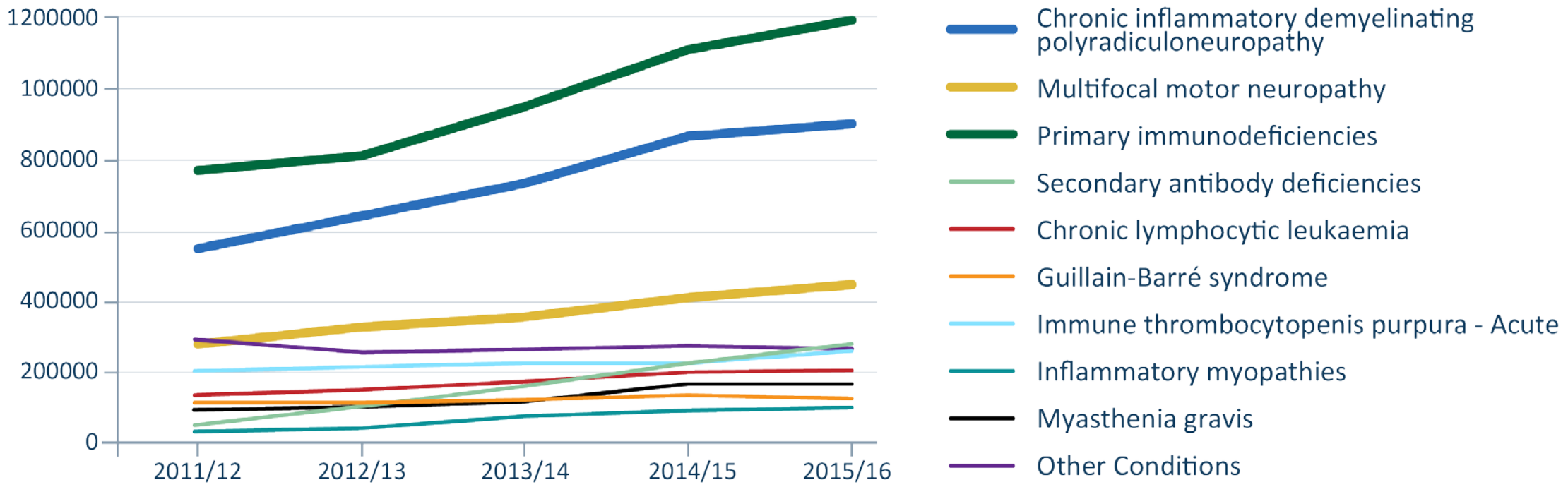
- Totals ~$10B with 6-8% CAGR
- Neurology taking 40-50% (CIDP, MG, MMN, GBS, etc.)
- Neurology showing rapid growth outside of PID
- MMN represents 4% of total IVIg market

References:

- Roberts 2015
- National Blood Authority
- Shire, Griffols annual reports; NHS UK IVIg report 2015/2016

Neuropathies Remain Highest Growth Indications for IVIg Consumption

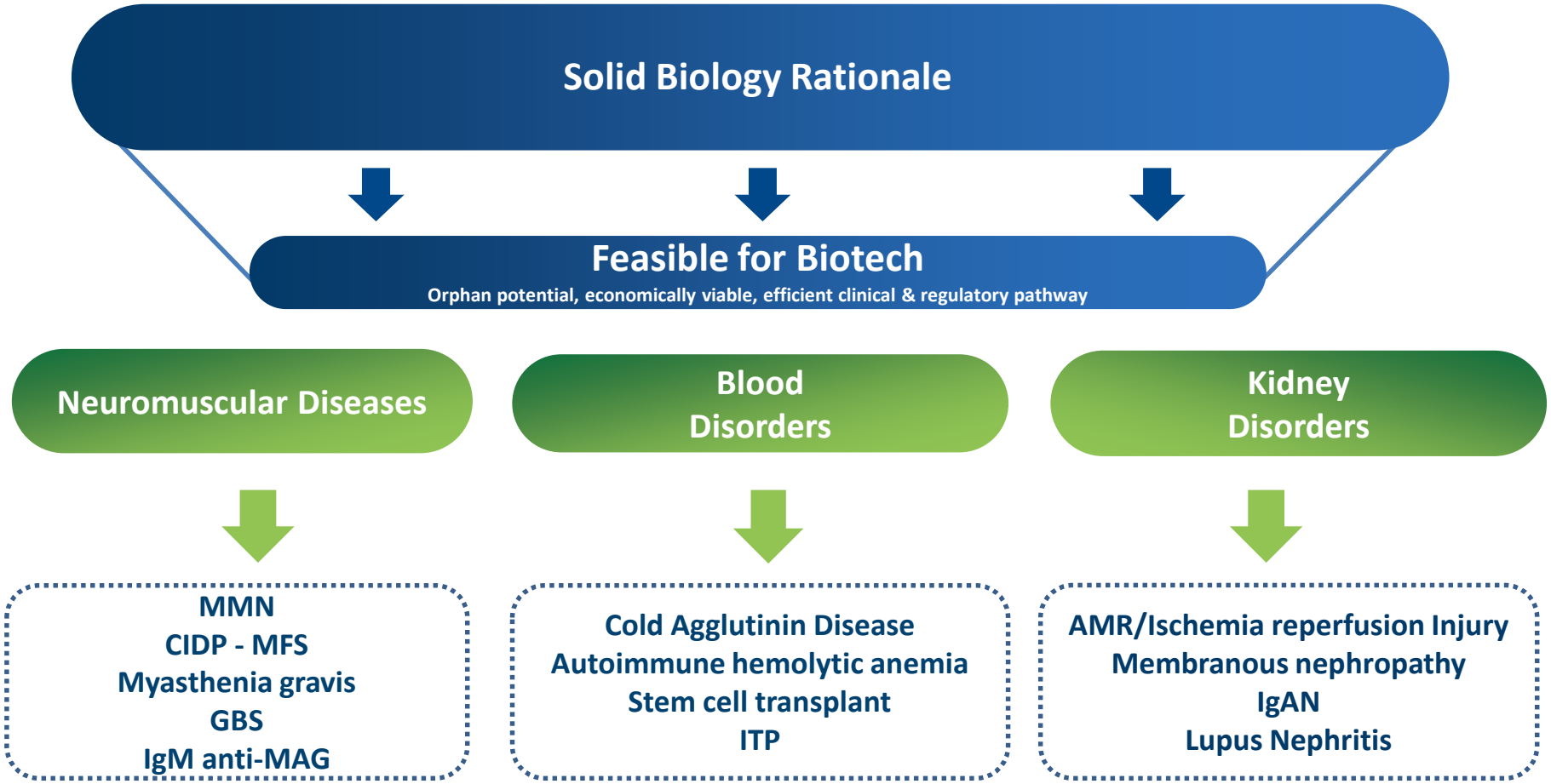
Recorded yearly immunoglobulin use for the top 10 diagnoses



MDSAS: Immunoglobulin Database Report 2015/16

ARGX-117: Pipeline-in-a-Product Opportunity

Classical and Lectin Pathway-mediated Severe Autoimmune Diseases



KOL Panel on Role of Complement in Kidney and Neurology Indications

Prof. Ludo van der Pol, M.D., Ph.D.

- Neurologist, Associate Professor of Neurology
- Head of the Netherlands SMA center at the University Medical Center Utrecht (UMCU), The Netherlands

Dr. Rafael Villicana, M.D.

- Associate Professor of Medicine
- Medical Director of Kidney Transplantation at Loma Linda University Medical Center, U.S.

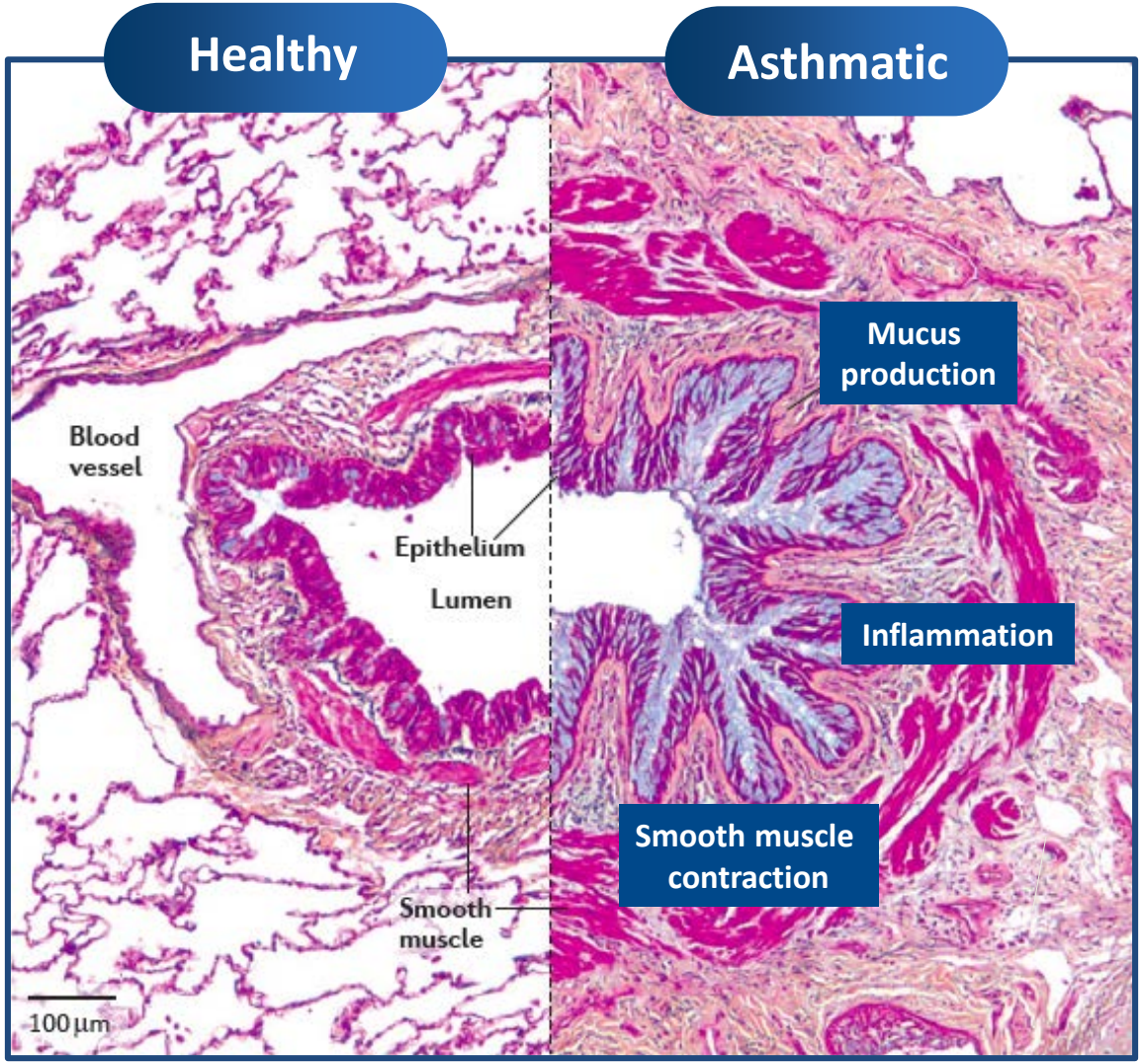
ARGX-118: Immunology Breakthrough for Airway Inflammation

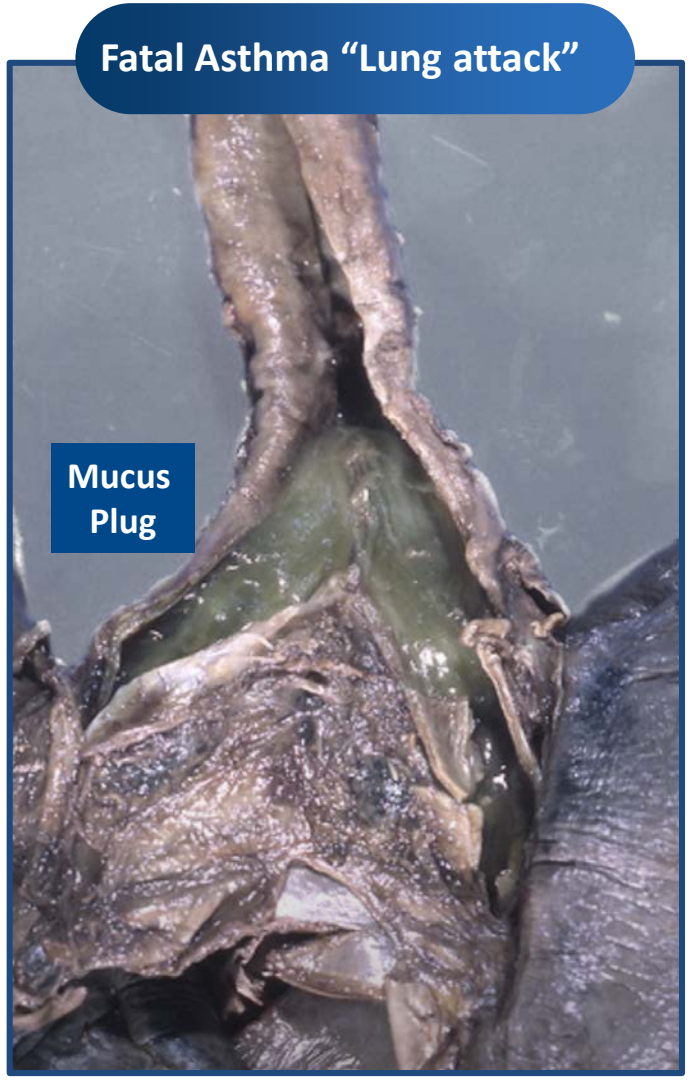
Bart Lambrecht | Prof. VIB-UGent

Professor Bart Lambrecht, M.D., Ph.D.

