

Supplemental Tables:

Supplemental Table 1. Properties of the FSHR ligands used.

Property of FSHR agonist	rh-follitropin- α	TOP5300	rh-follitropin- α /TOP5300
Molecular weight	24,000	580	41.4
Glycosylation termini	Sialic acid	None	-
Half-life in rodent	2-6 hr	5.5 hr	0.8
CHO-FSHR EC50	12 pM	9 nM	0.001

Supplemental Table 2. Patient characteristics.

Category	Normal Ovarian Reserve	Polycystic Ovarian Syndrome	Advanced Reproductive Age
Age	31.12	32.42	37.88
Anti-Mullerian Hormone	4.31	6.97	2.61*
Antral follicle count (AFC)	18.13	24.5	12.47*
Follicular fluid volume (mL)	69.38	121.58*	73.25
Number of oocytes retrieved	15.38	29.08	13.88
n	8	12	17

*p <0.05, paired t-test

Note: The 4 additional patients not listed in this table fell under the "other" category that included more than one diagnosis such as PCOS and ARA.

Supplemental Table 3. Cycle characteristics.

Patient	Diagnosis	Age	AMH	AFC	Cycle Type	rh-FSH (IU)	urinary FSH	Menopur (IU Menotropin)	GnRH Antag	Estrace Prim	Lupron micrc	Omnitrope	Other	Trigger Shot	Fluid Vol (ml)	Number of C	Pregnant	
1	NOR	29	5.73	11	GnRH Antag		1,350		1,350	1,250				Lupron + 3300 hCG	60	11	Y	
2	NOR	31	5.89	12+	GnRH Antag	2,625		1,350		1,000				Lupron + 3300 hCG	30	6	Y	
3	NOR	32	3.23	16	GnRH Antag		4,125		2,475	1,000				10k hCG	100	14	-	
4	NOR	32	2.28	23	GnRH Antag	2,175		1,200		1,250				Lupron + 3300 hCG	35	10	N	
5	NOR	33	4.36	19	GnRH Antag	2,925		1,425		1,500				Lupron + 3300 hCG	110	27	-	
6	NOR	33	6.8	22	GnRH Antag	2,250		750		1,250				Double Lupron	80	25	-	
7	NOR	34	2.4	16+	GnRH Antag		2,475		1,650	2,000				Lupron + 3300 hCG	50	14	Y	
8	NOR	25	3.77	26	GnRH Antag	1,875		1,650		1,500				Lupron + 3300 hCG	90	16	-	
9	ARA	39	1.53	1	GnRH Antag	5,475		1,950		1,250			X	Low dose hCG	Double Lupron	125	16	Y
10	ARA	35	1.008	7	GnRH Antag		2,400		2,400	1,000				10k hCG	50	8	-	
11	ARA	39	4.9	20	GnRH Antag		4,410		1,575	1,250				Lupron + 3300 hCG	80	9	N	
12	ARA	36	7.138	18	GnRH Antag		1,500		675	750				Double Lupron	170	26	Y	
13	ARA	35	1.75	9	Lupron Micrc	3,000		3,000				X	X	10k hCG	65	14	Y	
14	ARA	40	0.68	13	GnRH Antag		4,500		1,500	1,000	X			Clomid	10k hCG	22	3	-
15	ARA	39	1.7	5	GnRH Antag		5,850		1,950	1,250	X		X	10k hCG	90	14	Y	
16	ARA	41	2.9	16+	GnRH Antag		1,800		1,800	1,000				Lupron + 3300 hCG		12	Y	
17	ARA	36	1.18	15	GnRH Antag	3,150		2,025		750				10k hCG	80	10	Y	
18	ARA	38	2.48	13	GnRH Antag	4,275		2,700		1,250			X	10k hCG	64	22	Y	
19	ARA	40	1.47	15	GnRH Antag		5,400		2,550	1,250	X		X	10k hCG	35	6	-	
