**Abstract**

IL-17/IL-17Receptor Complexes Involve Substantial Protein-Protein Surfaces

- **IL-17A-MACROCYCLE**: E-35018 and E-35762 are highly potent in vitro, binding IL-17A with sub-nM affinity and competing with endogenous IL-17A binding to its cellular receptor.

- **IL-17A INHIBITORS**: E-35018 and E-35762 are highly potent in vitro, binding IL-17A with sub-nM affinity and competing with endogenous IL-17A binding to its cellular receptor.

**Synthetically Accessible Macrocyclic Chemical Matter: Unique Design Elements for Inhibiting Protein-Protein Complexes**

- **E-35018**
  - Inhibits IL-17A in human RASF and HT29 cells
  - Inhibits IL-17A in human RASF and HT29 cells

**Biochemical Characterization of IL-17A Binders**

- **E-35018**
  - Inhibits IL-17A in human RASF and HT29 cells
  - Inhibits IL-17A in human RASF and HT29 cells

**IL-17A Inhibitors Suppress IL-17A-Induced Cytokine and Chemokine Production in Human RASF and HT29 Cells**

- **E-35018**
  - Inhibits IL-17A in human RASF and HT29 cells
  - Inhibits IL-17A in human RASF and HT29 cells

**IL-17A Inhibitors Administered by Oral Gavage Suppress Edema and Cytokine Production in Murine DTH Model**

- **E-36041**
  - Inhibits IL-17A in human RASF and HT29 cells
  - Inhibits IL-17A in human RASF and HT29 cells

**Conclusion**

- Ensemble has identified and optimized inhibitors of human and murine IL-17A using its proprietary integrated macrocyclic drug discovery platform.

- The inhibitors show significant promise for the treatment of human and murine autoimmune/inflammatory diseases.