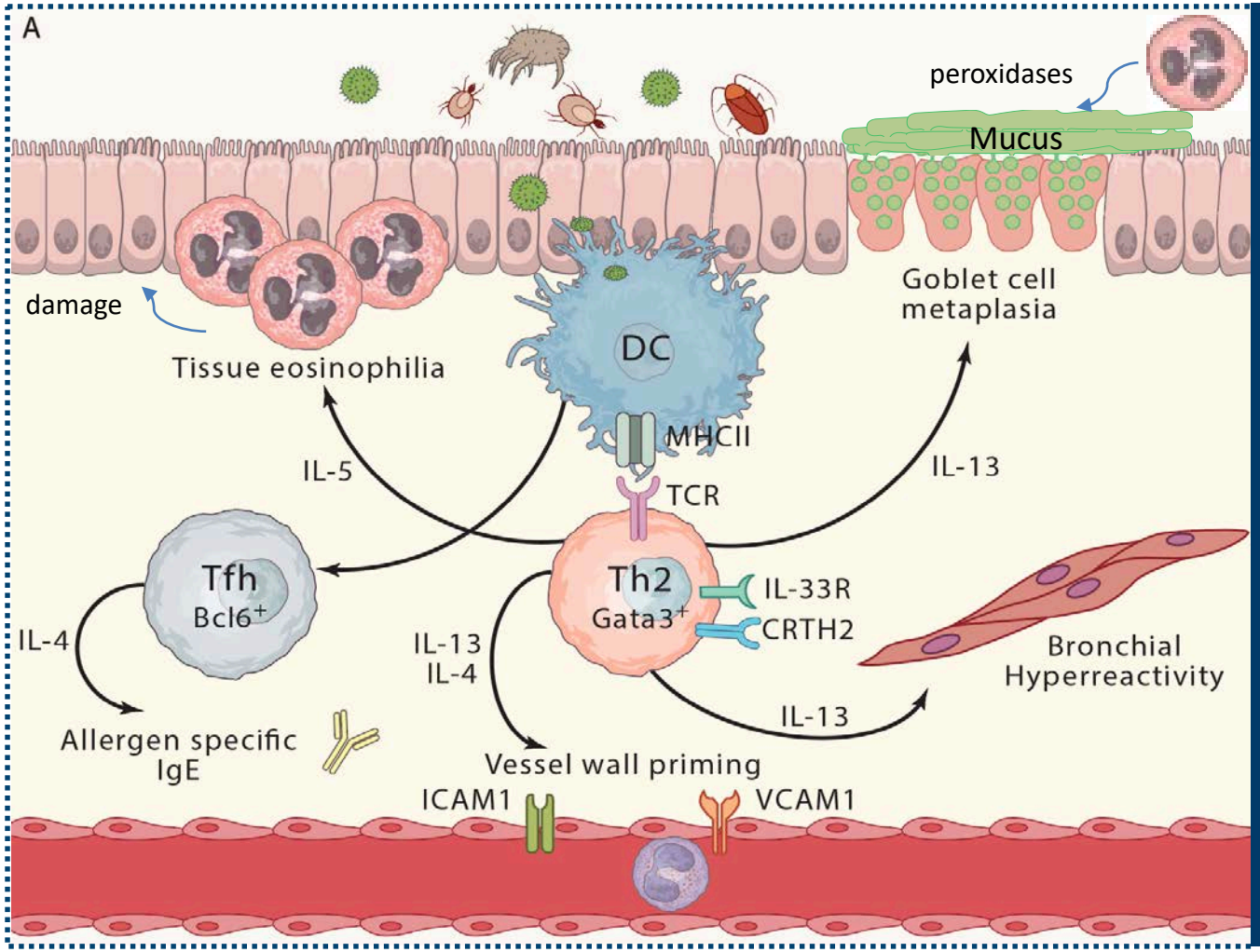
- Director of VIB Inflammation Research Center, UGent (280 scientists)
- Active clinician; Prof. of Pulmonary Medicine at Ghent University and Erasmus MC
- Author of 330 papers and 25 book chapters on asthma and allergy
- Research: the immunology of asthma; basic science and translational
- Theory on mechanisms of allergic sensitization are the basis of many research efforts globally, enabling new preventive and therapeutic avenues for asthma.

Mucus Plugs Remain Biggest Unmet Need in Asthma Management





Eosinophils Are Driver of Severe Asthma Pathology and Mucus Production

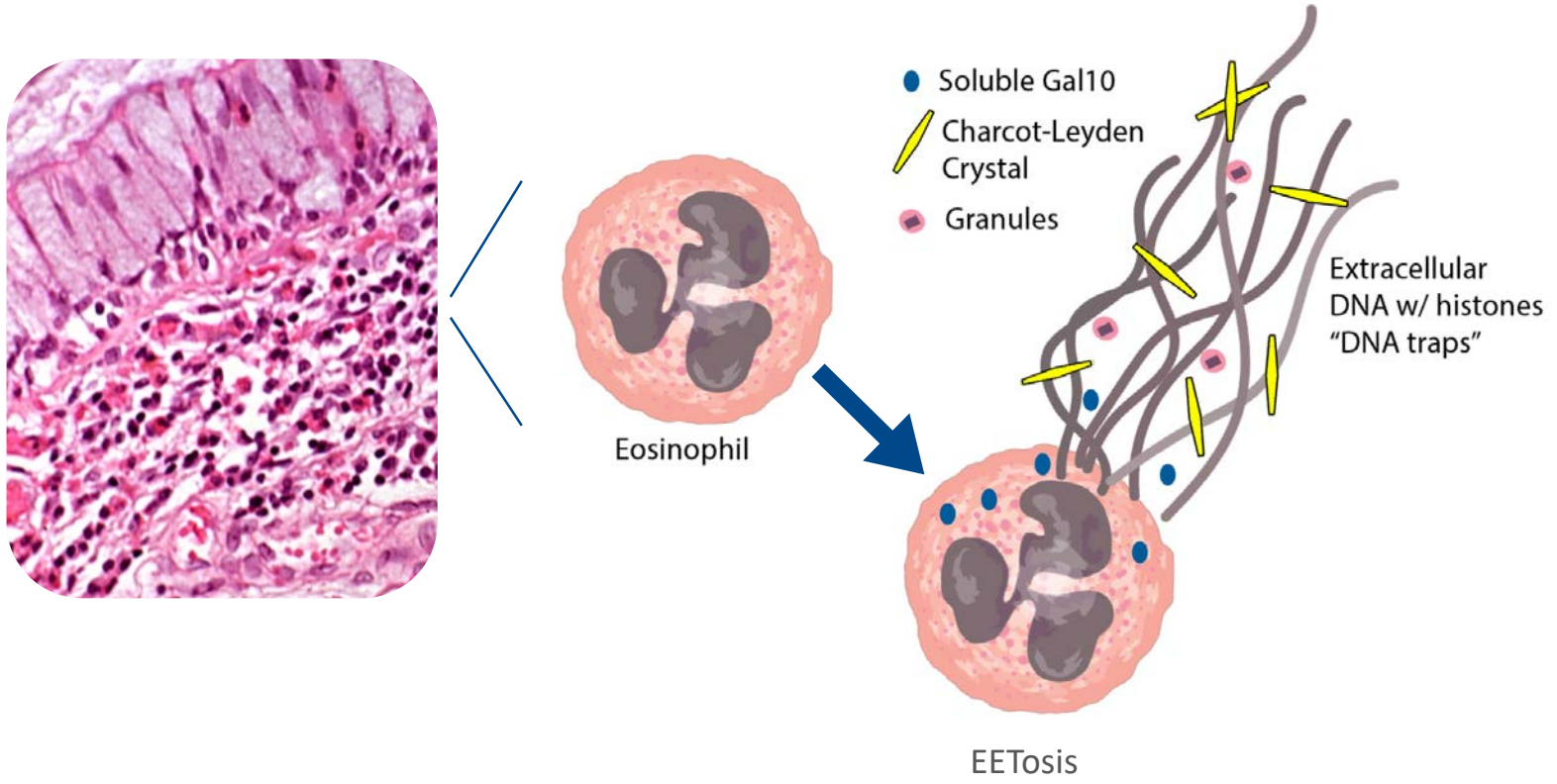


- Current therapies treat
  - Inflammation
  - smooth muscle contraction
- Currently no drugs to treat the mucus build up
- ARGX-118 potential first-in-class drug for mucus plugging and persistent airway obstruction

Lambrecht, Hammad and Fahy, Immunity, 2019

Charcot-Leyden Crystals (CLCs) and Galectin-10 Emerge from Eosinophil Burst

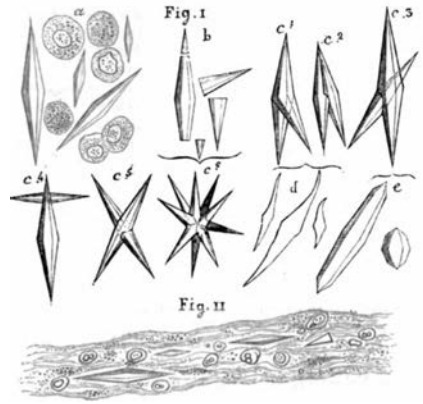
Asthma Biopsy



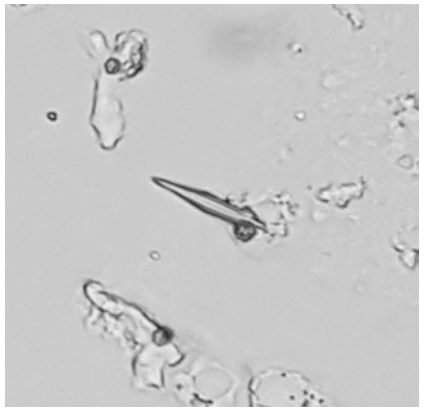
- Eosinophils seen in about 50% of severe asthmatics
- EETosis (burst of eosinophil): "Release of intracellularly formed CLCs and soluble Galectin-10 further contributes to formulation of large CLCs extracellular" (Ueki, Blood, 2018)
- Galectin-10 makes up 10% of all eosinophil protein content

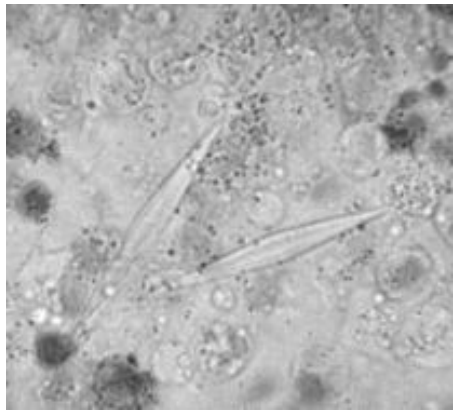
Charcot-Leyden Crystals Intuitive Yet Overlooked Asthma Target

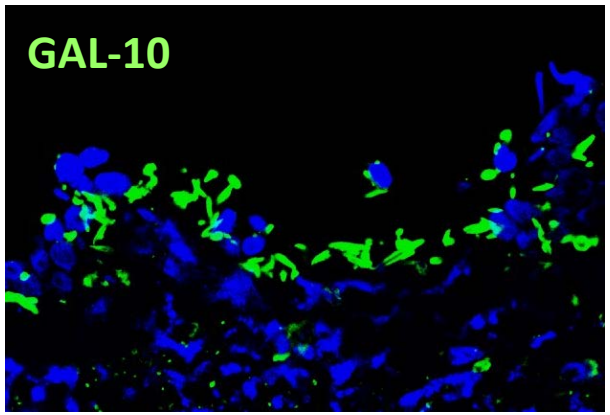
- Described in 1853 in sputum and mucus plugs of severe asthmatics
- Comprised of protein galectin-10
- Gal-10/CLCs serve as biomarker of mucus plugs
- Crystals present in “allergic mucin” in many diseases including:
  - Asthma and cystic fibrosis
  - Chronic rhinosinusitis (CRS) with nasal polyps



