Identification of a novel non-brain penetrant A2AR inhibitor and proof-of-concept of CD73 and A2AR/CD73 small-molecule inhibitors for cancer immunotherapy

Overview
- Partnership to discover adenosinergic medicines for immune-oncology therapies established between Exscentia and Evotec
- Strategy: Create potent non-specific high quality assets and value in immune-oncology

Objectives
- Preclinical candidate identification for A2AR inhibitor
- Evaluate in human or mouse CD-7 T-cells

In vitro assays developed at Evotec/Exscentia
- SPR screening assay with A2AR bound to the C-terminal domain of A2AR
- In vivo functional assay on human or mouse CD-7 T-cells

Crystallography is providing insights on ligand binding to CD73

X-Ray crystal structure of literature compound (from GSK), located away from 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
- Partnership to discover bispecific small molecule immuno-oncology therapeutics established between Exscentia and Evotec
- Expansion of existing partnership to discover novel immuno-oncology therapeutics
- Rapid progress has been made on both specific A2AR antagonists and CD73 specific molecules have been identified
- Program is placed to deliver a development candidate by mid-2018
- Potential to also extend bispecific approach within adenosinergic franchise

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Abstract #3768

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Evotec, Toulouse, France; ‘Glistening’, Oxford, United Kingdom; ‘Milateral Discovery’, Ohay, United Kingdom

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