PHASE 1 EVALUATION OF THE SAFETY, ACCEPTABILITY, AND PHARMACOKINETIC PROFILE OF AN OB-002H GEL

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Background & Objective

- **OB-002** is a small recombinant protein (69 amino acid residues) analog of RANTES/CCL5, a natural ligand of the CCR5 receptor.
- **OB-002** is currently under development by Orion Biotechnology for both HIV prevention & cancer indications. Topical OB-002 prevents vaginal transmission of SHIV in a non-human primate (NHP) model of HIV infection. (Veazey & al. *JID* 2009)
- **OB-002** is best-in-class, based on functional inhibition potency, compared to other CCR5 antagonists (Maraviroc and Leronlimab/PRO-140; Figure 1A). These data are supported by strong anti-HIV potency (human PBMC; Figure 1B) & efficacy (NHP vaginal challenge; Figure 1C) data.

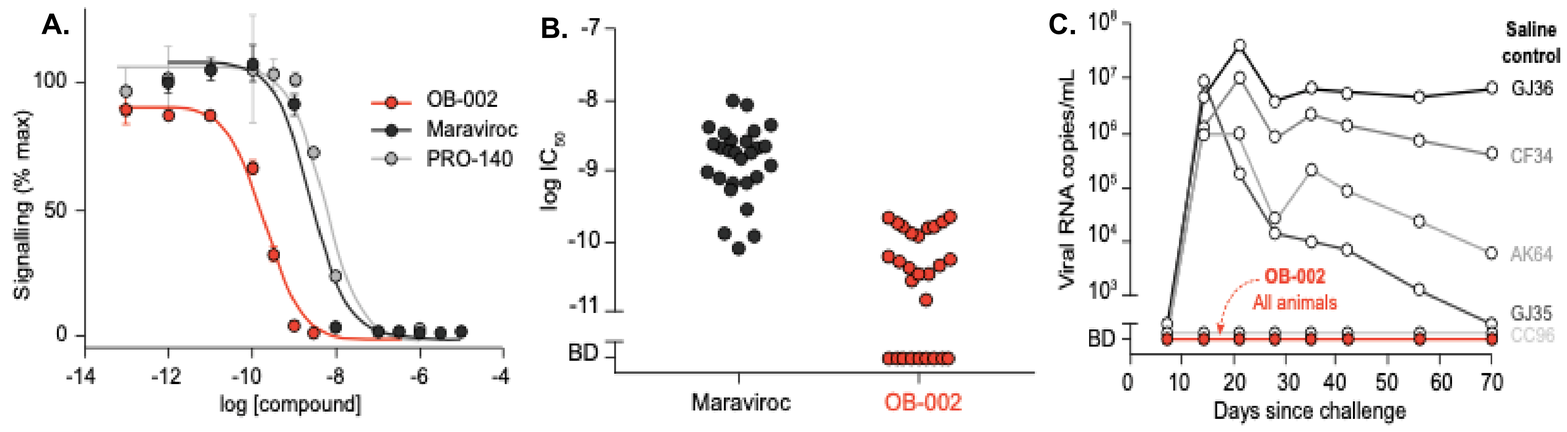

Figure 1 (A) Functional inhibition assay *in vitro*; OB-002 potency (0.2 nM) is 13-fold higher than that of Maraviroc (2.6 nM) & 28-fold higher than that of PRO-140/Leronlimab (5.6 nM). **(B)** HIV replication assay; OB-002 showed potency consistently higher than that of Maraviroc. **(C)** Positive SHIV protection in NHPs; OB-002 is fully efficacious against vaginal SHIV challenge in macaques

- In this Phase I clinical trial, we sought to characterize the safety, acceptability, and pharmacokinetic profile of a gel formulation of OB-002 (OB-002H). The study was conducted in two parts: a single-dose vaginal/rectal application (Part 1) and a randomized placebo-controlled multiple-dose vaginal application (Part 2).
- In Part 1, 12 participants were allocated to either Cohort A1 (vaginal application; N=6 women) or Cohort B1 (rectal application; N=3 women, N=3 men).
- In Part 2, 18 female participants were allocated to either Cohort A2 (N=3) or Cohort A3 (N=15). Participants of Cohort A2 received open label OB-002H gel and Cohort A3 were randomised in a 2:1 ratio to either OB-002H (N=10) or placebo (N=5) vaginal gel application.

Results: Safety & Pharmacokinetics

- The gel formulation of OB-002 was safe, well tolerated. Product-related genital adverse events were mild (Grade 1) or moderate (Grade 2) and transient.
- In Part 1, one participant experienced Grade 2 hyperkalemia which was deemed not to be related to product use.
- In Part 2, seven TEAEs were reported to be related to product use, including genital burning sensation, vulvovaginal pruritus, and vaginal discharge (all Grade 1) and vulvar disorder (Grade 2).
- Serum concentration of OB-002 was below the limit of quantification in all analysed samples at each time point, indicating that there was no systemic absorption of the gel.

