IMVT-1401 (RVT-1401), A Novel Anti-FcRn Monoclonal Antibody, Was Well Tolerated in Healthy Subjects and Reduced Serum IgG Following Subcutaneous or Intravenous Administration

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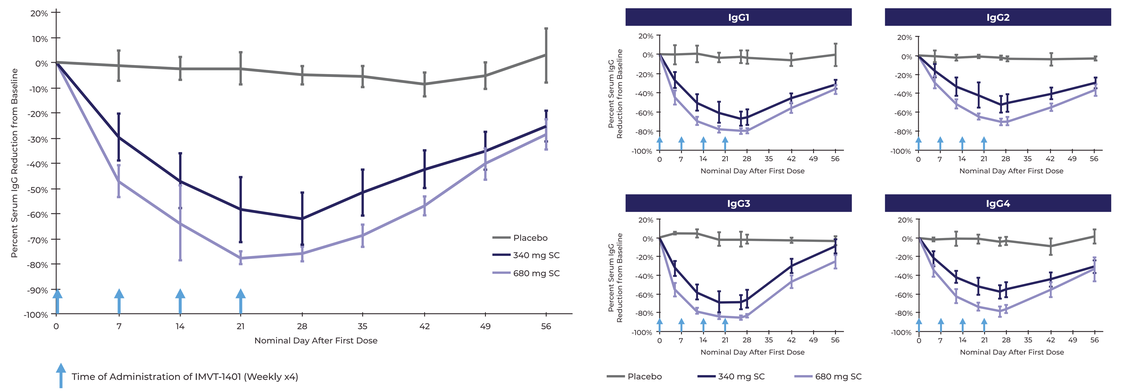
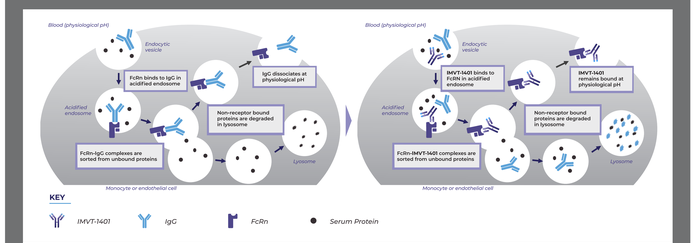
INTRODUCTION

- IMVT-1401 is a novel, fully human monoclonal antibody that selectively binds to and inhibits FcRn, and is designed for:
  - *Subcutaneous injection (SC)*
  - *Simple SC dosing schedule*
  - *Reduced immunogenicity risk*
  - *Reduced effector function*
- FcRn plays a pivotal role in preventing the degradation of IgG antibodies, thus inhibition of FcRn by IMVT-1401 is expected to lead to a reduction in levels of pathogenic IgG
- IMVT-1401 is being developed as a fixed-dose subcutaneous injection for several IgG-mediated autoimmune disorders including Myasthenia Gravis
- An ongoing study is being conducted to evaluate the safety, pharmacokinetics, and pharmacodynamics in healthy adult subjects following single and multiple doses of IMVT-1401 or placebo
- Preliminary data presented here are from this first in human study

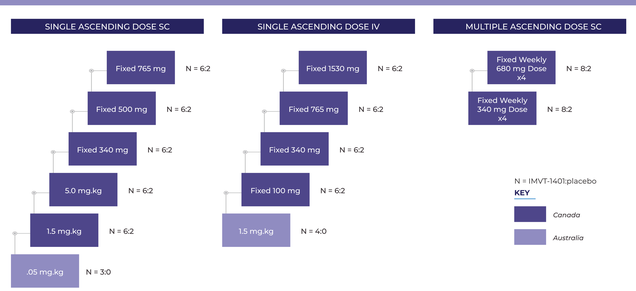
PHARMACODYNAMIC RESULTS – IgG REDUCTION



MECHANISM OF ACTION FOR IMVT-1401



STUDY DESIGN



- *Randomized double blind placebo-controlled study in healthy volunteers assessing both single and multiple doses of IMVT-1401*

PHARMACOKINETIC RESULTS

- Single dose exposures (C_{max} and AUC) following SC and IV administration increased in a non-dose proportional manner across the dose ranges evaluated
- Following subcutaneous injection of IMVT-1401, the median time to peak concentration ranged from less than a day at the lowest administered dose to ~ 3 days for the highest dose of 765 mg
- The pharmacokinetic profile of IMVT-1401 is consistent with target mediated drug disposition