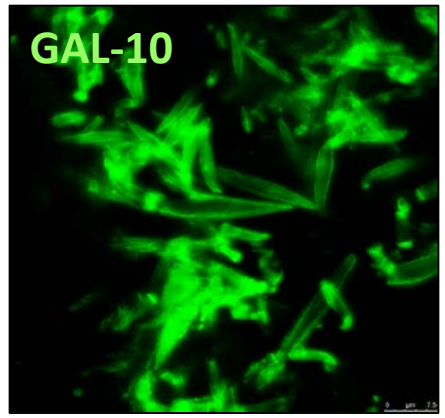
Charcot & Vulpian, Gaz. Hebd, 1870


Fresh sputum from asthma patient


Mucus plug from ABPA patient



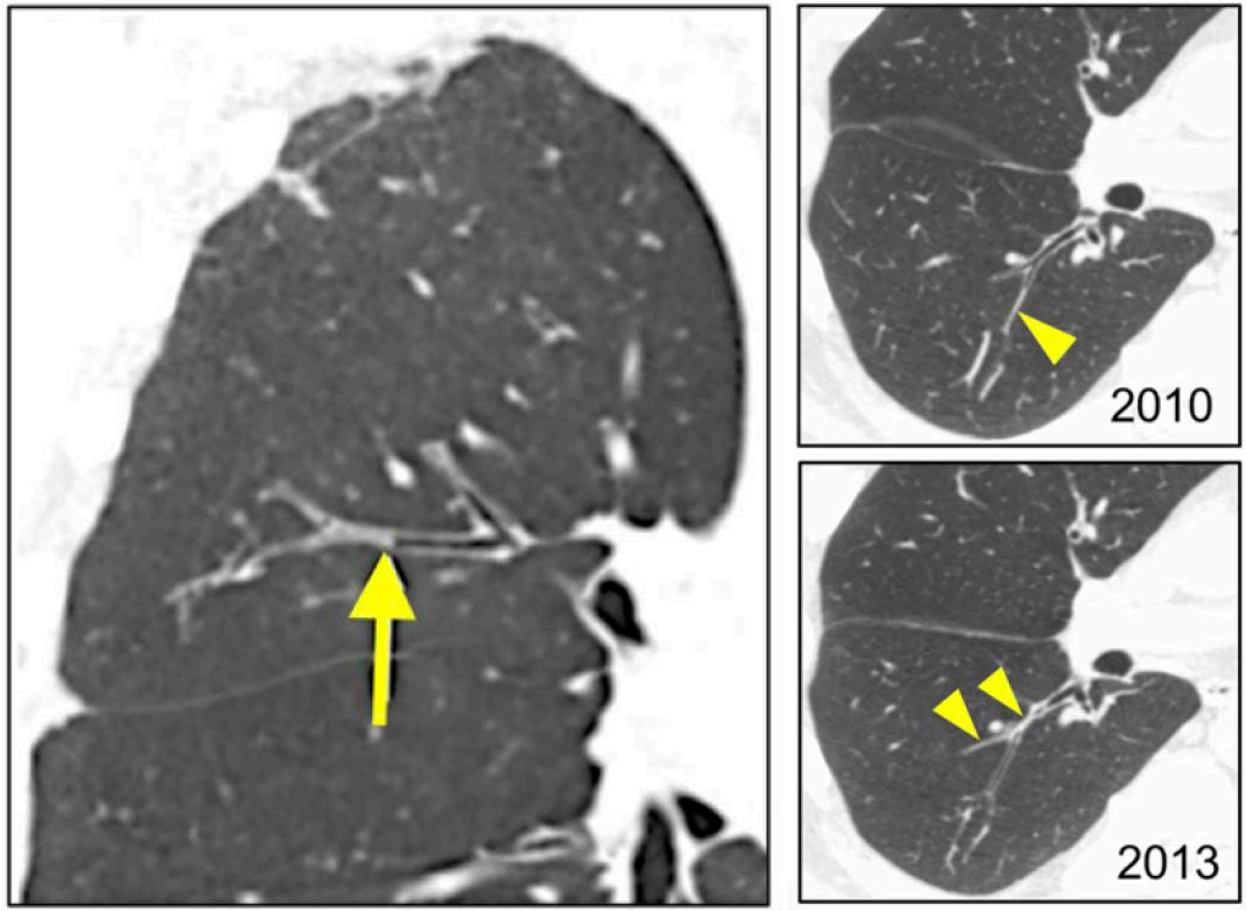
Mucosal biopsy from CRS with nasal polyps



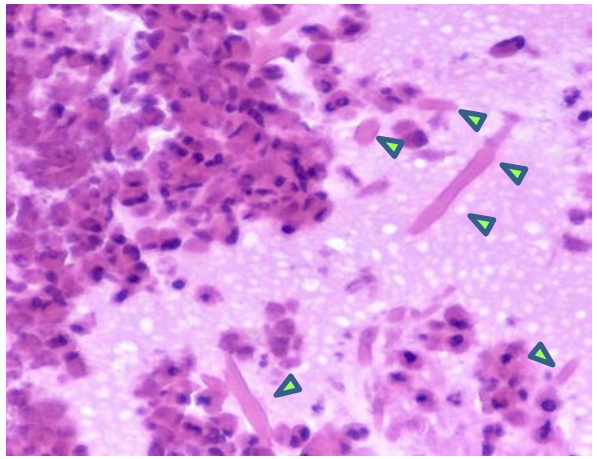
”Peanut butter” from CRS with nasal polyps

Mucus Plugging Seen in 70% of Severe Asthmatics with Persistently Low Lung Function

Mucus plugs on chest CT scan - Very chronic



Asthma mucus plugs contain numerous CLCs

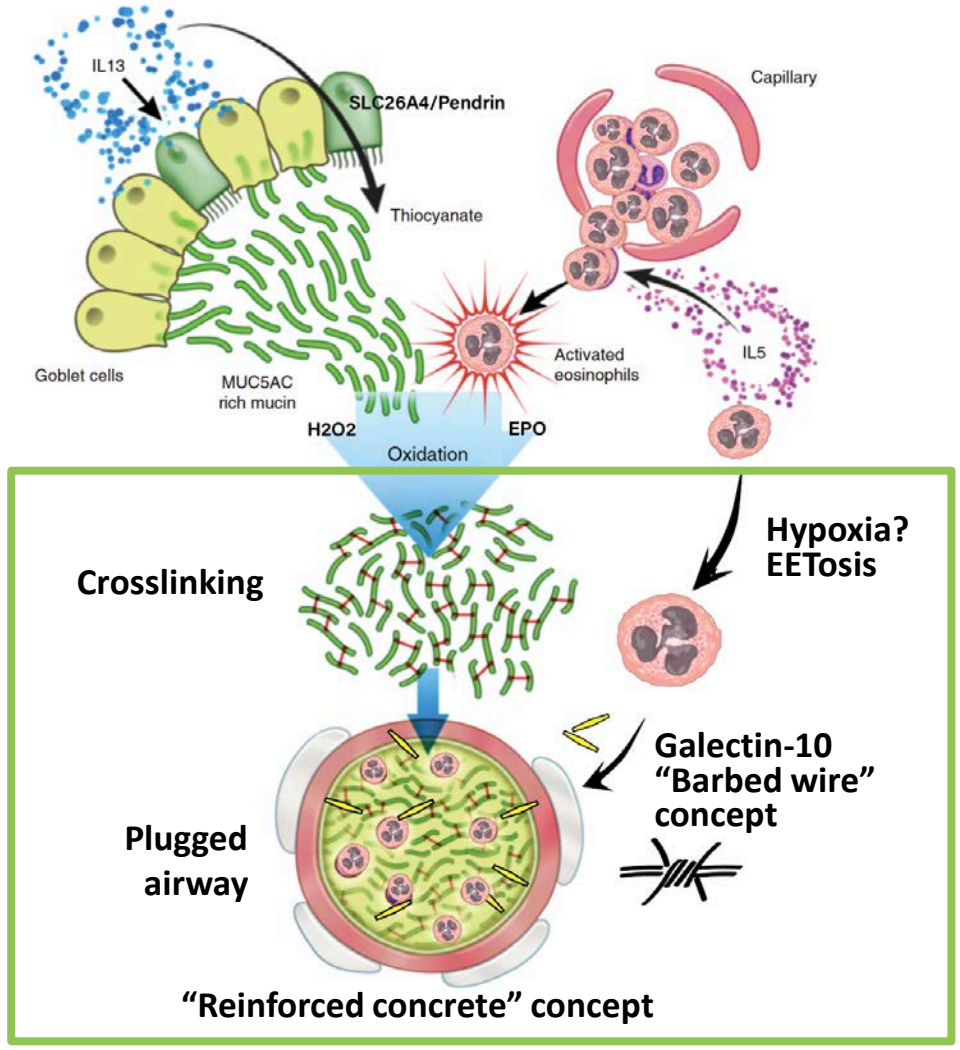


Dunican & Fahy J., Journal of Clin. Invest. , 2018

Charcot-Leyden Crystals and Galectin-10 Are Basis of Mucus Plug Persistence

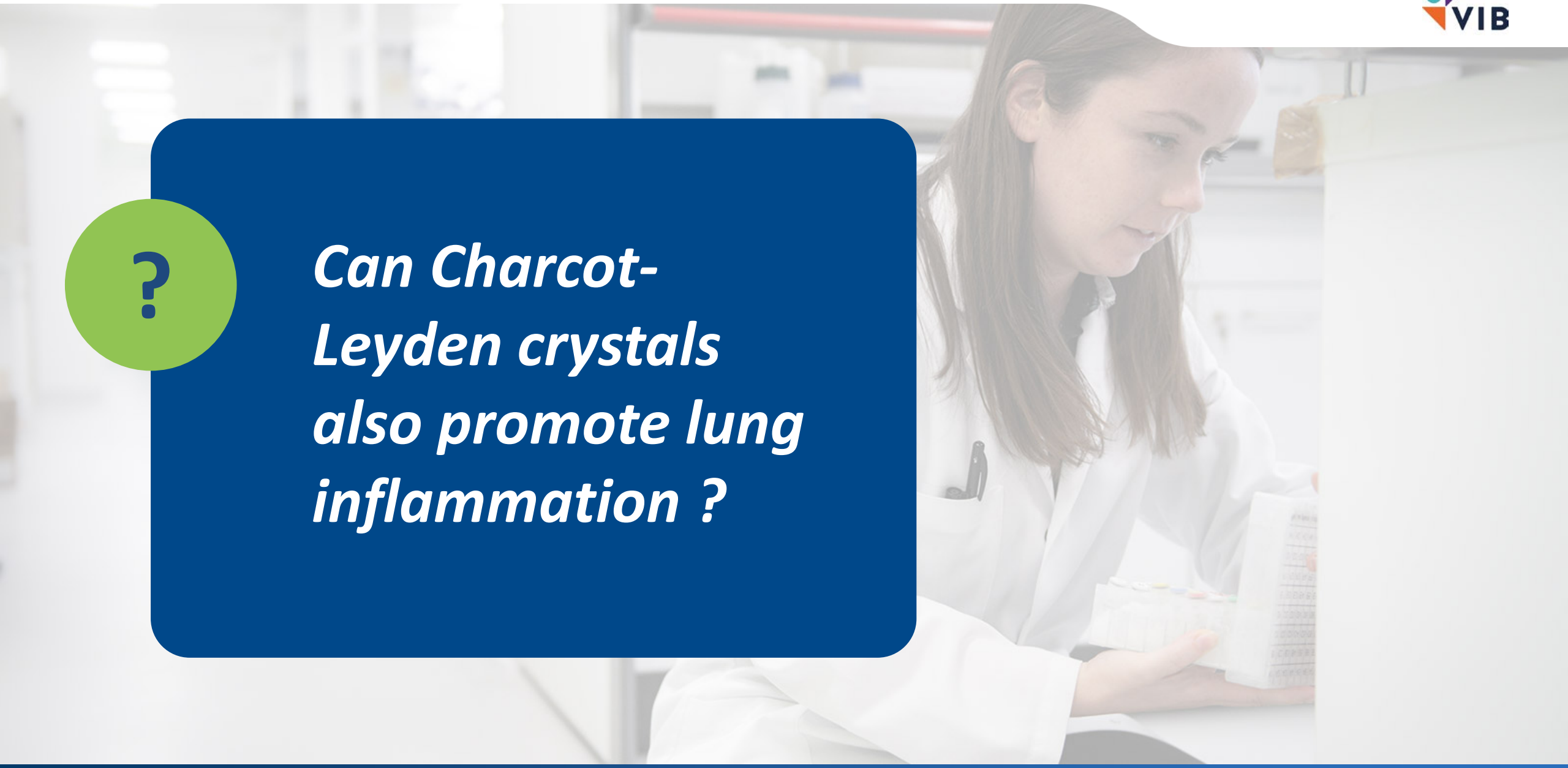
Generation (days-weeks)

Persistence (months-years)



- CLCs together with crosslinked mucin form "barbed wire" which makes the plug stick in the airways
- Once mucus plugs are formed, they are persistent for years
- High unmet need for treatment that can resolve the plugs
  - Only interventional therapies available to reduce pre-existent plugs

