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# COVA322: Overcoming Limitations Of Current Biologics In Rheumatoid Arthritis By a Novel, Bispecific Tumor-Necrosis-Factor-Alpha / Interleukin-17A (TNF/IL-17A) Inhibitor Moving Towards The Clinic

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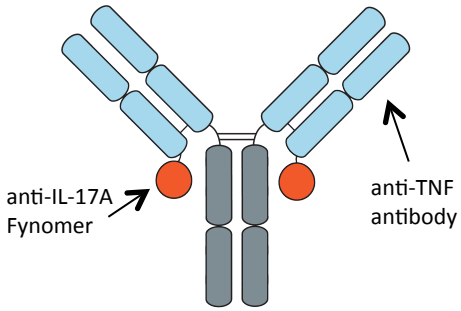
## INTRODUCTION

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:**

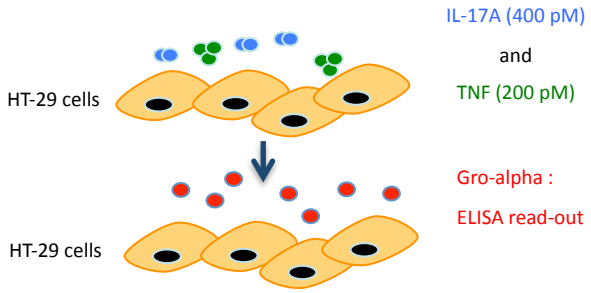
- High expression yields (3.3 g/l obtained from 1000 liter GMP run)
- COVA322 is highly stable
- In vivo half-life as unmodified antibody
- IND/IMPD enabling primate toxicology study: No clinical signs observed

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

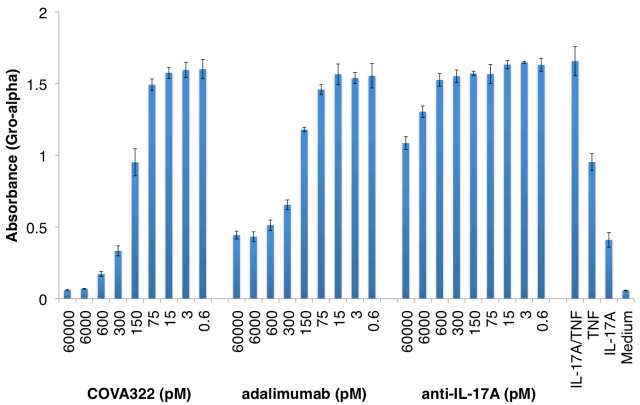
## RESULTS

### *COVA322 Inhibits Simultaneously TNF and IL-17A*

***a) Method: HT-29 Inhibition Assay***




***b) Results: Dose-dependent Inhibition***

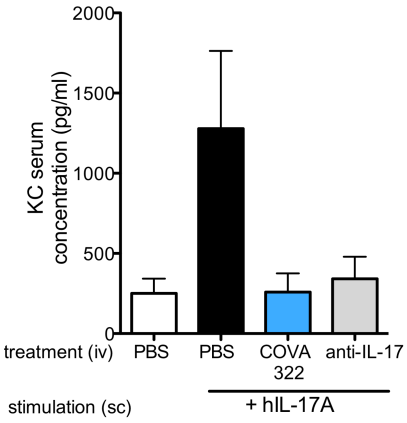



| Compound | COVA322 | adalimumab | anti-IL-17 Ab |
|---|---|---|---|
| $IC_{50}$ value | 169 pM | 187 pM | 8570 pM |

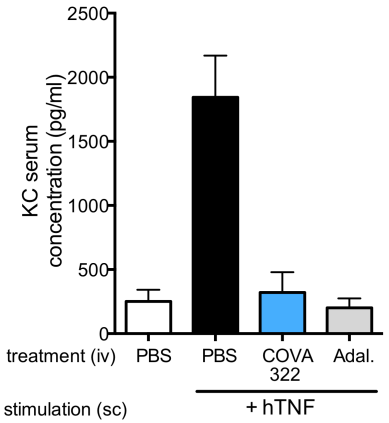
### *Animal Model:*

***COVA322 Inhibits TNF and IL-17A in an Acute Inflammation Animal Model***

***a) IL-17A***




***b) TNF***




Mice were injected i.v. with COVA322, adalimumab, anti-IL-17A antibody or PBS followed by s.c. injection of human IL-17A or human TNF. Two hours after administration, blood samples were taken and IL-17/TNF induced KC levels were detected by ELISA. As a control, basal KC levels are shown. Mean KC levels of 5 mice per group are shown (± SEM).

## CONCLUSION

These encouraging results indicate that COVA322 has highly promising biophysical 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.