Development of a Pipeline of Macrocyclic Peptides for Disorders of the Complement System

6th Annual Peptides Congress

April 24, 2019, London, UK

Ra Pharma®

Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the safety, efficacy, regulatory and clinical progress, and therapeutic potential of our product candidates, including zilucoplan and PLGA XR formulation of zilucoplan, plans and timing for the presentation of clinical data, expectations surrounding the initiation of a Phase 3 clinical program evaluating zilucoplan for the treatment of gMG and timing thereof, plans and timing for entering into human clinical studies for each of zilucoplan XR and an oral small molecule inhibitor of C5, expectations surrounding the announcement of a new neuromuscular indication for zilucoplan and timing thereof, our market opportunities, the anticipated pricing of our product candidates, if approved, including zilucoplan, and management's estimates about the potential size and characteristics for the patient populations that our product candidates are targeting. All such forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include the risks that Ra Pharma's product candidates, including zilucoplan and PLGA XR formulation of zilucoplan, will not successfully be developed or commercialized, as well as the other factors discussed in the "Risk Factors" section in Ra Pharma's most recently filed Annual Report on Form 10-K, as well as other risks detailed in Ra Pharma's subsequent filings with the Securities and Exchange Commission. There can be no assurance that the actual results or developments anticipated by Ra Pharma will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, Ra Pharma. Except as noted, all information in this presentation is as of April 24, 2019, and Ra Pharma undertakes no duty to update this information unless required by law.

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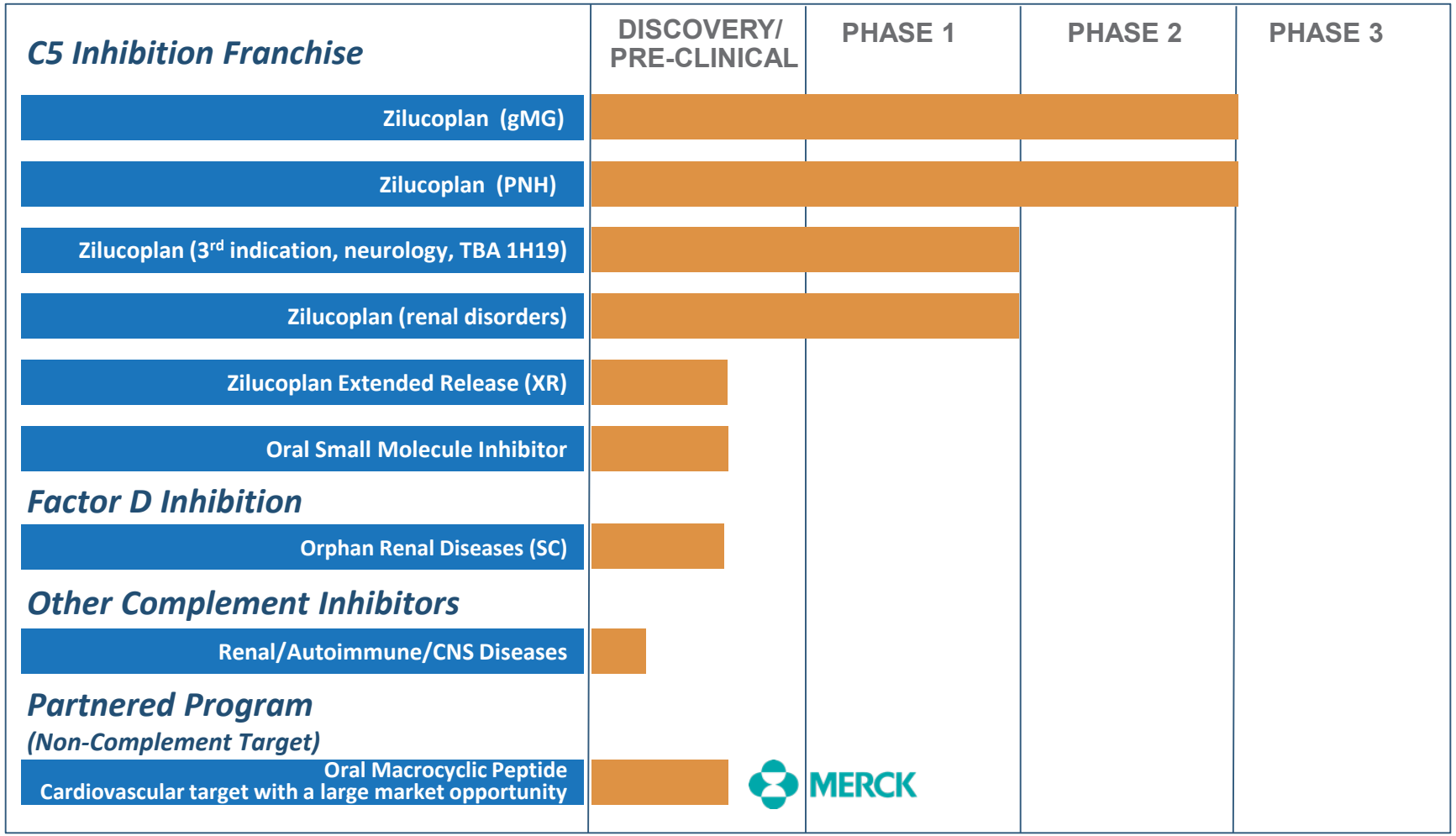
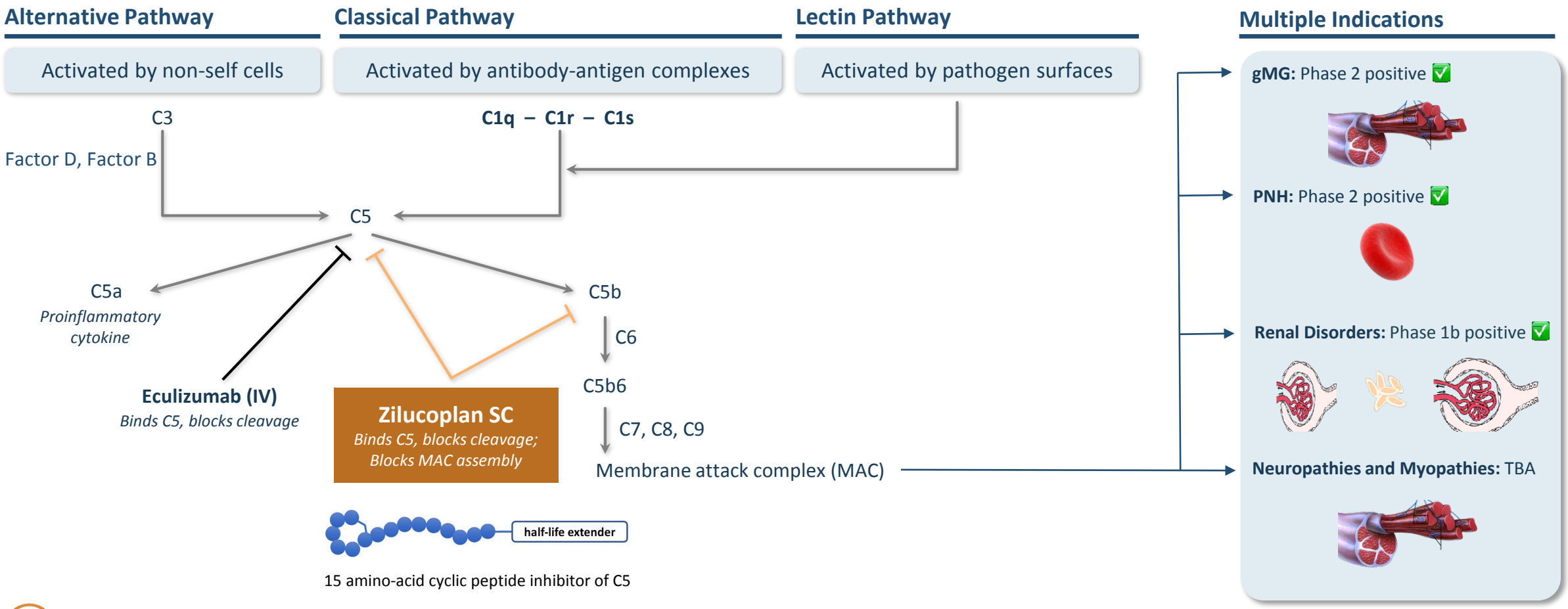
- **Focused on delivering innovative and accessible therapies to patients with rare diseases**
- **Macrocyclic / constrained peptides have "come-of-age"**
- **Zilucoplan: A convenient, self-administered, subcutaneous macrocyclic inhibitor of C5**
  - Single, pivotal, 12-week, placebo-controlled, Phase 3 clinical trial in generalized myasthenia gravis (gMG) to initiate in the second half of 2019
- **Zilucoplan extended release (XR) program**
  - Non-human primate (NHP) studies support once weekly or less frequent dosing
  - Anticipate entering human clinical studies in the first half of 2020
- **Exploiting PK/PD advantages of zilucoplan's improved tissue biodistribution compared to mAbs**
  - Small macrocyclic peptides have improved biodistribution to tissues
  - Announcing second tissue-based neuromuscular indication in the second quarter of 2019
- **Continue to leverage our proprietary drug discovery engine and expand the pipeline**
  - Oral, small molecule inhibitors of complement C5 entering human clinical studies in the first half of 2020
  - Macrocyclic peptide inhibitors of Factor D
  - Merck collaboration: Oral peptide targeting a large CV market opportunity