Fahy and Lambrecht



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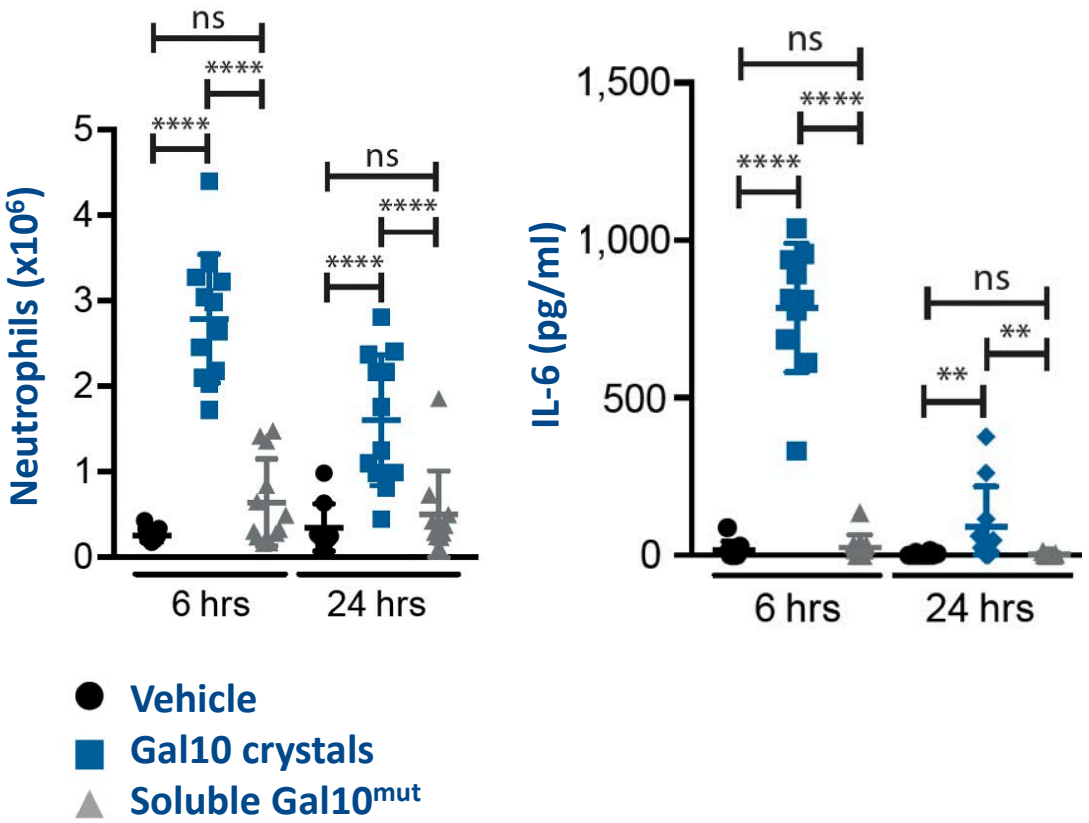
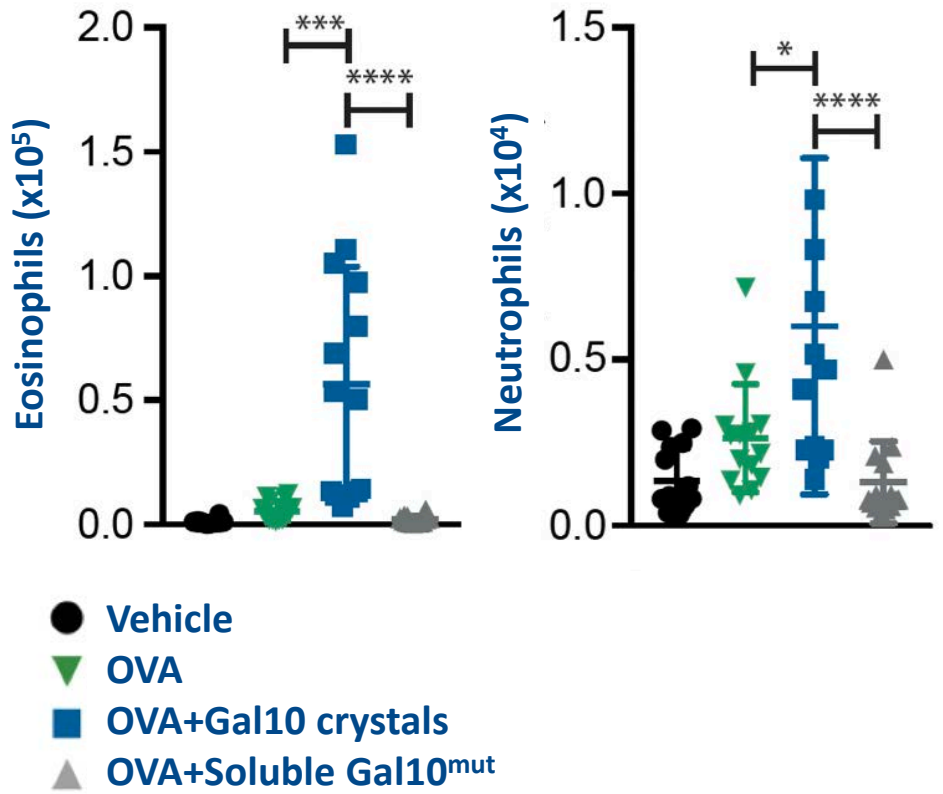
Can Charcot-Leyden crystals also promote lung inflammation ?

CLCs Induce Inflammation and Promote Development of New Allergies *in vivo*

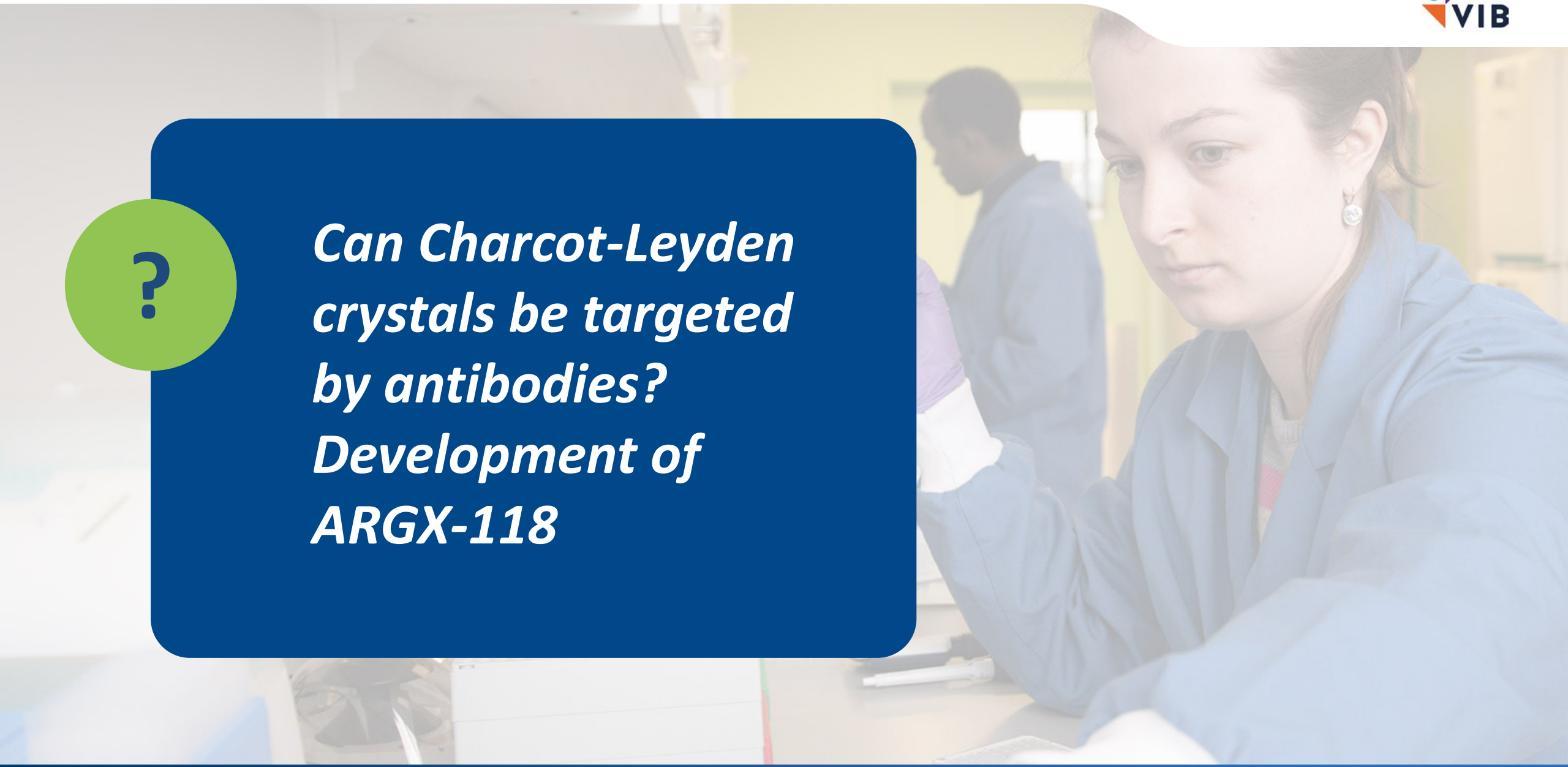
CLCs induce inflammation when injected in lungs of mice



CLCs promoter development of new allergies in mice



Persson et al., *in press*



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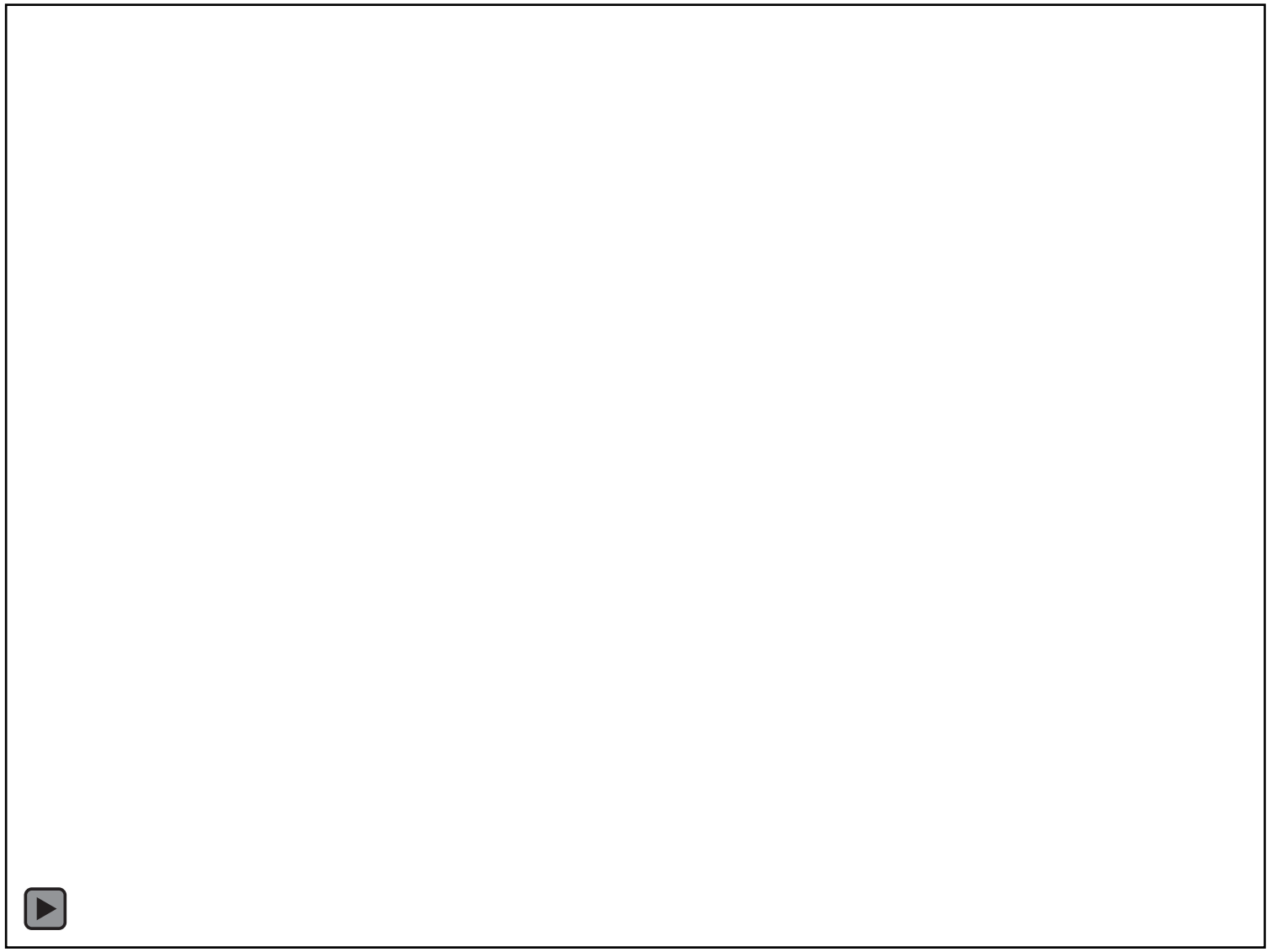
Can Charcot-Leyden crystals be targeted by antibodies? Development of ARGX-118

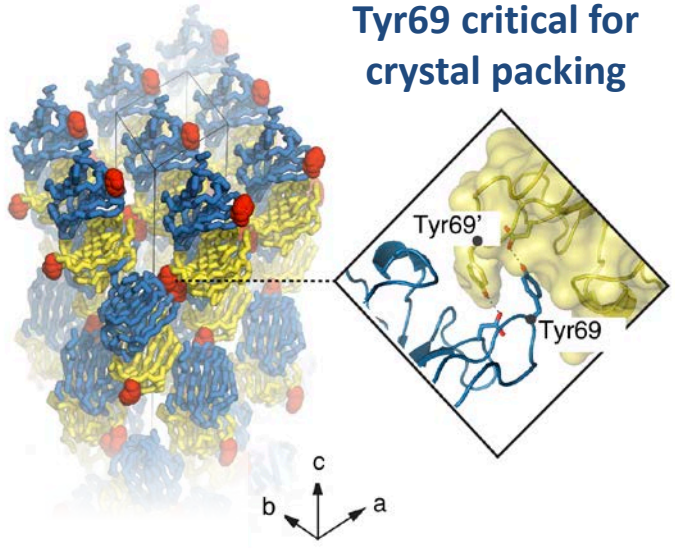
ARGX-118 Solubilizes Charcot-Leyden Crystals



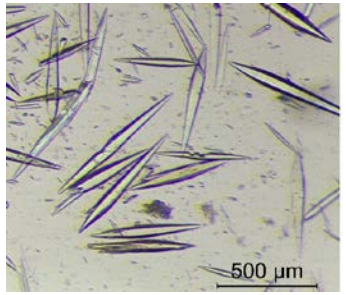
ARGX-118 Binds Critical Residue for Crystal Packing