PHARMACODYNAMIC RESULTS

- 680 mg weekly SC administration
  - *Average maximum IgG reduction from baseline of 78.4% (+/- 2.4)*
- 340 mg weekly SC administration
  - *Average maximum IgG reduction from baseline of 62.7% (+/- 10.7)*
- Sustained IgG reduction (≥ 35%) maintained one month beyond the last dose
- No clinically relevant changes were observed in IgM or IgA
- Dose-dependent and reversible albumin reductions were observed in the single and multiple ascending dose cohorts
  - *Reductions were not associated with any AEs or clinical symptoms*
  - *Albumin was 20% below baseline on day 28 following 4 weekly doses of 340 mg and 31% below baseline on day 28 following 4 weekly doses of 680 mg*
  - *Across both cohorts, on average, individuals were within 95% of their baseline concentration 5 weeks after the last dose*

IMMUNOGENICITY RESULTS

- In a preliminary analysis of immunogenicity, no subject in either multiple-dose cohort developed confirmed ADA to IMVT-1401 through the last sampling timepoint; 5 weeks after the last dose
- Across the single dose cohorts, 8 subjects out of 61 receiving IMVT-1401 tested positive for low levels of ADA
  - *3 of these subjects tested positive for ADA at baseline*

SAFETY RESULTS

Across all dosed cohorts of IMVT-1401 (IV & SC) the following safety observations were noted:

- IMVT-1401 has been observed to be well-tolerated with no Grade 3 or Grade 4 AEs and no withdrawals due to AEs
- AEs were mild to moderate in severity
- Most commonly reported AE has been mild erythema and swelling at the injection site, which typically resolved within hours and had a similar incidence between subjects receiving IMVT-1401 and placebo
- Other AEs reported more frequently than placebo and >5% of the pooled safety population were headaches, upper respiratory infection, oropharyngeal pain, and insomnia
- Two serious adverse events (1 appendicitis and 1 skin cancer) have been reported, neither related to study drug as determined by study investigator

TREATMENT EMERGENT AEs FOLLOWING MULTIPLE SC INJECTION

MedDRA Preferred Term	340 mg	680 mg	Placebo
	n=8	n=8	n=4
Abdominal pain	1		
Abdominal pain upper	1		
Back pain	1		
Calculus urinary			1
Chest pain	1		
Constipation	1		
Dermatitis contact		1	
Diarrhoea	2		
Dizziness			1
Dry skin		1	
Erythema		1	
Headache	2		
Hot flush		1	
Hypoaesthesia	1		
Injection site erythema	8	7	4
Injection site pain	2		1
Injection site swelling	7	6	2
Insomnia	4		
Lymphadenopathy	1		
Muscle spasms		1	
Myalgia	1	1	
Nasal congestion	1		
Nausea		1	1
Ocular hyperaemia		2	
Oropharyngeal pain	2		
Pruritus	1		
Rash		1	
Skin plaque	1		
Upper respiratory tract infection	1		

CONCLUSION

- Dosing of IMVT-1401 in this ongoing trial has been observed to be well-tolerated following both single (IV and SC) and multiple doses (SC) in healthy subjects
- IMVT-1401 rapidly lowered and maintained the reduction of total IgG and IgG subclasses following multiple SC injections
- To our knowledge, IMVT-1401 is the first anti-FcRn antibody delivered by convenient subcutaneous injection to be investigated in patients with Myasthenia Gravis (ClinicalTrials.gov Identifier: **NCT03863080**)

Disclosure Statement: *JC, LJ, CC, and RF have an equity interest in Immunovant Sciences Ltd, and are employees of, and have received personal compensation from, Immunovant, Inc., MS has received personal compensation from Altavant Sciences, Inc, PG has received personal compensation from Q-Pharm Pty Ltd, ES has received personal compensation from Algorithme Pharma Inc, SP has received personal compensation from Dermavant Sciences, Inc , LW has received personal compensation from Axovant Sciences, Inc., and JC, LJ, CC, RF, MS, SP, LW have all received personal compensation from Roivant Sciences, Inc.*