Pipeline Programs



Zilucoplan
A Subcutaneously Self-Administered, Macrocyclic Peptide Inhibitor of Complement C5

Multiple validated indications, pipeline-in-a-product potential



gMG – generalized myasthenia gravis; PNH – paroxysmal nocturnal hemoglobinuria

Generalized Myasthenia Gravis (gMG) Is a Rare, Debilitating, C5-Mediated Disease[1]

FREQUENCY

150-250/Million, ~60,000 (US), ~100,000 (EU), ~24,000 (JP)[2]

CAUSE

Autoantibodies block signals from nerves to muscles and complement activation destroys the neuromuscular junction[3]

DIAGNOSIS

Acetylcholine receptor antibody positive[2]

CONSEQUENCES

Serious and progressive

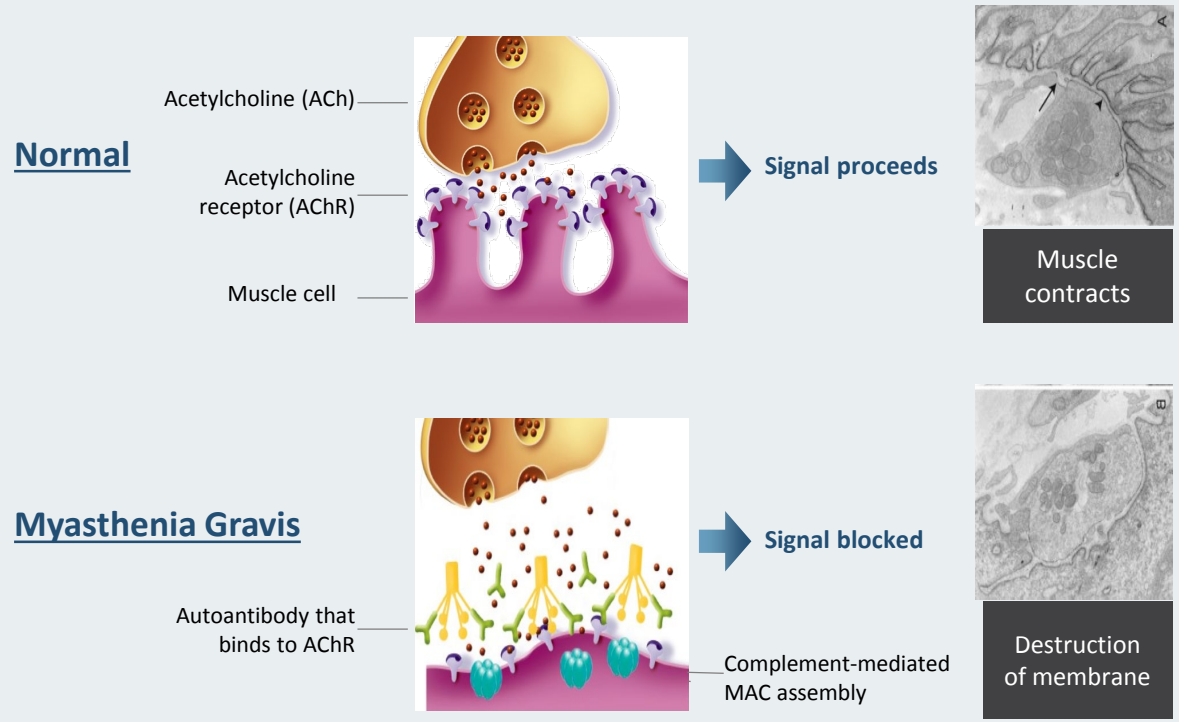
- Significantly impacts quality of life[1,2]
- ~80% progress to generalized muscle weakness[4]
- ~20% experience crisis[5]

TREATMENT

Sporadic, expensive, and often non-specific

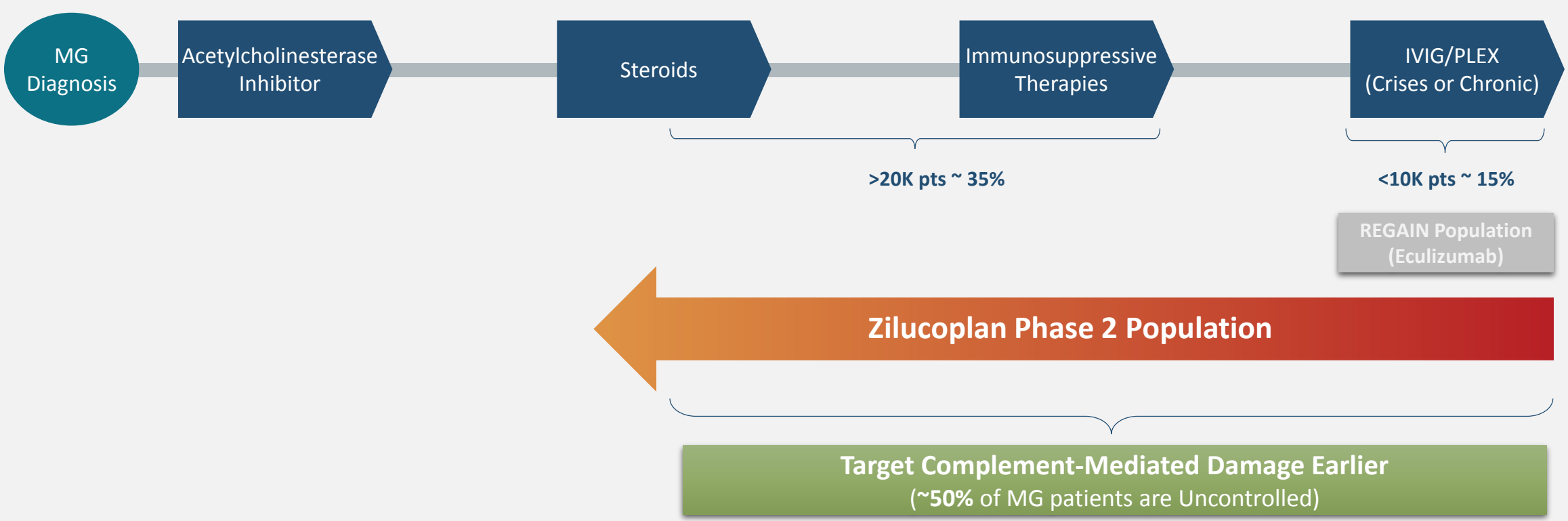
- Cholinesterase inhibitors, corticosteroids, ISTs, thymectomy
- IVIG, PLEX total maintenance costs ~$150,000[6,7] per year
- Eculizumab (Soliris®; Alexion), bi-weekly IV therapy approved in 2017[8]; ~$700,000[9]