Galectin-10 crystal

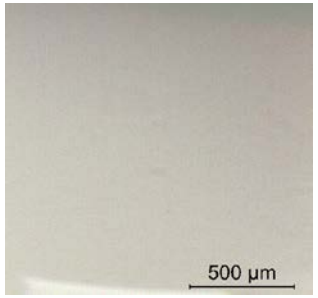
Tyr69 critical for crystal packing



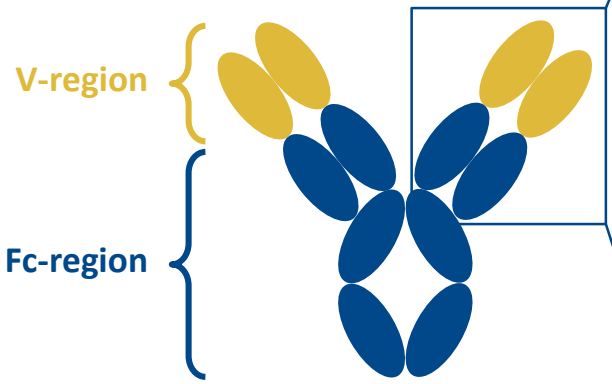
GAL10-WT

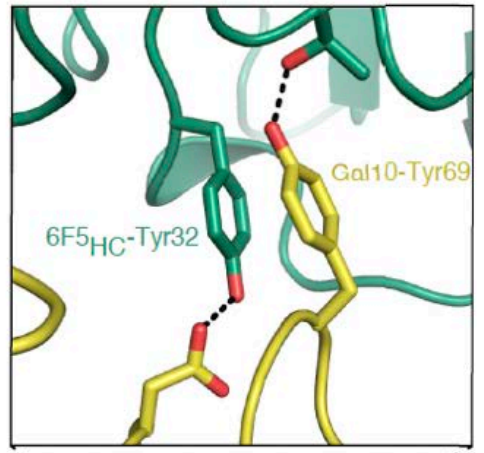


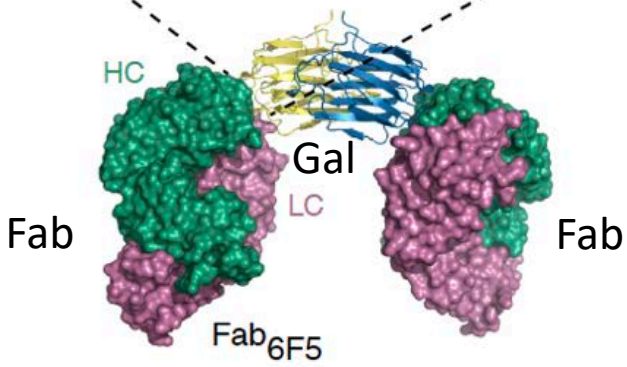
GAL10-Tyr69GW



ARGX-118 binds Galectin-10 Tyr69



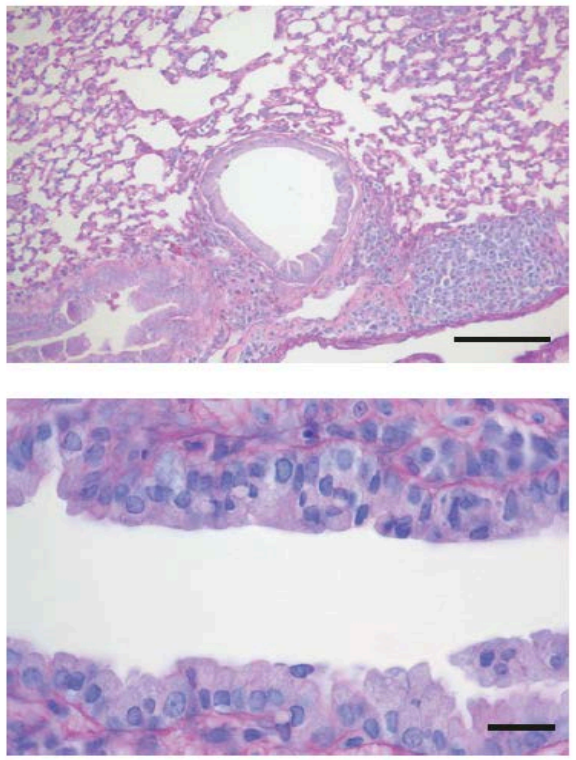




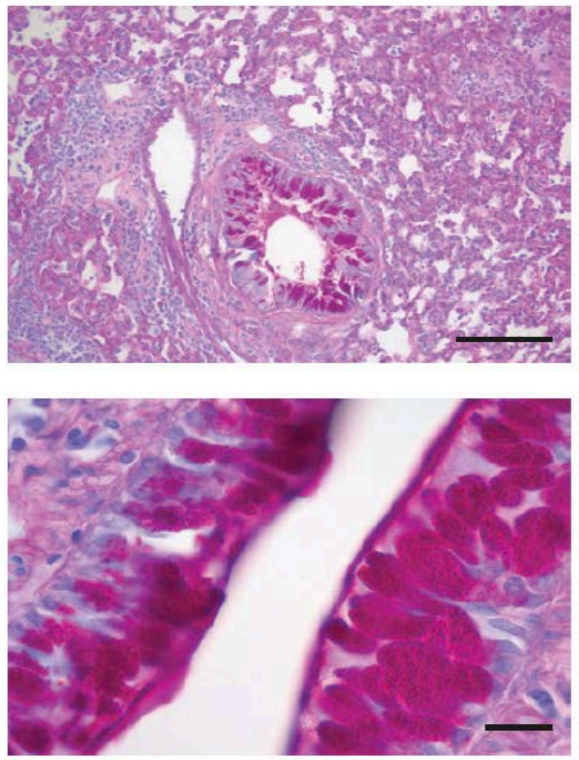
Targeting Tyr69 solubilizes the crystal

ARGX-118 Reverses Goblet Cells Metaplasia Caused by Charcot-Leyden Crystals in Mice

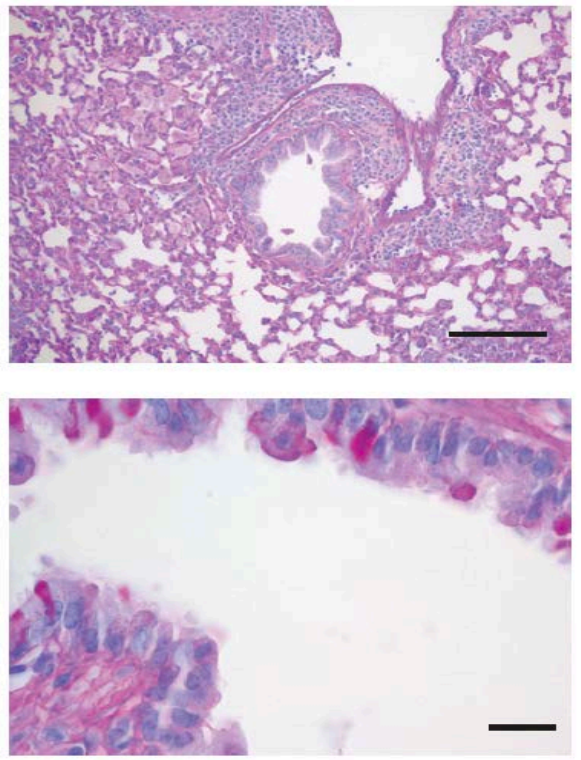
HDM Isotype Ab



HDM + CLC Isotype Ab



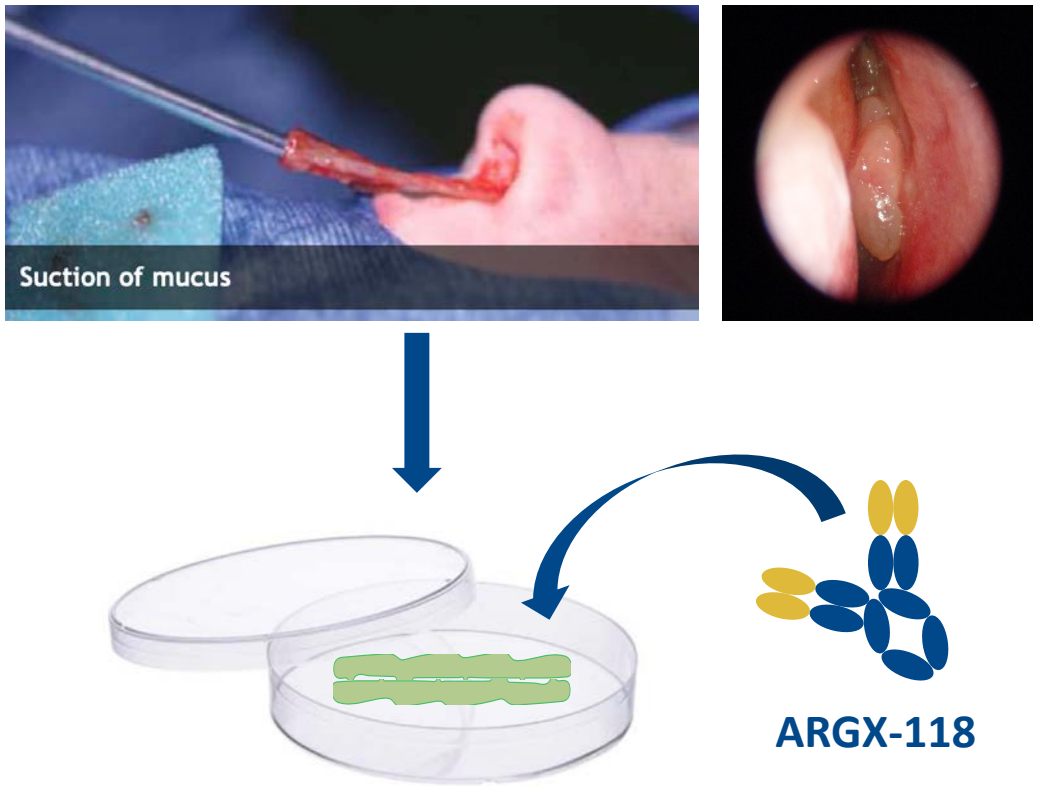
HDM + CLC ARGX-118



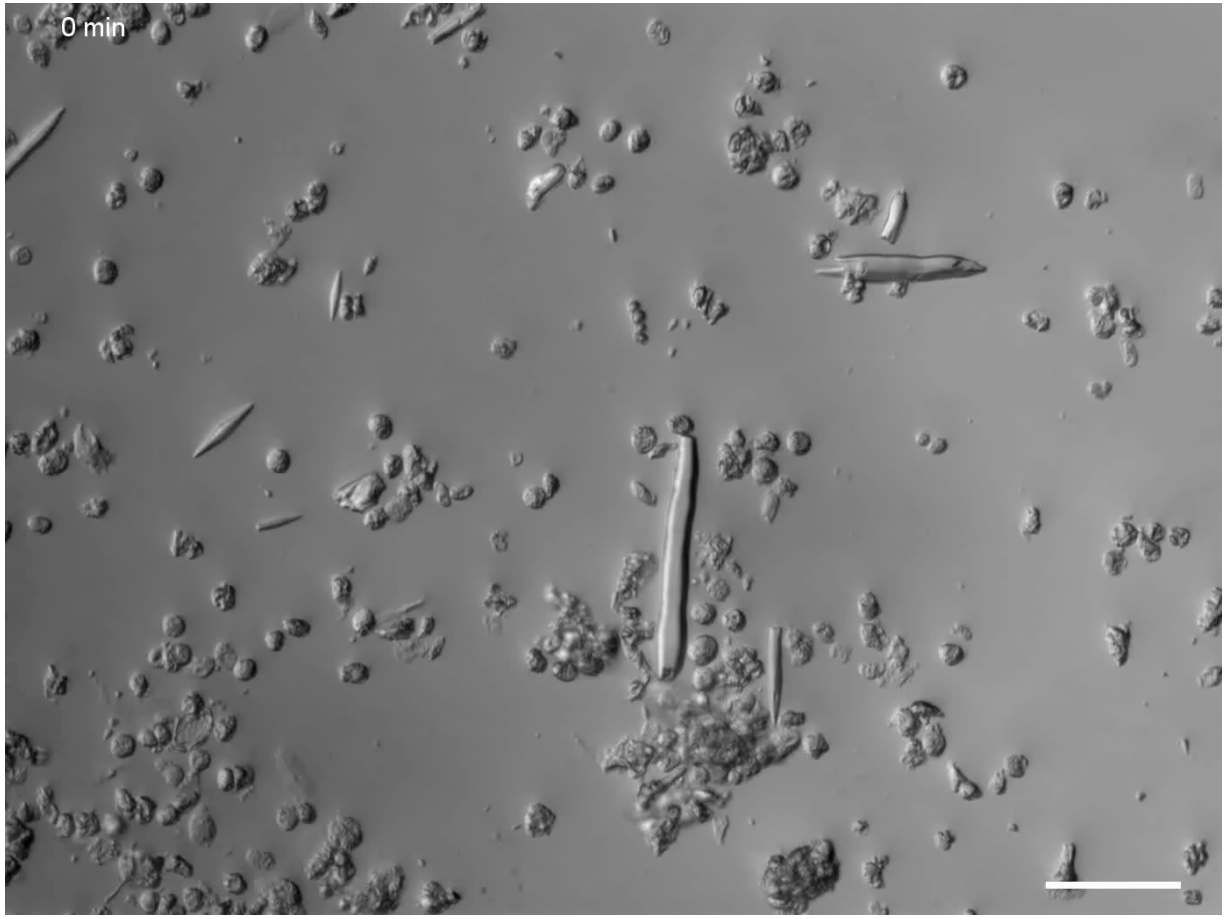
Persson et al., *in press*

ARGX-118 Dissolves Charcot-Leyden Crystals Within Native Patient Mucus

Allergic mucin protruding from nasal sinus

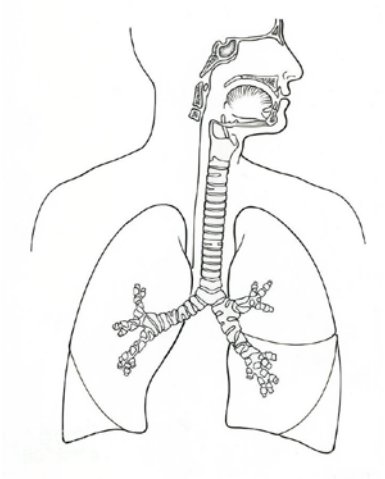


Persson et al., *in press*



Video shot over 16 h

Multiple Crystallopathies Induced by Charcot-Leyden Crystals



ARGX-118 targets Gal-10,
The only component of Charcot-Leyden Crystals (CLCs)