20	ARA	38	4.37	22	GnRH Antag	2,700		1,350		1,250				Lupron + 3300 hCG	70	17	Y	
21	ARA	37	1.6	6	Lupron Micrc	1,800		600			X	X		10k hCG	40	9	-	
22	ARA	44	1.26	5	GnRH Antag	2,700		1,350		1,000				Lupron + 5k hCG	60	11	-	
23	ARA	37	4.46	14	GnRH Antag	3,525		1,500		1,000				Lupron + 3000 hCG	72	20	Y	
24	ARA	35	1.3	16	GnRH Antag	2,400		1,200		1,000				Lupron + 3000 hCG	78	15	-	
25	ARA	35	4.57	17	GnRH Antag	3,825		1,650		1,250				Lupron + 3000 hCG	71	24	-	
26	PCOS	32	4.06	33	GnRH Antag	3,075		2,100		1,500		X		Lupron + 3300 hCG	150	34	-	
27	PCOS	34	4.15	21	GnRH Antag	1,200		975		1,000				Lupron	132	23	-	
28	PCOS	32	6	20+	GnRH Antag		1,500		825	1,000				Lupron	92	36	Y	
29	PCOS	31	8.08	20+	GnRH Antag	1,425		1,275		750				Low dose hCG	Lupron + 1500 hCG	250	56	-
30	PCOS	33	10.4	28	GnRH Antag	900		525		1,000				Lupron + 3000 hCG	100	15	-	
31	PCOS	32	4.56	25	GnRH Antag	3,000		1,350		1,250				Lupron + 3000 hCG	90	28	Y	
32	PCOS	32	6.31	11+	GnRH Antag	2,775		1,500		1,500				Lupron + 3300 hCG	50	16	-	
33	PCOS	34	6.54	21	Lupron Microflare		2,625		2,625		X	X		10k hCG	100	14	N	
34	PCOS	32	>16	40+	GnRH Antag	1,800		1,500		1,250				Low dose hCG	Lupron + 4800 hCG	200	82	N
35	PCOS	34	2.27	22	GnRH Antag	3,000		1,800		1,000				10k hCG	120	10	-	
36	PCOS	30	11.59	45	GnRH Antag	2,250		2,475		1,000				Double Lupron	100	25	Y	
37	PCOS	33	3.72	8 (one ovary)	GnRH Antag	2,475		2,475		1,250				10k hCG	75	10	Y	
38	Other	36	6.78	29	GnRH Antag		2,475		825	1,250				Lupron + 3300 hCG	185	26	Y	
39	Other	37	7.96	11	GnRH Antag	1,200		600		1,250				Lupron + 3300 hCG	85	17	-	
40	Other	39	4.04	26	GnRH Antag		3,000		1,800	1,250		X		10k hCG		11	N	
41	Other	26	1.06	13	GnRH Antag	2,850		1,350		1,000				10k hCG	40	6	-	

Supplemental Table 4. Progesterone concentrations in conditioned media after 48 hr culture with vehicle, rh-FSH or TOP5300.

Trigger	Compound concentration (nM)	Mean Progesterone [ng/mL] (+/- SEM)
10,000 IU hCG	FSH-100	2.49 (0.75)
	FSH-20	1.59 (0.44)
	FSH-4	1.76 (0.44)
	FSH-0.8	1.57 (0.40)
10,000 IU hCG	TOP-400	4.72 (1.58)
	TOP-80	4.62 (1.5)
	TOP-16	2.30 (0.62)
	TOP-3.2	1.72 (0.39)
Lupron + 3300 IU hCG	FSH or TOP-100	>40.0 (UL)
	FSH or TOP-20	>40.0 (UL)
	FSH or TOP-4	>40.0 (UL)
	FSH or TOP-0.8	>40.0 (UL)

UL: Progesterone concentrations were beyond the upper limit of detection in these samples, and insufficient sample was left to repeat assay.

Note: for only progesterone determinations, samples were exposed to high ambient temperatures during shipment due to logistical errors of shippers during COVID-19 pandemic.