Autoantibodies and complement-mediated destruction of the neuromuscular junction cause pathology in gMG[1,2]



References: **1.** Howard JF. Lancet Neurol. 2017;16(12):976-986. **2.** Gilhus N, N Engl J Med 2016;375:2570-812015 **3.** Conti-Fine BM. J Clin Invest. 2006; 116(11):2843-2855. **4.** Wang et al. BMC Neurology. 2017;17:77-83. **5.** Renton AE, et al. JAMA Neurol. 2015 Apr;72(4):396-404. **6.** Heatwole C, et al. J Clin Neuromuscul Dis. 2011; 13(2): 85–94. **7.** MG Cost Calculator, Data on File. **8.** Soliris® [package insert]. Alexion Pharmaceuticals Inc; revised 1/2017. **9.** Prime Therapeutics. AMCP 2018, April 23-26, Boston.

Extending Complement Inhibition to More Patients with anti-AChR Seropositive Generalized Myasthenia Gravis



US Prevalence: ~200 per million (~60K pts)

Data source: IQVIA market projections (93% retail, 1.5B LRx & Dx claims, CDM ~350 hospitals, PharMetrics health plan 150M pts)
Jan 2016 – Dec 2017 selection period (patients with at least 1 MG diagnosis claim ICD-10 G70.00 or G70.01); 5 years history for treatment and procedures (starting Jan 2013)
Applied best practice eligibility controls and apply appropriate pre-screener/end-treater rules
Used Rx/Dx intersection to project Rx and office-based treatments, and projected hospital utilization of relevant therapies (ie. IVIG, PLEX) using CDM
Segment size projected with Pharmetrics Plus data, therapy usage does not use Pharmetrics Plus; therapy analysis on steroid dosage used to allocate patients on high dose steroid to Uncontrolled

Phase 2 Study Targets Broad gMG Patient Population

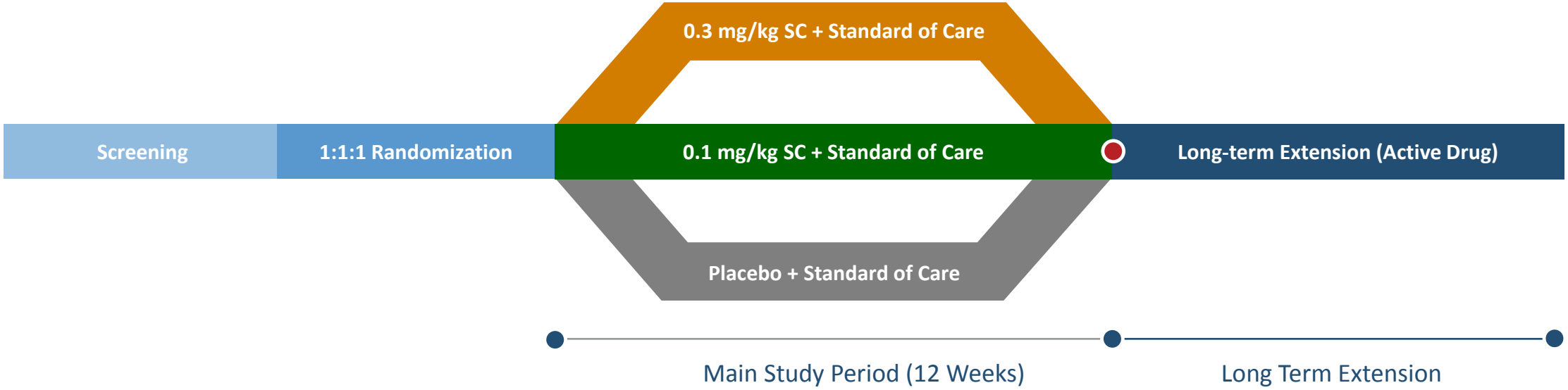
Broad Patient Population:

- Generalized MG (Myasthenia Gravis Foundation of America class II-IVa)
- AChR-antibody positive
- Quantitative Myasthenia Gravis (QMG) score of ≥ 12
- Stable doses of corticosteroids and/or immunosuppressants
- No requirement to be “refractory” or have failed multiple prior therapies

Endpoints:

- Primary: Change in QMG score from baseline to week 12
- Key Secondary: Change in MG-ADL score from baseline to week 12
- Pre-specified significance testing at 1-sided alpha of 0.1

Enrollment: 44 patients (vs. target of 36)



Randomized, double-blind, placebo-controlled, multi-center study followed by an open-label, long-term extension (LTE)

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Baseline Characteristics Confirm Breadth of gMG Study Population

Variable	Placebo (n=15)	Zilucoplan 0.1 mg/kg (n=15)	Zilucoplan 0.3 mg/kg (n=14)
Age, mean years (± SD)	48 (15.7)	46 (15.7)	55 (15.5)
Male, n(%)	4 (27%)	7 (47%)	10 (71%)
Race, n(%) • White • Asian • Black or African American	 12 (80%) 1 (7%) 2 (13%)	 13 (87%) 0 2 (13%)	 11 (79%) 1 (7%) 2 (14%)
MGFA Class at Screening • II • III • IVa	 7 (47%) 8 (53%) 0	 5 (33%) 10 (67%) 0	 5 (36%) 5 (36%) 4 (29%)
Duration of Disease, mean years (min, max)	8.0 (0.1, 20.9)	8.7 (1.6, 24.1)	8.3 (0.5, 26.0)
Baseline QMG Score, mean (± SD)	18.7 (4.0)	18.7 (4.0)	19.1 (5.1)
Baseline MG-ADL Score, mean (± SD)	8.8 (3.6)	6.9 (3.3)	7.6 (2.6)
Baseline MG Composite Score, mean (± SD)	18.7 (5.7)	14.5 (6.3)	14.6 (6.3)
Baseline MGQoL15r Score, mean (± SD)	15.9 (7.4)	19.1 (5.0)	16.5 (7.3)
Prior MG Therapies (Standard of Care) • Pyridostigmine, n(%) • Corticosteroids, n(%) • Immunosuppressants, n(%)	 14 (93%) 13 (87%) 12 (80%)	 15 (100%) 13 (87%) 12 (80%)	 14 (100%) 14 (100%) 9 (64%)
Prior IVIG, n(%)	9 (60%)	8 (53%)	10 (71%)
Prior Plasma Exchange, n(%)	7 (47%)	9 (60%)	7 (50%)
Prior Thymectomy, n(%)	5 (33%)	8 (53%)	7 (50%)
Prior MG Crisis Requiring Intubation, n(%)	3 (20%)	4 (27%)	2 (14%)