Charcot-Leyden crystals (CLCs) shown to:
- **Stimulate innate and adaptive immunity**
- **Act as a type 2 adjuvant when administered to the airways**
- **Stimulate mucus production**

Biology rationale supports potential role of CLCs as disease-drivers in eosinophilic diseases like asthma

Lung attack or asthma exacerbation

- Acute intratracheal treatment for asthma attack by bronchoscopy
- Chronic Nebulization for persistent plugging
- MoA: reverse mucus plugging

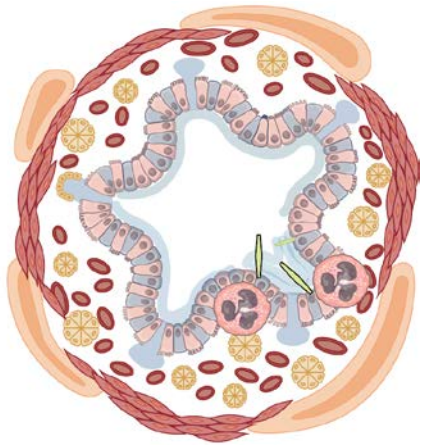
ABPA

- Chronic treatment
- Nebulization
- MoA: block type 2 immunity trigger (IgE) plus mucus plugging

CRS with Nasal Polyps

- Chronic treatment
- Nebulization
- Following sinus surgery
- MoA: block type 2 immunity trigger plus mucus stickiness

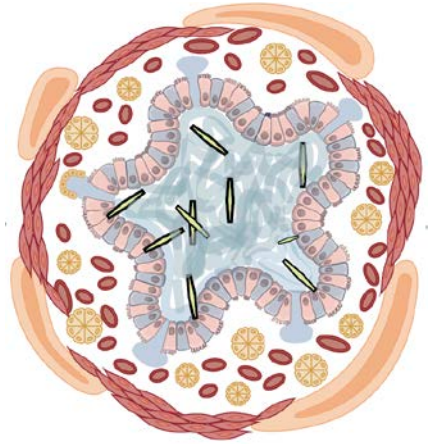
Mucus Plugging Requires an Interventional Procedure or Chronic Inhaled Therapy



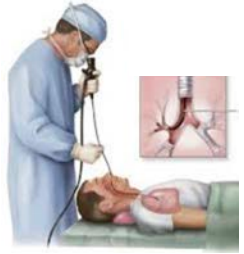
Bronchus is narrowed
Exacerbation

Prevention by biologicals

Mepolizumab
Benralizumab
Dupilumab

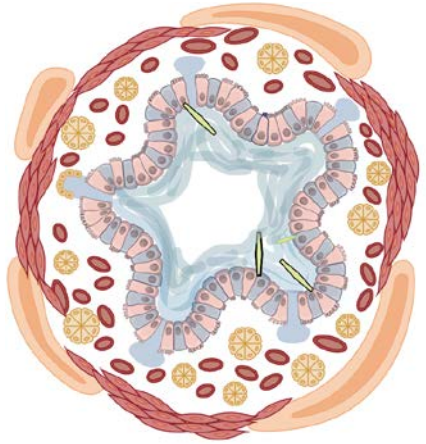


Acute occlusion
by mucus plugging



Bronchoscopy
Mucolysis

Potential for
ARGX-118



Healing with persistent
airway obstruction caused
by residual mucus

Inhaled mucolytic
therapy

Potential for
ARGX-118

Innovative Access Program in Action

argenx

Antibody expertise

VIB - UGent

Disease Biology expertise

Development of unique Simple Antibody™ ; track record in drug development

High risk - high gain: early collaboration focused on science, feeling of ownership on both ends

Open communication; fair economics; aligned expectations

Cusatuzumab Development Plan

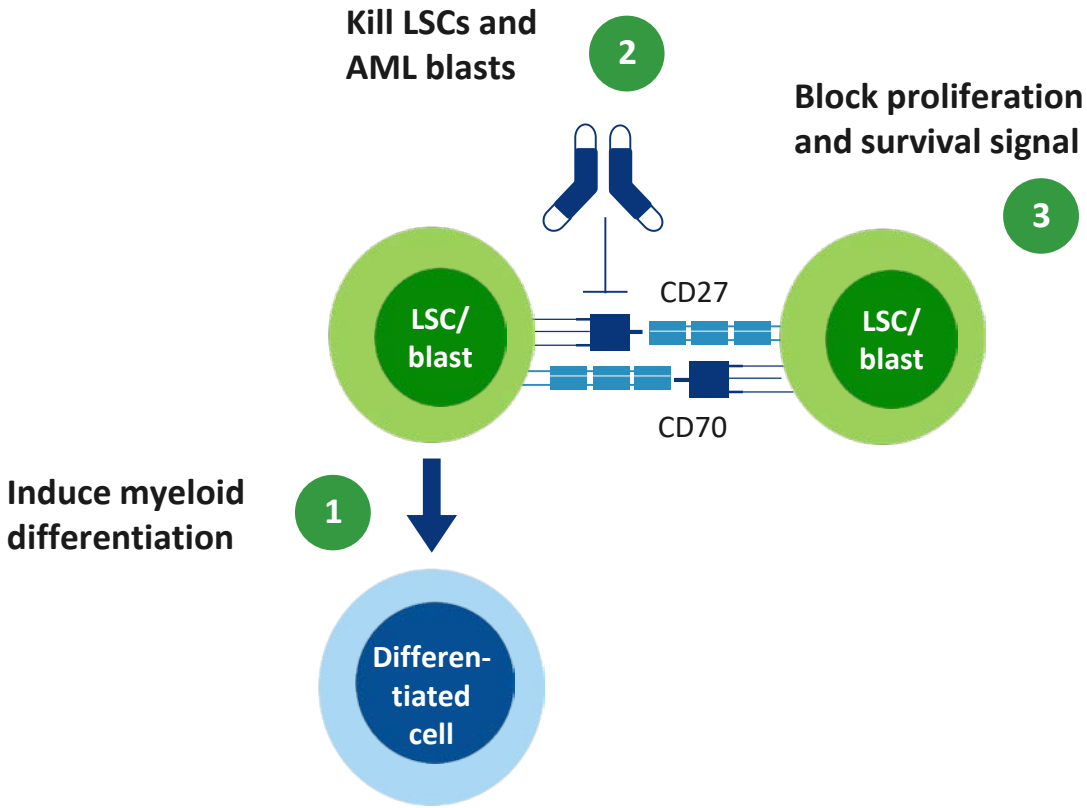
Wim Parys | Chief Medical Officer

Wim Parys, M.D. – Newly Appointed CMO

- MD from KUL (Belgium)
- Janssen Research Foundation (BE) - developed Reminyl™ / Razadyne™ for Alzheimer's Disease
- Head of Development at Tibotec (BE), established Tibotec Inc. (USA) - developed and launched Prezista™, Intelence™ & Edurant™, three innovative HIV drugs
- Head of Development of Janssen's Infectious Diseases and Vaccines therapeutic - discovery and development of novel medicines for HIV, Hepatitis C (Incivo™, Olysio™/Sovriad™), TB (Sirturo™) and respiratory viral diseases
- Head of R&D of Janssen's Global Public Health group, responsible for a portfolio including programs in HIV, TB, other mycobacterial infections, Dengue and Malaria

Cusatuzumab: Potential Foundational, Novel Therapy for Acute Myeloid Leukemia

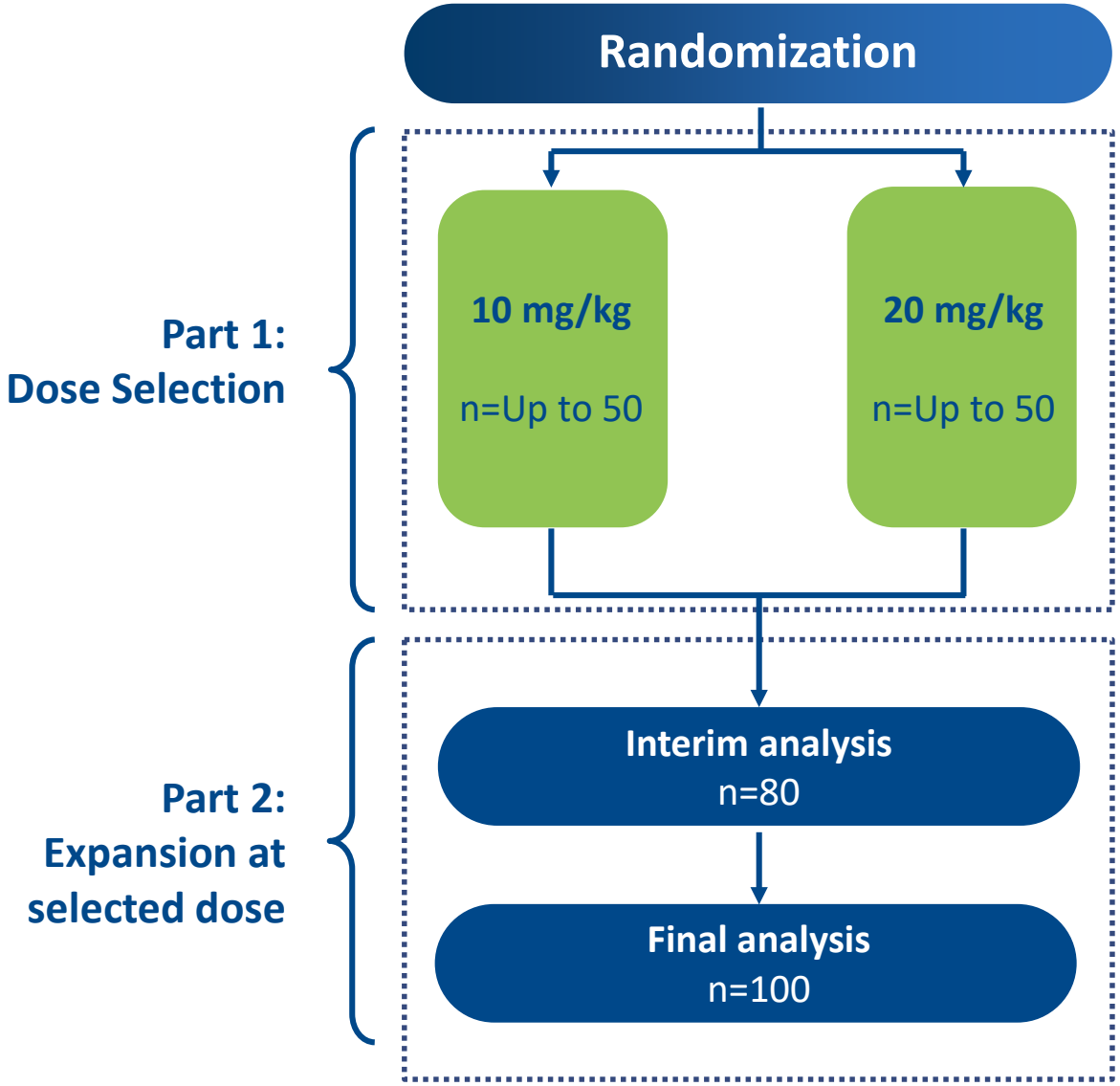
Cusatuzumab Induces LSC Differentiation



- Novel target and mechanism of action[1]
- Biologic with potential for combination therapy and extended dosing[2]
- Inhibition of CD70 pathway leads to differentiation and death of leukemia cells[3]
- Single-agent biologic activity in AML
- Phase 1/2 study: 92% response rate with 10 of 12 patients showing a complete response (CR/CRi) after Cusatuzumab treatment in combination with azacitidine (AZA) in newly diagnosed AML patients[4]
- IAP Program with Bern University – Prof. Ochsenbein

LSC, leukemic stem cells; sCD27, soluble CD27 | 1. Silence K, et al. MAbs. 2014;6:532232 | 2. Riether C, et al. J Exp Med. 2017;214:359–80
3. Hinterbrandner M, et al. ASH 2017; abstract 2652 (poster presentation) |. 4. argenx ASH 2018 investor meeting

Phase 2 Clinical Study in Newly Diagnosed, Unfit AML Patients



Combination therapy: Cusatuzumab + Azacytidine

Patient Population: Newly diagnosed AML patients unfit for intensive chemotherapy (total n= up to 150)

Primary Objective: To determine the efficacy (CR rate)

