375 AHR Inhibitor for Hematological Malignancies

Asset Overview

Product Type	Small Molecule
Indication	Oncology
Current Stage	Lead identification / optimization
Target(MoA)	Aryl Hydrocarbon Receptor (AHR) inhibitor
Brief Description	• AHR has an important role in hematopoiesis and lymphocyte development • AHR is preferentially expressed by myeloma tumor cells and expression level correlates with overall survival • AHR antagonism with off-patent tool inhibitor induces direct cell death of myeloma stem cells and tumor cells and favorable immunomodulatory effects (expansion, enhanced activation, and increased cytotoxicity of immune effector cells & increased susceptibility of myeloma cells to immune mediated recognition and lysis) *(2014)* • Now designing novel candidate AHR inhibitors and further developing assays to interrogate their biology
Organization	The Ohio State University

Differentiation

□ **AHR as a therapeutic target**

- AHR is a transcription factor that acts as a master regulator of the immune system
- The enzymes IDO1, IDO2 and TDO are overexpressed in tumours and convert tryptophan into kynurenine (KYN) in the tumour microenvironment. KYN is then actively transported into dendritic cells and effector T-cells that are mobilised to detect and kill tumour cells. KYN signalling via AhR in these cell types converts them into regulatory T-cells, suppressing the immune system and preventing it from attacking tumor cells
- AHR mediates all the major steps of cancer development including initiation, promotion, progression, and metastasis

□ **AHR pipelines**

- BAY-2416964 (Bayer): Phase Ⅰ (2019) for advanced solid tumors including NSCLC and HNSCC, oral administration, by antagonizing AhR, inhibition of the motility and invasion ability of highly invasive cancer cells and preventing metastasis
- AHR antagonist (JAGUAHR, JV of ASLAN and Bukwang): Preclinical for the treatment of cancer
- HP-163 (Hercules Pharmaceutical): Preclinical for the treatment of TNBC, CRC and other solid tumors, oral administration, block of spreading of the tumor by reducing the number and function of cancer stem cells, Antagonism of AhR reduces clonogenic survival and invasiveness of cells. The drug candidate enhances tumor-specific immune response by inhibiting immune checkpoints
- BAY-218 (Bayer): Discovery for the treatment of cancer as a single agent or in combination with existing immuno-oncology drugs, oral administration

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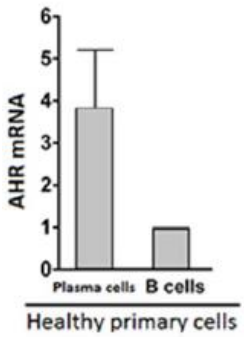
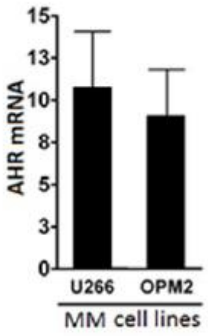
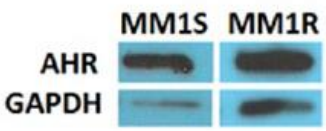
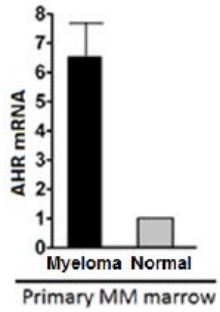
Key Data

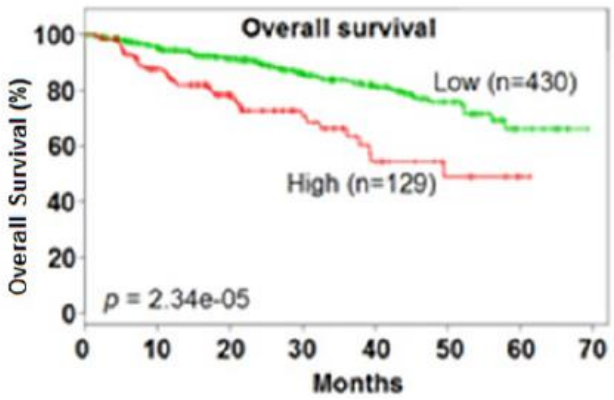
AHR is preferentially expressed by myeloma tumor cells and expression level correlates with overall survival.











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Intellectual Property

Patent No.	PCT/US2016/017338 PCT/US2016/061062 PCT/US2017/041948
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Country	US, EP, JP, CN, CA, AU

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