High Unmet Medical Need

Non-Refractory Patients Included

9% no prior steroids
25% no prior ISTs
39% no prior IVIG
48% no prior PLEX

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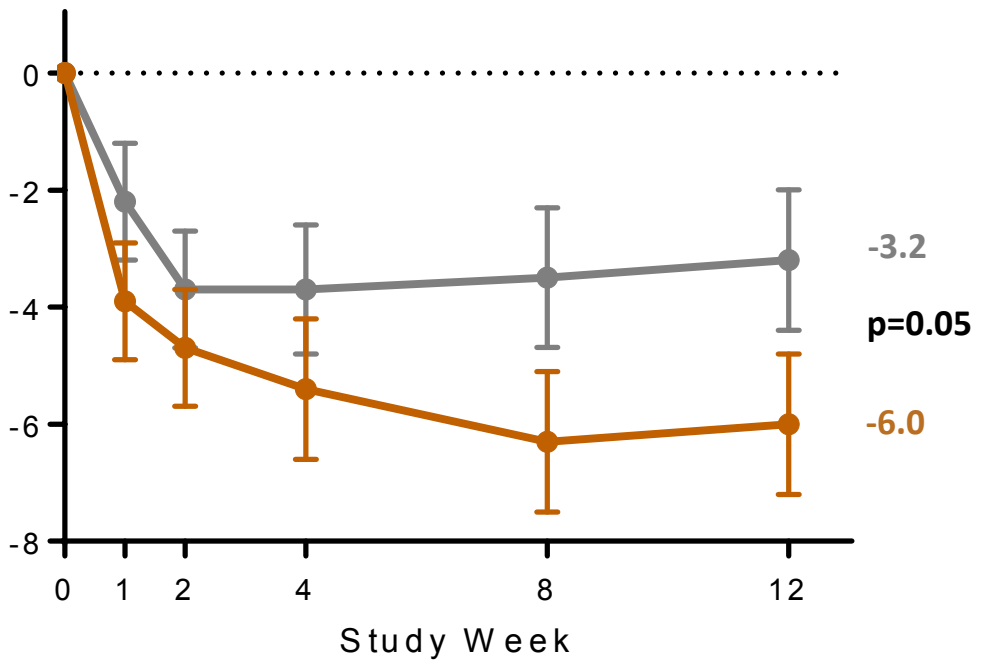
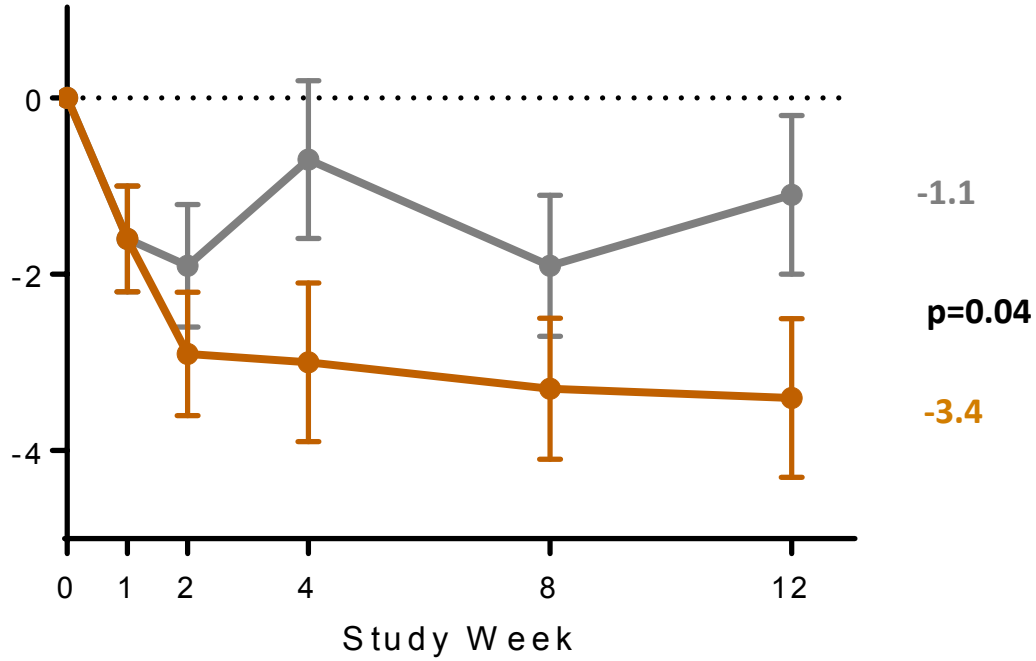
Primary and Key Secondary Endpoints Met with 0.3 mg/kg Zilucoplan Dose:
Rapid, Clinically Meaningful, and Statistically Significant Reductions in QMG and MG-ADL

Change from Baseline in QMG



Change from Baseline in MG-ADL



Placebo
0.3 mg/kg Zilucoplan

Pre-specified significance testing at 1-sided alpha of 0.1 with LOCF ANCOVA p values shown; error bars denote standard errors of least squares mean; mITT

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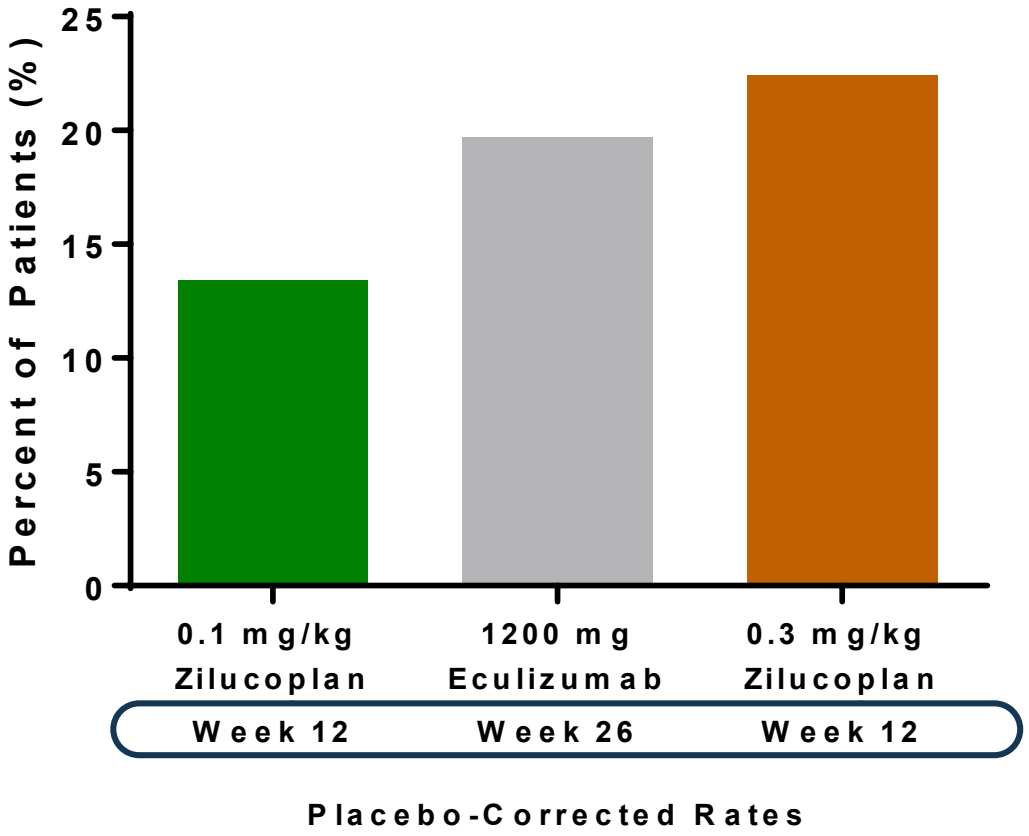
Patients Can Achieve Minimal Symptom Expression by Week 12