Secondary Objective: To assess

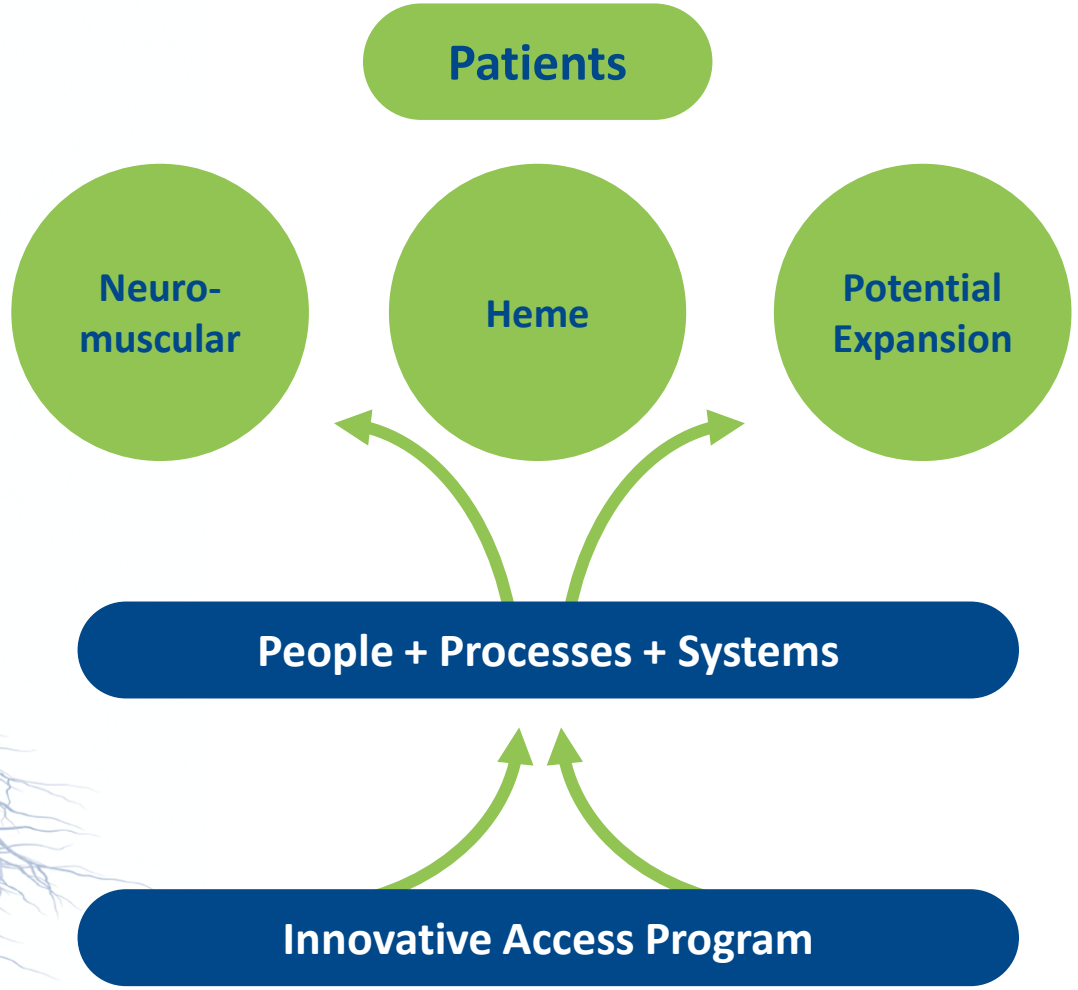
- ORR = (CR + CRh + CRi)
- Time to response and duration of response
- Event-free survival
- Overall survival
- Safety
- PK/immunogenicity
- MRD

Anticipate start Phase 2 study in US: mid 2019

argenx 2021: Global Commercial Vision

Keith Woods| Chief Operating Officer

argenx 2021: Our Path To An Integrated Immunology Global Biotech



Building Immunology Franchises

Neuromuscular Core

- MG
- CIDP
- MMN

Expansion Opportunities

- GBS
- MGUS
- Other?

Hematology Core

Malignant Heme

- AML
- MDS

Benign Heme

- ITP

janssen

50/50 share in economics (costs/profits)

Expansion Opportunities

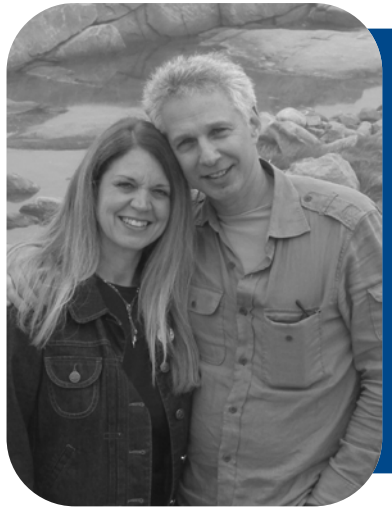
- CAD
- Hemolytic Anemias
- Thalassemias

New Horizons:
Complement or IgG-mediated Disease in Kidney and Skin

- IgAN
- AMR
- Lupus Nephritis
- Membranous Neph
- Myositis
- PV
- Bullous Pemphigoid

Neuromuscular and Hematology Opportunities

High unmet medical need



Dave, 66, lives with CIDP

"The weakness was the most difficult symptom to deal with. Simple activities like walking to my car became an exhausting task."

Sharon, 70, lives with pemphigus vulgaris (PV)

"The specialist was at a loss and couldn't give me a diagnosis. He basically shrugged his shoulders, wished me good luck, and closed the door behind me."

Lauren, 32, lives with generalized MG

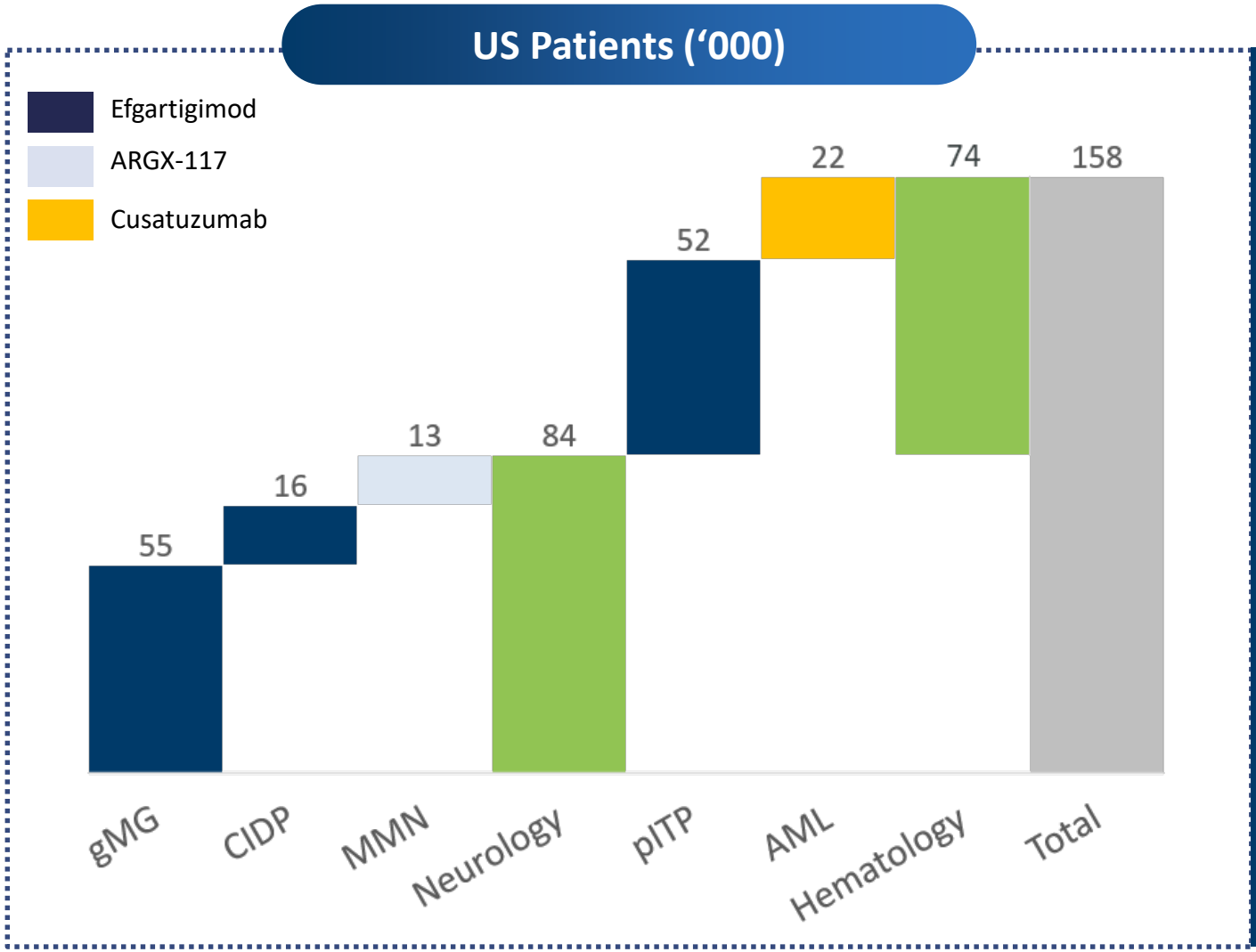
"I also know that the treatment is mostly a band aid at this point; it's not solving my issues, but rather just patching them.

Barbara, 61, lives with ITP

"I wasn't on medication for most of my childhood. We kept in touch with doctors, but we didn't get my platelet counts regularly. Since there was a great lack of treatment options, my parents thought, *what is the use in knowing?*"

Pipeline-in-product assets create scaling opportunity across our franchises

To add sources



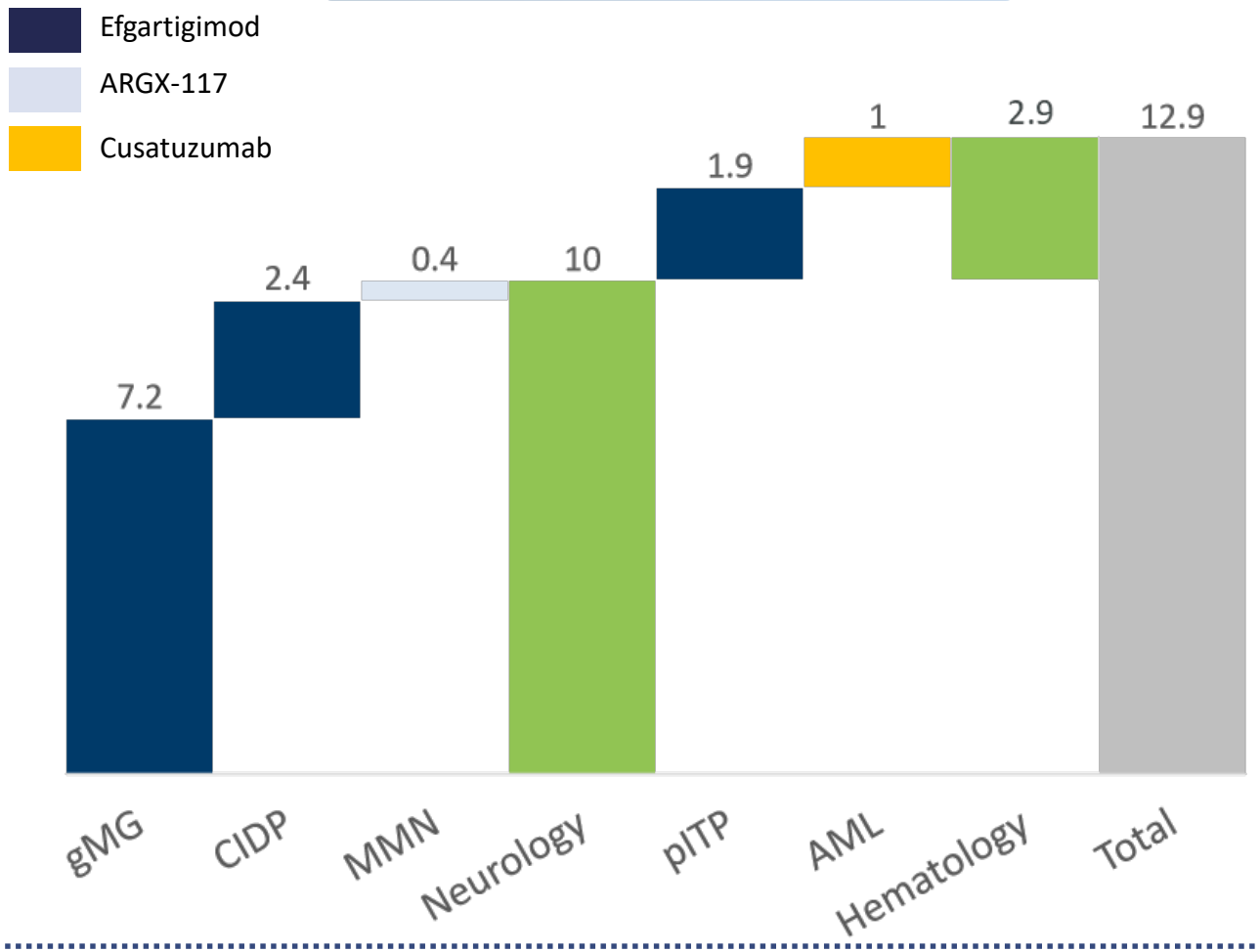
Global opportunity

- Indication prevalence comparable to US across other key geographies (EU / JP), meaning **~370,000 patients** in US / EU5 / JP for current indications
- Neurology / hematology opportunities are growing at double digit percent overall
- Will expand and announce new indications for efgartigimod and ARGX-117 [in Q1 2020]

Pipeline-in-product assets create scaling opportunity across our franchises

To add sources

Global Opportunity ($ Bn)



