Identification of a novel non-brain penetrant A2A R inhibitor and proof-of-concept of CD73 and A2A R/CD73 small-molecule inhibitors for cancer immunotherapy


Overview
- Partnership to discover adenosinergic molecules for immuno-oncology therapeutics established between Evotec and Exscientia.

In vitro assays developed at Evotec/Exscientia

Crystallography is providing insights on ligand binding to CD73

- X-ray crystal structure of literature compound (from GSK), located away from the adenosine pocket.
- The protein can exist in open and closed conformations.
- In contrast EVOEXS compounds bind in the adenosine pocket.

First CD73 inhibitor lead compounds active in the in vitro CD3-T cell functional assay

Conclusion
- Adenosinergic Franchise is a new platform in Evotec to accelerate drug discovery in the field of Immuno-oncology.
- Rapid progress has been made on both specific A2A R antagonists and CD73 specific molecules.
- Program is placed to deliver a development candidate by mid-2018.
- Potential to also extend bispecific approach within adenosinergic franchise.