Minimal symptom expression (MSE) = Achieving MG-ADL score of 0 or 1



23% of patients (placebo-corrected) achieved MSE in 12 weeks in 0.3 mg/kg zilucoplan arm

*Vissing J, Jacob S, Fujita K, et al. Minimal Symptom Expression with Eculizumab in Myasthenia Gravis. AANEM 2018

Safety and Tolerability Profile Supports Continued Development

	Placebo (n=15)	Zilucoplan 0.1 mg/kg (n=15)	Zilucoplan 0.3 mg/kg (n=14)
Patients Requiring Rescue with IVIG or PLEX	**3 (20%)**	**1 (7%)**	**0 (0%)**
Patients with adverse events (AEs)	12	15	12
Patients with related AEs	3	8	3
Patients with serious AEs	3	0	5
Patients with related serious AEs	0	0	0
Patients with most common related AEs:			
Nausea	0	2	2
Injection site bruising	1	2	0
Injection site scab	0	3	0
Contusion	0	1	1
Headache	1	4	2
Patients with injection site reactions	3	4	3

No patients required rescue in 0.3 mg/kg zilucoplan arm

- No meningococcal infections
- Profile consistent with Ph1 and Ph2 PNH studies
- All 44 subjects completed 12-week study; No early withdrawals
- 42/44 subjects (95%) entered long-term extension

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MedDRA Version 20.0 Adverse Event Preferred Terms; injection site reactions defined as pain, tenderness, erythema, or induration

Zilucoplan in gMG: Phase 2 Top-Line Data Summary

- **Positive Phase 2 study in broad gMG population (not restricted to “refractory”)**
- **Primary and key secondary endpoints met with clinically meaningful and statistically significant reductions in QMG and MG-ADL in both 0.3 mg/kg and 0.1 mg/kg dose groups**
- **Magnitude and speed of effect, no rescue therapy required, and higher rate of minimal symptom expression all favor 0.3 mg/kg dose over 0.1 mg/kg dose for Phase 3**
- **Favorable safety and tolerability profile with no early withdrawals in the study; Safety and PK/PD profile consistent with Phase 1 healthy volunteer and Phase 2 PNH studies**
- **Single, pivotal, 12-week, placebo-controlled, Phase 3 clinical trial to initiate in 2H19**
- **Phase 2 data, including long-term extension data, to be presented at the 2019 American Academy of Neurology Annual Meeting, Philadelphia, PA, from May 4 to 10, 2019**

Development of Zilucoplan XR

Poly(D,L-lactic-co-glycolic Acid) (PLGA):
A Validated Delivery Platform for Peptides

- **Poly(D,L-lactic-co-glycolic acid) (PLGA)/poly (lactic acid) (PLA) microspheres/nanoparticles are one of the most successful drug delivery systems for extended release**
- **An established platform for sustained release of parenteral peptides in both adults and pediatric patients with at least 15 products available on the US market, e.g.:**
  - Bydureon® (exenatide)
  - Lupron / Lupron Depot® (leuprolide)
  - Lupron depot PED® (leuprolide)
  - Sandostatin® LAR (octreotide)
  - Trelstar® (triptorelin)
  - Risperdal Consta® (risperidone)
  - Signifor® LAR (parsireotide)
  - Zoladex® (goserelin)
- **PLGA XR formulation of zilucoplan is consistent with Ra's life-cycle extension vision to improve accessibility and simplify disease management**
  - Delivers stable concentrations of drug with once weekly or less frequent dosing
  - Single, low volume injection without requirement for on body infusion devices
  - Therapeutic concentrations of drug maintained at all times without significant fluctuation in PD
  - Potential for room temperature storage
  - Low cost-of-goods to support improved accessibility

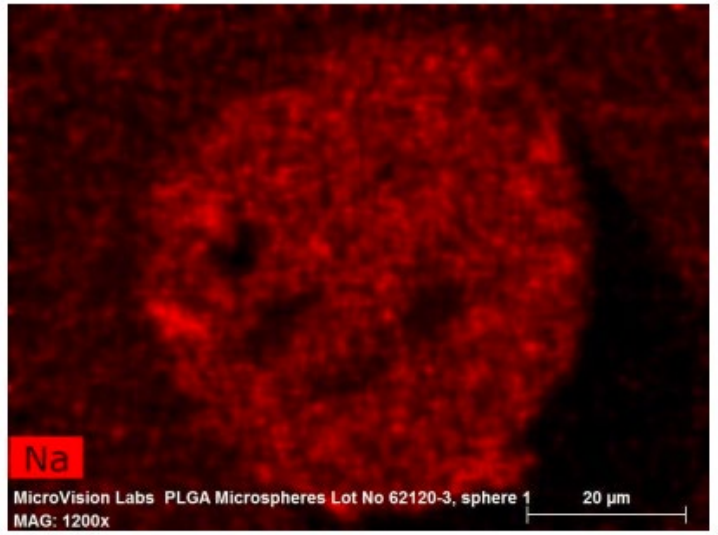
PLGA XR Formulation of Zilucoplan

Designed to Have Uniform Microsphere Morphology with High Drug Loading and Homogeneous Distribution

Zilucoplan PLGA microsphere (A) Surface morphology by scanning electron microscopy and (B) Drug distribution by Na+ Energy Dispersive X-Ray Spectroscopy*

A)

B)



Optimization of process has delivered a uniform particle with homogenous distribution of zilucoplan throughout microspheres

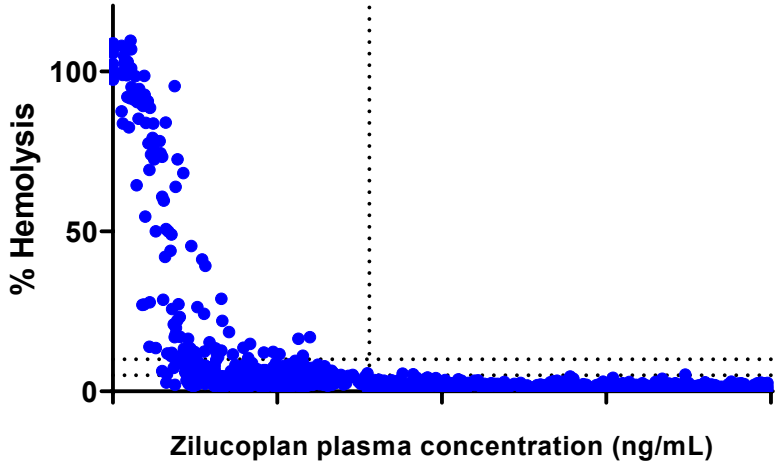
- Target drug load achieved: Morphology and size range enable good syringeability
- Homogeneous distribution of drug in particle expected to ensure predictable drug release with minimal burst (<5%)