System Organ Class *Preferred Term*	SINGLE-DOSE COHORTS									MULTIDOSE COHORTS												
	Cohort A1 OB-002H (N=6)			Cohort B1 OB-002H (N=6)			Total (N=12)			Cohort A2 OB-002H (N=3)			Cohort A3 OB-002H (N=10)			Cohort A3 Placebo (N=5)			Cohort A3 Total (N=15)			Total (N=18)		
	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E	n	(%)	E
Participants with at least one TEAE	1		1	0		0	1	8.3	1	0		0	4	40.0	9	0		0	4	26.7	9	4	22.2	9
Metabolism and nutrition disorders	**1**	**16.7**	**1**	**0**		**0**	**1**	**8.3**	**1**	**0**		**0**	**0**		**0**	**0**		**0**	**0**		**0**	**0**		**0**
Hyperkalaemia	1	16.7	1	0		0	1	8.3	1	0		0	0		0	0		0	0		0	**0**		**0**
Reproductive system and breast disorders	**0**		**0**	**0**		**0**	**0**		**0**	**0**		**0**	**3**	**30.0**	**7**	**0**		**0**	**3**	**20.0**	**7**	**3**	**16.7**	**7**
Genital burning sensation	0		0	0		0	0		0	0		0	2	20.0	2	0		0	2	13.3	2	2	11.1	2
Vulval disorder	0		0	0		0	0		0	0		0	2	20.0	2	0		0	2	13.3	2	2	11.1	2
Vulvovaginal pruritus	0		0	0		0	0		0	0		0	2	20.0	2	0		0	2	13.3	2	2	11.1	2
Vaginal discharge	0		0	0		0	0		0	0		0	1	10.0	1	0		0	1	6.7	1	1	5.6	1
Nervous system disorders	**0**		**0**	**0**		**0**	**0**		**0**	**0**		**0**	**2**	**20.0**	**2**	**0**		**0**	**2**	**13.3**	**2**	**2**	**11.1**	**2**
Headache	0		0	0		0	0		0	0		0	2	20.0	2	0		0	2	13.3	2	2	11.1	2

N = number of participants in the safety set
n = number of participants that experienced adverse events
E = number of adverse events

Results: Acceptability

- The majority of the feedback related to acceptability profile of the gel's consistency, feeling, and lubrication was positive.

Characteristics	Parameter	Single-Dose Cohorts			Multi-Dose Cohorts				
		Cohort A1 OB-002H (N=6) n (%)	Cohort B1 OB-002H (N=6) n (%)	Total (N=12) n (%)	Cohort A2 OB-002H (N=3) n (%)	Cohort A3 OB-002H (N=10) n (%)	Cohort A3 Placebo (N=5) n (%)	Cohort A3 Total (N=15) n (%)	Total (N=18) n (%)
Consistency	Positive opinion on gel's consistency	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	7 (70.0)	4 (80.0)	11 (73.3)	14 (77.8)
	Ease to use gel consistently based on gel's consistency	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	9 (90.0)	5 (100.0)	14 (93.3)	17 (94.4)
	Gel's consistency better relative to other lubricants	6 (100.0)	6 (100.0)	12 (100.0)	2 (66.7)	9 (90.0)	5 (100.0)	14 (93.3)	16 (88.9)
Feeling	Positive opinion on gel's feeling inside	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	9 (90.0)	5 (100.0)	14 (93.3)	17 (94.4)
	Ease to use gel consistently based on gel's feeling inside	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	9 (90.0)	5 (100.0)	14 (93.3)	17 (94.4)
	Gel's feeling inside better relative to other lubricants	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	10 (100.0)	5 (100.0)	15 (100.0)	18 (100.0)
Lubrication	Positive opinion on gel's lubrication	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	9 (90.0)	5 (100.0)	14 (93.3)	17 (94.4)
	Ease to use gel consistently based on gel's lubrication	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	10 (100.0)	5 (100.0)	15 (100.0)	18 (100.0)
	Gel's ability to provide better lubrication relative to other lubricants	6 (100.0)	6 (100.0)	12 (100.0)	3 (100.0)	9 (90.0)	5 (100.0)	14 (93.3)	17 (94.4)

- The majority of participants confirmed their willingness to use the gel against HIV, pregnancy, or both.

Characteristics	Parameter	Single-Dose Cohorts			Multi-Dose Cohorts				
		Cohort A1 OB-002H (N=6) n (%)	Cohort B1 OB-002H (N=6) n (%)	Total (N=12) n (%)	Cohort A2 OB-002H (N=3) n (%)	Cohort A3 OB-002H (N=10) n (%)	Cohort A3 Placebo (N=5) n (%)	Cohort A3 Total (N=15) n (%)	Total (N=18) n (%)
HIV protection	Likely usage for protection against HIV infection	4 (66.7)	4 (66.7)	8 (66.7)	2 (66.7)	7 (70.0)	3 (60.0)	10 (66.7)	12 (66.7)
Pregnancy protection	Likely usage for protection against pregnancy	3 (50.0)	5 (83.3)	8 (66.7)	2 (66.7)	5 (50.0)	3 (60.0)	8 (53.3)	10 (55.6)
HIV and pregnancy protection	Likely usage for protection against pregnancy and HIV infection	3 (50.0)	5 (83.3)	8 (66.7)	2 (66.7)	7 (70.0)	3 (60.0)	10 (66.7)	12 (66.7)

Participants were provided with a placebo gel applicator and encouraged to inspect the applicator and dispense a sample of placebo gel in order to make an informed assessment on the acceptability of the gel characteristics

Conclusions & Outlook

- The gel formulation of OB-002 was safe, well tolerated, and product-related genital adverse events were mild (Grade 1) or moderate (Grade 2) and transient.
- The majority of participants expressed satisfaction with the product and the intent to use an OB-002H gel for prevention of HIV infection if the gel was available.
- There was no evidence of systemic absorption of OB-002 following single or multiple vaginal/rectal OB-002H gel administration.
- Further trials will be necessary to evaluate the safety and pharmacokinetic profile of rectal administration, as well as the optimal dosage for rectal and vaginal administration of OB-002H.

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