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A Phase 1 Study of FPA008, an Anti-Colony Stimulating Factor 1 Receptor (anti-CSF1R) Antibody in Subjects with Rheumatoid Arthritis (RA): Preliminary Results

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Background/Purpose:FPA008 is a humanized IgG4 anti-CSF1R antibody that blocks the binding of CSF1 and IL34 ligands to CSF1R, resulting in inhibition of the activation and survival of inflammatory macrophages and osteoclasts, thus providing a potential therapeutic benefit in RA. Data from healthy volunteers in this 3-part Phase 1 study were reported previously (***J Hambleton et al., ACR Annual Meeting 2014***). Here, we report preliminary results from Part 3 in RA pts.

Methods: Part 3 consists of open-label dose escalation and randomized portions. In the open-label portion, FPA008 is being evaluated at 1, 3, and 6 mg/kg IV every 14 days for 2 or 3 doses. Three to 9 RA pts without adequate response to biologic or nonbiologic disease modifying anti-rheumatic drugs (DMARDs) are treated in each dose cohort. All pts are required to be on stable dose methotrexate (MTX) during the study. ACR 20/50/70, EULAR responses as well as change in DAS 28 from baseline and MRI are assessed at wks 4 and 12. The randomized portion will be based upon the open-label results.

Results: As of May 13, 2015, 3 pts each were treated with FPA008 at 1 or 3 mg/kg for 2 doses. The median age was 59, ranging from 53 to 66 yrs old. Five were female and one was male. No pts had prior biologic DMARDs. Median MTX dose was 17.5 mg, ranging from 10 mg to 25 mg wkly with 3 pts requiring methylprednisolone 2 to 4 mg daily. All 3 pts receiving 1 mg/kg completed the study (through Study Day 141) and all 3 pts receiving 3 mg/kg completed the Study Day 85 visit. Reduction in CD14+CD16++ nonclassical monocytes were observed as expected. Reported treatment-related AEs were periorbital edema/eyelid edema in the 3 mg/kg cohort and all were self-limiting. Expected, reversible dose-dependent asymptomatic elevations of AST, ALT, LDH and CK were noted, but not associated with abnormalities in total bilirubin, troponin, aldolase or EKGs.

Preliminary efficacy data are reported below:

FPA008 Dose Cohort		Day-1	Week 4					Week 12				
Dose regimen	Subjects	DAS28CRP	ACR 20/50/70	ACR hybrid	EULAR	DAS28CRP	DAS28 change	ACR 20/50/70	ACR Hybrid	EULAR	DAS28CRP	DAS28 change
1 mg/kg x 2 doses	3101	3.44	0	-5.14%	no	3.74	-0.31	0	-6.00%	no	3.83	-0.39
	3102	4.35	0	11%	moderate	3.26	1.09	0	6.29%	moderate	3.22	1.13
	3103	7.06	ACR50	52.86%	moderate	3.87	3.19	ACR50	53.86%	moderate	5.22	1.83
3 mg/kg x 2 doses	3104	4.17	ACR 20	49.99%	good	2.94	1.23	0	19.99%	moderate	3.55	0.62
	3105	5.40	0	19.99%	good	2.28	3.12	0	8.57%	moderate	4.44	0.96
	3106	4.50	0	-1.43%	no	4.13	0.37	0	8.71%	moderate	3.73	0.77

Conclusion: FPA008 was well tolerated up to 3 mg/kg in RA pts with no new safety signals. Dose escalation is ongoing. Updated safety, PK/PD and preliminary efficacy from open-label dose escalation will be presented.