*Data on record at Ra Pharma

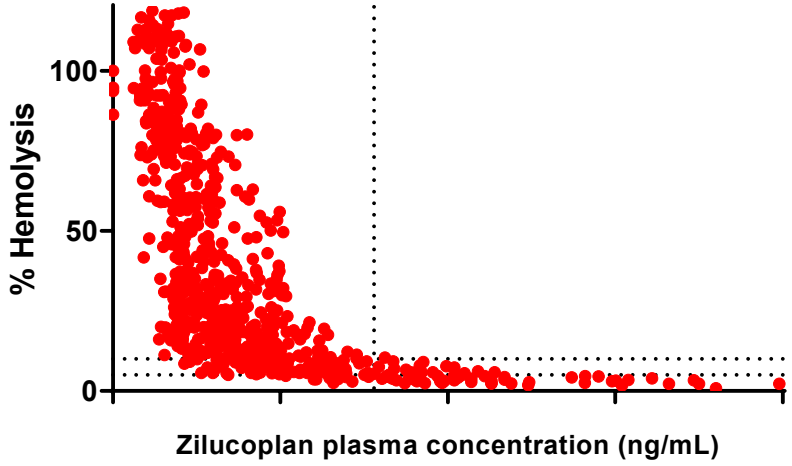
NHP and Human PK/PD
Highly Comparable Across Species

Comparable concentration dependence of complement inhibition observed in pre-clinical NHP and Phase 1 and Phase 2 human clinical studies

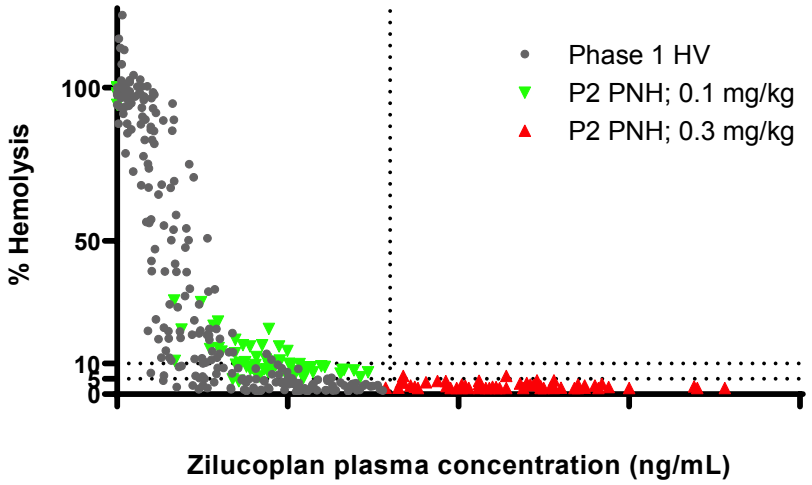
NHP PK/PD Zilucoplan Immediate Release (IR)*



NHP PK/PD Zilucoplan XR*



Human PK/PD Zilucoplan IR*



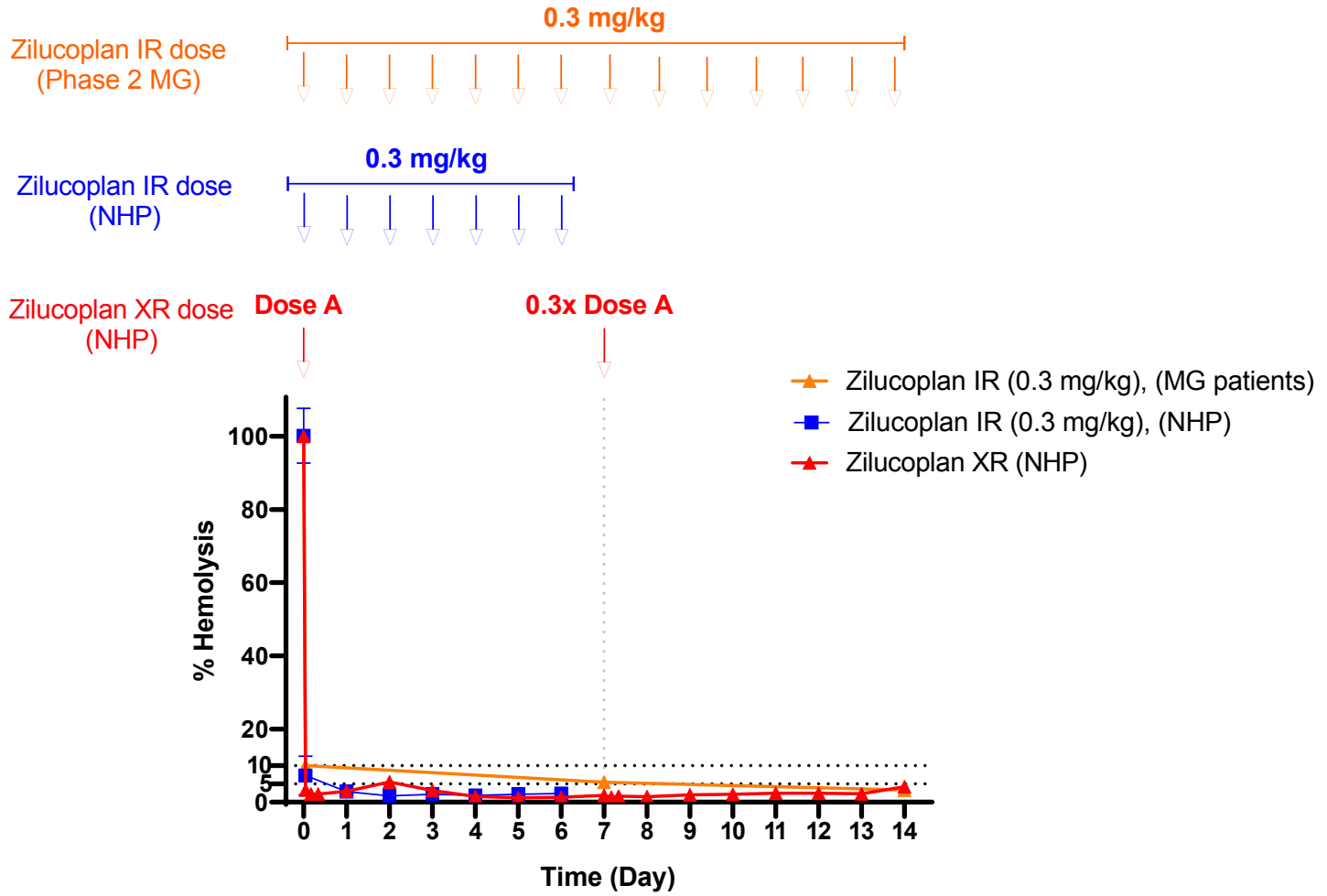
For reference across species, vertical dotted line represents clinical trough concentration for daily 0.3 mg/kg

*Data on record at Ra Pharma

Performance Comparison of PLGA XR Formulation of Zilucoplan

Once Weekly XR Rapidly Achieved Target C5 Inhibition Equivalent to Daily Administration

