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Abstract No. 2225

COVA322: A Novel, Bispecific Tumor-Necrosis-Factor-Alpha / Interleukin-17A (TNF/IL-17A) Inhibitor With Excellent Pharmacokinetic Properties In Mice and Cynomolgus Monkeys

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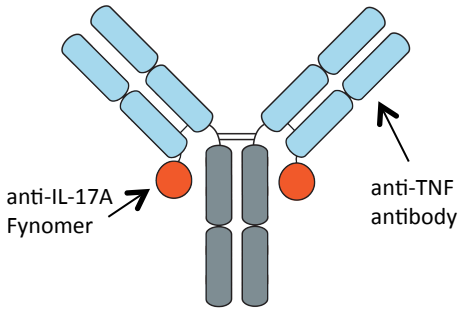
INTRODUCTION

Fynomers are small binding proteins (7 kDa) derived from the fully human Fyn SH3 domain that can be engineered to bind to any target antigen of interest (1). In addition, Fynomers can be fused to any antibody to provide bispecific fusion proteins (FynomAbs) with enhanced activity compared to the unmodified antibody.

COVA322 is a bispecific anti-TNF/IL-17A FynomAb, consisting of the anti-IL-17A Fynomer B6 fused to the C-terminus of the light chain of a fully human anti-TNF antibody:



COVA322 Properties:

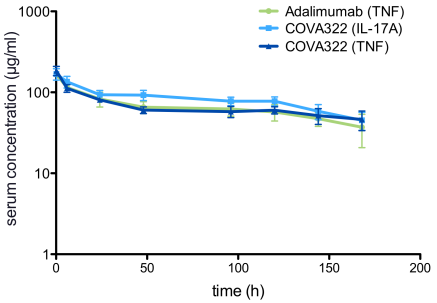
- High expression yields (3.3 g/l obtained from 1000 liter GMP run)
- COVA322 is highly stable
- In vivo half-life as unmodified antibody
- IND/IMPD enabling primate toxicology study: No clinical signs observed

Ref: (1) Grabulovski D . et al. (2007) *J Biol Chem* 282 (5): 3196-3204

RESULTS

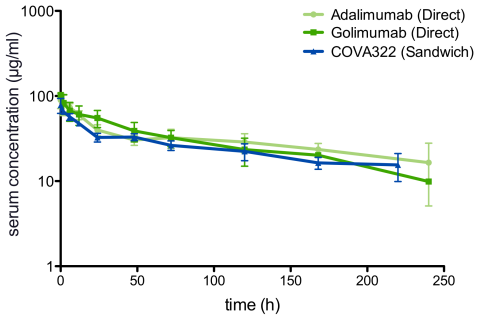
Pharmacokinetic Properties In Mice:

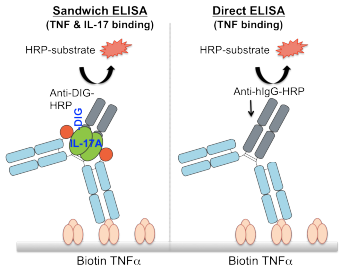
COVA322 Has Comparable Serum Concentrations as The TNF Inhibitor Adalimumab In Mice



Serum concentrations of COVA322 and the anti-TNF antibody control Adalimumab at different time-points after a single i.v. injection at a dose of 10 mg/kg into C57Bl/6 mice (n=5). For COVA322, concentration in serum was determined by ELISA using both TNF and IL-17A as capturing agents (indicated in brackets).

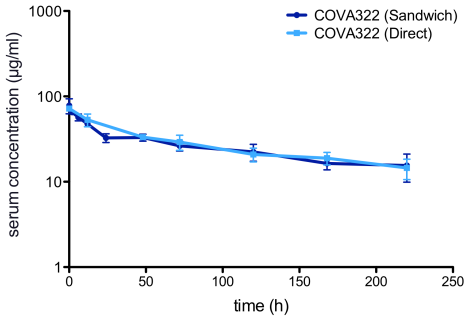
COVA322 Has Comparable Serum Concentrations as TNF Inhibitors In Cynomolgus Monkey

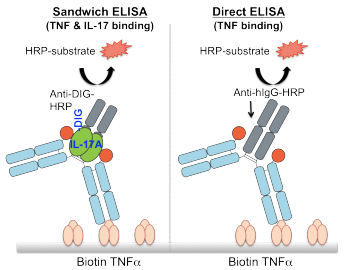




Serum concentrations of COVA322 and the anti-TNF control antibodies Adalimumab and Golimumab at different time-points after a single i.v. injection (3 mg/kg) into cynomolgus monkeys (n=3).

COVA322 Stays Intact In Cynomolgus Monkeys For At Least 10 Days





Serum concentrations of COVA322 in cynomolgus monkeys determined by Sandwich ELISA and Direct ELISA. The determined serum concentrations are comparable for both detection methods, indicating that COVA322 is stable in cynomolgus monkeys for at least 10 days.

CONCLUSION

These encouraging preclinical results indicate that COVA322 has highly promising pharmacokinetic properties. Through its unique mode-of-action of inhibiting simultaneously TNF and the IL-17A/A homodimer, COVA322 has game changing potential in the treatment of inflammatory diseases and is anticipated to enter clinical trials in Q1/2014.