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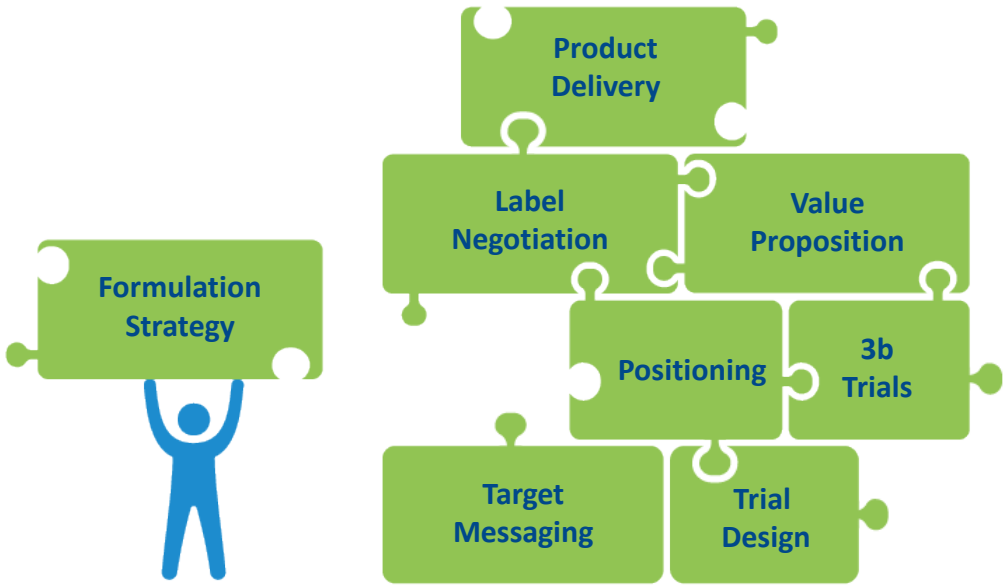
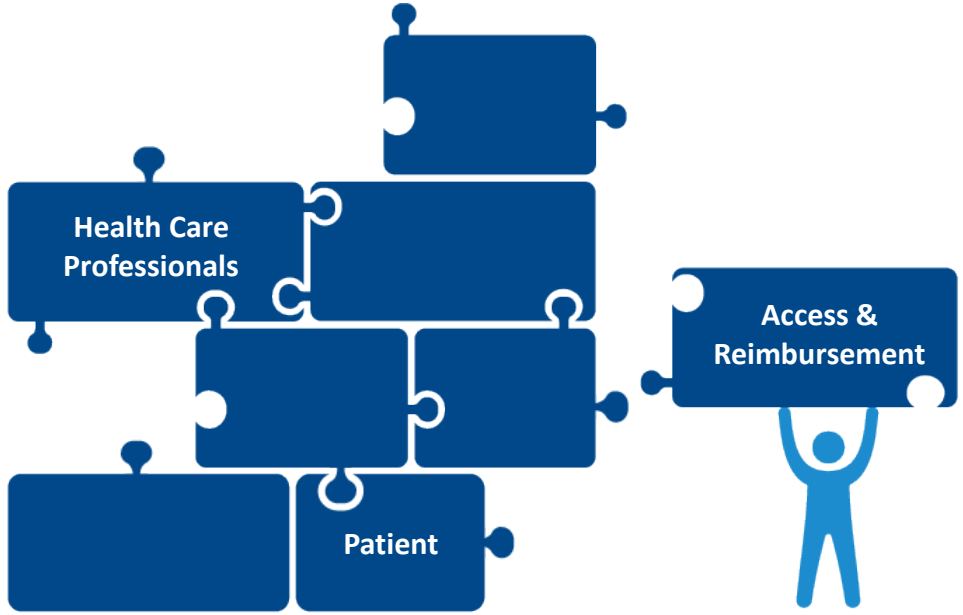
Building Efgartigmod/MG Franchises

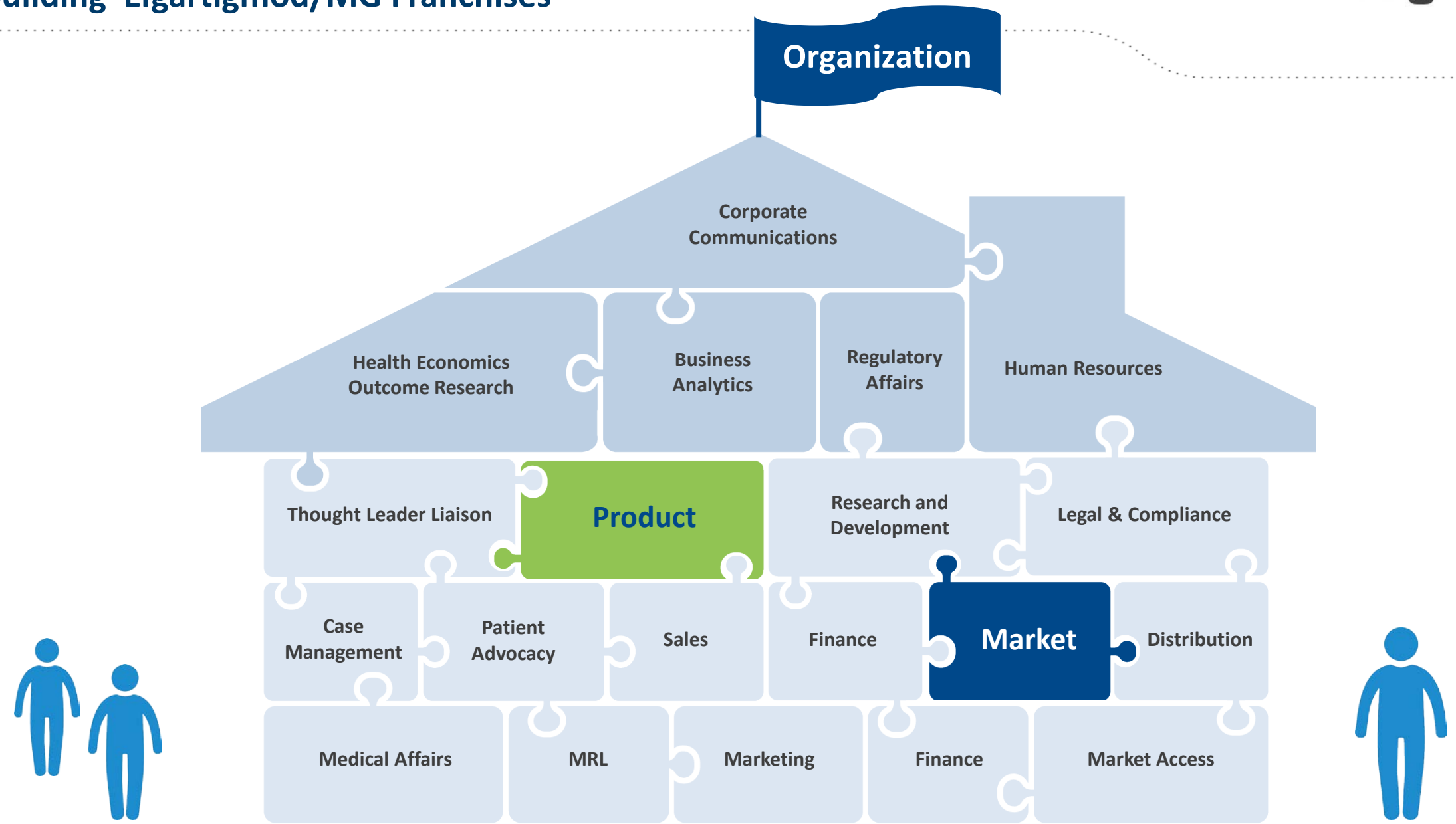
Product



Market



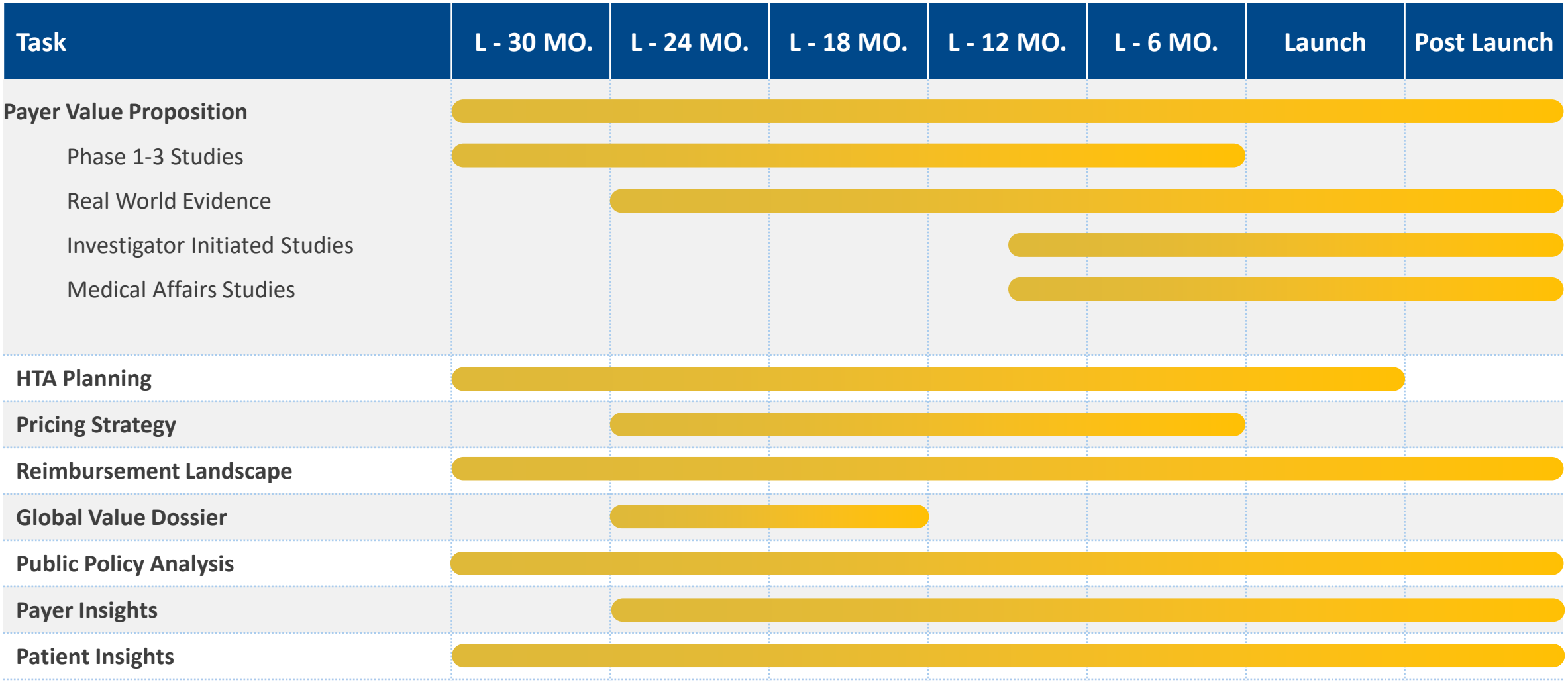
Building Efgartigmod/MG Franchises



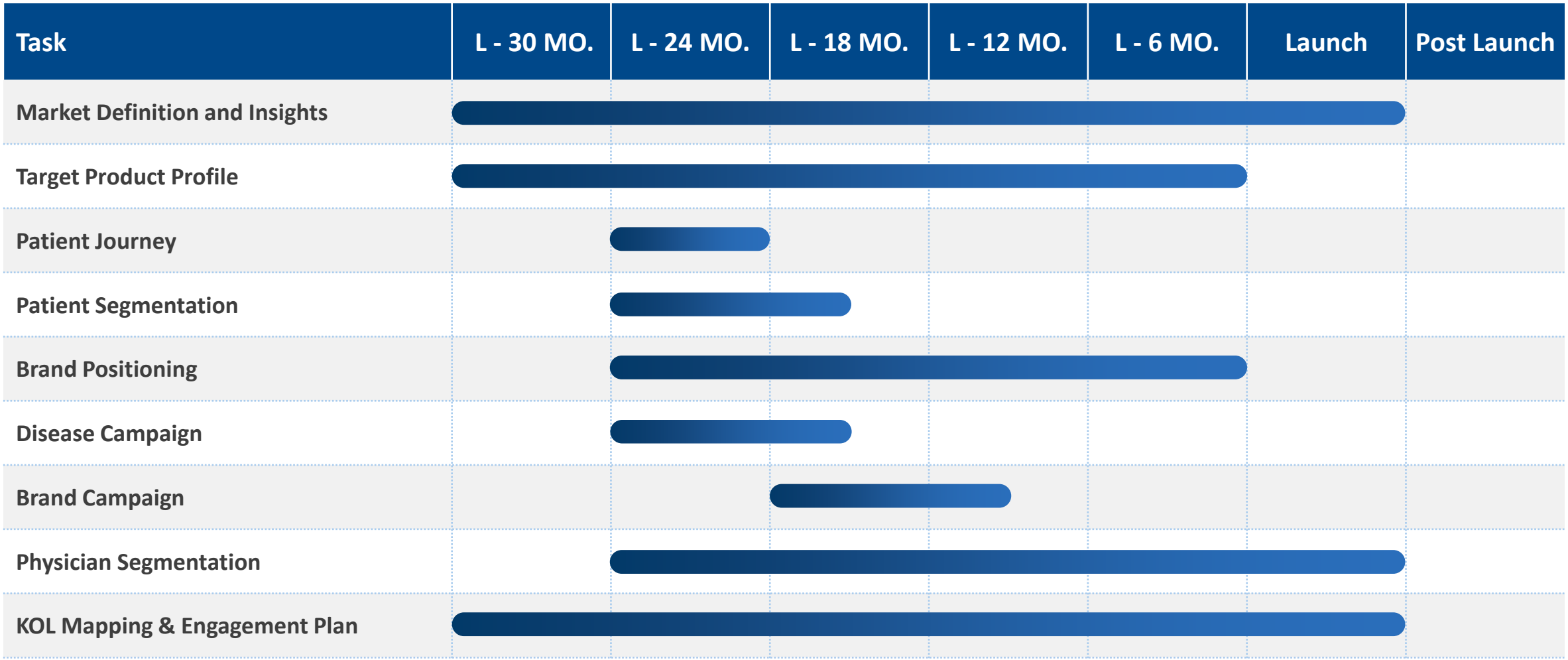
Ensuring Adequate Data and Insights

Task	L – 30+ MO.	L - 24 MO.	L - 18 MO.	L - 12 MO.	L - 6 MO.	Launch	Post Launch
Scientific Communications							
Data Gap Analysis							
Data Generation Plan							
Publication Planning & Execution							
Competitive Intelligence							
KOL Plan & execution							
Medical Research Liaison Engagement							
Congresses & Advisory Boards							
Medical Education Plan & Execution							

Ensuring Access Before the Launch



Commercial Preparation Well in Advance



Building the Right Organization

Thank you!