Comparison of PLGA XR formulation of zilucoplan Q1W PD to zilucoplan IR daily in NHP and myasthenia gravis patients

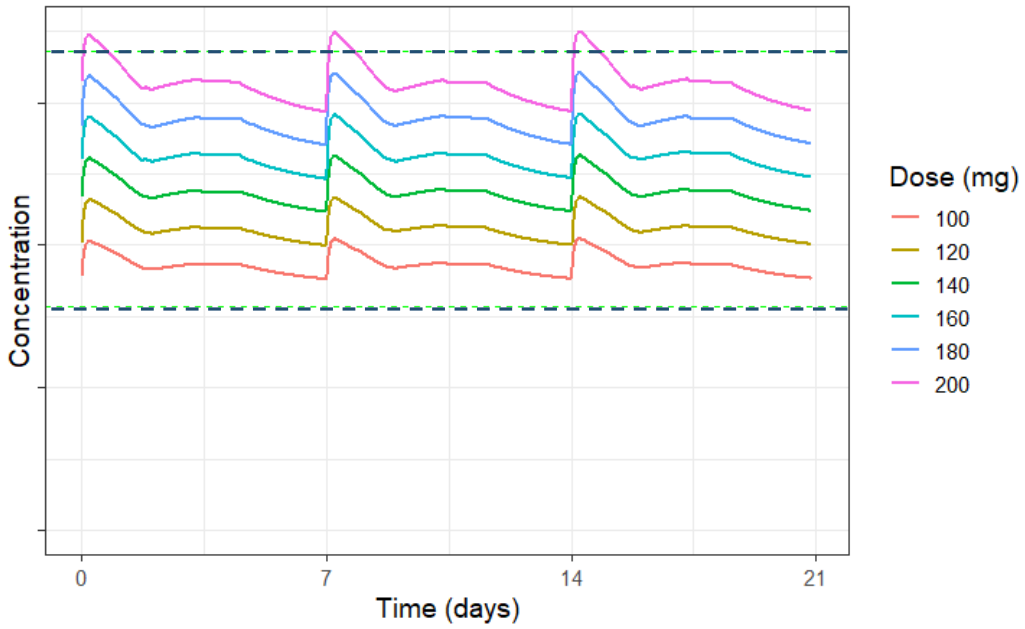


Dose-to-Man Modeling at Steady State

Release Profile of PLGA XR Formulation of Zilucoplan Q1W Indicates Potential to Deliver Meaningful Dose Efficiency

Steady state concentration range observed in Phase 2 gMG study zilucoplan IR (0.3 mg/kg)

Human Dose Projection Zilucoplan XR Q1W



Human Dose Projection

- Human target mediated drug disposition pharmacokinetic model
- Input profile based upon deconvolution of zilucoplan XR release in non-human primates
- Green dashed lines: Zilucoplan IR concentration range at steady state in Phase 2 gMG study

Model indicates XR dose of 100 mg (Q1W) has potential to maintain meaningful drug concentrations
Approximately 33% dose efficiency realized compared to 7 daily doses of immediate release product*

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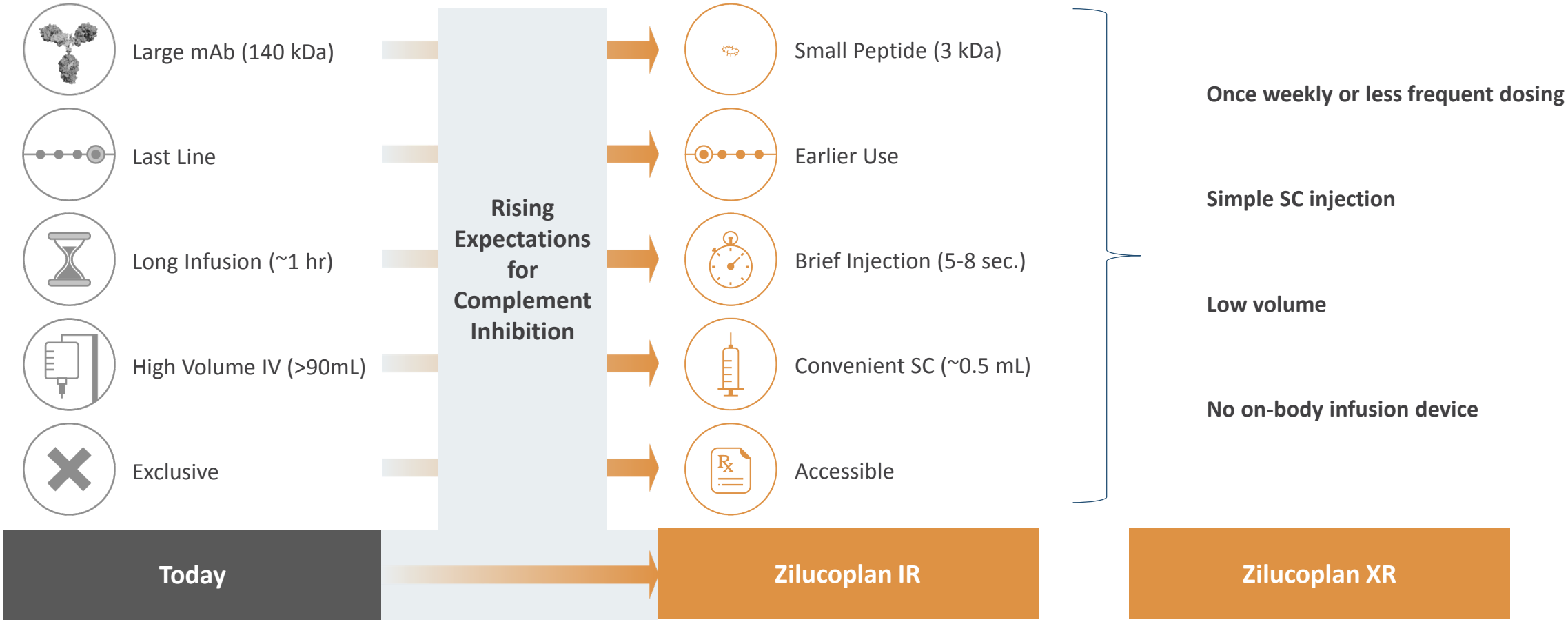
*Based on 70 kg adult and 0.3 mg/kg per day for current daily product

The Zilucoplan Life Cycle – Positioned for Success

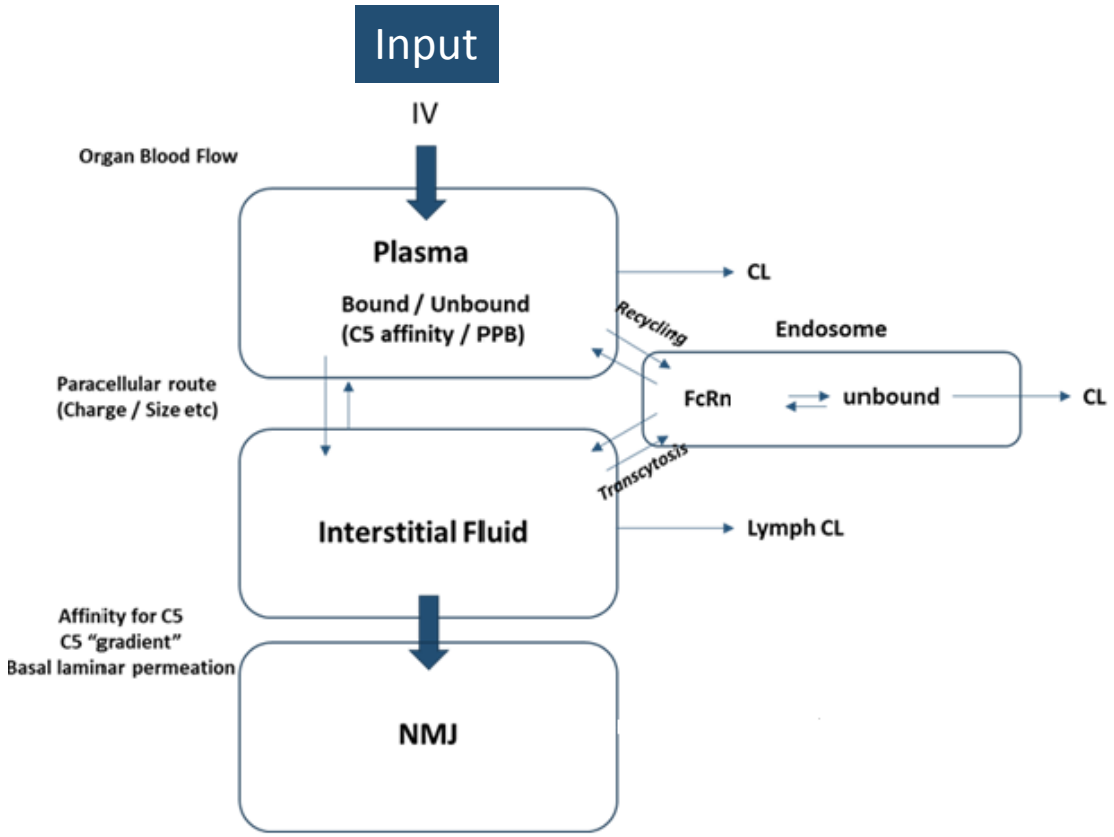


Advantages of a Peptide-Based Approach to MG and Other Tissue-Based Diseases

Rodent QWBA: Size and Biodistribution to Muscle

Zilucoplan Has Improved Biodistribution into Tissue vs. Typical mAb

	Antibody Biodistribution[1] (%)	Zilucoplan Biodistribution[2] (%)
Lung	14.9	**37.5**
Heart	10.2	**22.9**
Muscle	3.97	**7.0**
Small Intestine	5.22	**10.9**
Large Intestine	5.03	**21.7**
Spleen	12.8	**15.5**
Liver	12.1	**27.1**
Bone	7.27	**15.3**
Stomach	4.98	**8.5**
Lymph nodes	8.46	**12.8**
Fat	4.78	**16.2**
Brain	0.35	**0.9**
Pancreas	6.4	**15.8**
Testes	5.88	**15.5**
Thymus	6.62	**7.8**

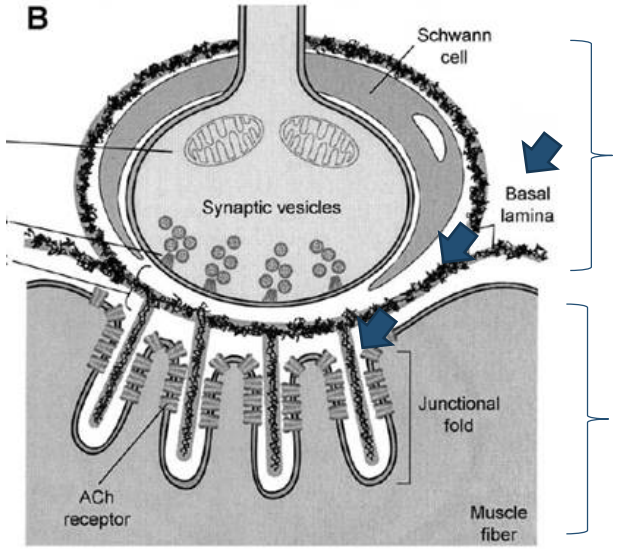


1. Shah DK, Betts AM. Antibody biodistribution coefficients: Inferring tissue concentrations of monoclonal antibodies based on the plasma concentrations in several preclinical species and human. mAbs 2013; 5:297-305
2. Ra Internal Data – Rat QWBA Study using radiolabeled zilucoplan; Data represent tissue AUC0-24 as a percentage of Plasma

Modeling Permeability Across the Basal Lamina

Zilucoplan Exhibited Improved Diffusion in Matrigel Model

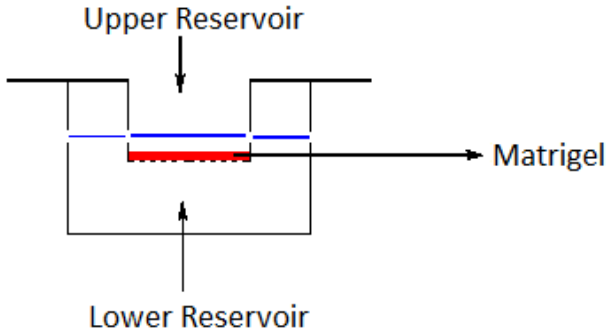
Schematic of neuromuscular junction*



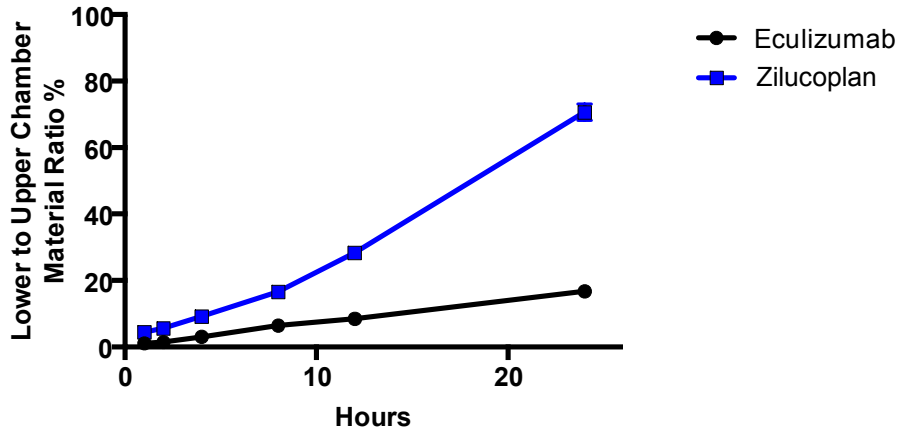
Passage of drug from interstitial fluid

Site of action

Model of basal lamina diffusion using matrigel membrane



Zilucoplan demonstrates a 4x improvement in permeability across matrigel membrane at 24 hours compared with eculizumab**



* Composition and Function of the Extracellular Matrix in the Human Body: *Biophysical Properties of the Basal Lamina: A Highly Selective Extracellular Matrix By Fabienna Arends and Oliver Lieleg. DOI: 10.5772/62519*

***Data on record at Ra Pharma*

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  - Single, pivotal, 12-week, placebo-controlled, Phase 3 clinical trial in generalized myasthenia gravis (gMG) to initiate in the second half of 2019
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- **Continue to leverage our proprietary drug discovery engine and expand the pipeline**
  - Oral, small molecule inhibitors of complement C5 entering human clinical studies in the first half of 2020
  - Macrocyclic peptide inhibitors of Factor D
  - Merck collaboration: Oral peptide targeting a large CV market opportunity