AstraZeneca (including affiliates) Oncology Portfolio Opportunities for Local Sponsorship via Combinations Alliance

"Open EOI Call" October 2017

Further to the request from the Combinations Alliance for clarity on which drugs and areas of scientific interest are open for collaboration under the master terms of agreement, AstraZeneca (and affiliates) are pleased to provide the following details.

Any proposals that are of interest and that AZ and affiliates and our Alliance partners would be keen to progress, will be reviewed by AZ (and affiliates as relevant) internal governance in order to secure appropriate funding prior to a decision.

The areas outlined below for each project are not at the exclusion of others with a strong scientific rationale, and all proposals will be considered on a case-by-case basis for External Sponsored Research (ESR) via the Combinations Alliance.

AZD9150 (STAT3 antisense oligonucleotide) Project representative: esha.gangolli@astrazeneca.com

- Development stage - Phase II, combination RP2Ds with durvalumab (D) and durvalumab/tremelimumab (D/T) available. Ongoing trials in SCCHN, DLBCL, NSCLC, CRC, pancreatic and bladder cancers in combination with D and in SCCHN with D/T.
- Availability – Open to expressions of interest, with drug supply available for collaborative trials only in Q32018. Proposals will be prioritised based on scientific merit and fit with the core development program.
- Settings of Interest – Immunotherapy combinations in indications not already covered, in particular studies with a strong investigative biomarker component; chemotherapy or radiation combinations (with the caveat that dose-finding will be required). Collaborators may need to generate additional preclinical work to support clinical settings of interest.

AZD6738 (ATR inhibitor) Project representative: simon.a.smith@astrazeneca.com

- Development stage – Phase 1/2, with combination RPh2Ds with olaparib, durvalumab, paclitaxel and radiotherapy available now or being developed; expansion of the olaparib combination ongoing or planned in gastric cancer, ovarian cancer, small cell lung cancer, non-small cell lung cancer, triple negative breast cancer, and ARID1A-deficient cancers; expansion of the durvalumab combination ongoing or planned in NSCLC, gastric cancer, and small cell lung cancer; expansion of the paclitaxel combination planned in gastric cancer
- Availability – open to expressions of interest. Proposals will be prioritised based on scientific merit and fit with the core development program
- Settings of interest (gaps where there is interest) – +olaparib includes prostate, haematologic cancers, and cervix; +durvalumab includes head & neck cancer; mono therapy hypotheses exploring novel patient selection biomarkers; novel DDRi-DDRi combinations. All the above supported by a strong scientific rationale and (ideally) a pre-clinical platform of evidence

AZD0156 (ATM inhibitor) Project representative: andrew.reynolds1@astrazeneca.com

- Development stage – Phase I
- Availability – Open to expressions of interest. Proposals will be prioritised based on scientific merit and fit with the core development program.
- Settings of interest – AZD0156 monotherapy, AZD0156 in combination with DNA damaging chemotherapy (but not irinotecan), AZD0156 in combination with radiation, AZD0156 in combination with immunotherapy. We are also interested in window of opportunity studies, or other innovative study designs, with the potential to elucidate AZD0156 mechanism of action and / or discover predictive biomarkers of response for AZD0156.
- Additional notes: (1) setting could be a solid tumour type or a haematological malignancy, (2) studies should select a well-defined patient segment supported by a strong hypothesis pertaining to why these patients would be likely to respond to an ATM inhibitor (in this regard, supporting preclinical data would be desirable), (3) we also encourage studies with a strong translational component, with the potential to (a) elucidate mechanism of action, and / or (b) identify predictive biomarkers of response, (4) we encourage investigators to consider the line of sight – if their study was successful, what study would they do next?

Durvalumab (Imfinzi) (PD-L1 inhibitor) Project representative: Asud.Khaliq@astrazeneca.com

- Development stage – Phase III
- Availability – Open to expressions of interest. Proposals will be prioritised based on scientific merit and fit with the core development program and the GMA ESR strategies. A recommended fixed dose of 1500mg q4 weekly
- Settings of interest
    - NSCLC (early stage and advanced), SCLC, HNSCC (locally advanced and recurrent/metastatic), Urothelial Carcinoma, GI cancers (hepatocellular, pancreatic, oesophageal, gastric, biliary tract, CRC), Triple Negative Breast Cancer (TNBC) and other tumours with credible scientific rationale

- combinations or sequencing with chemotherapy, radiation, other IO therapies, novel targeted agents
- data generation in special populations
- evidence in post-IO treatment settings
- understanding safety, irAEs and the MOA in depth
- understanding mechanisms of resistance
- exploration of biomarkers for efficacy

Tremelimumab (CTLA-4) Project representative: Asud.Khaliq@astrazeneca.com

- Development stage – Phase III (only in combination with durvalumab)
- Availability – open to expressions of interest for combination studies with durvalumab. Proposals will be prioritised based on scientific merit and fit with the core development program and GMA ESR strategies. A recommended fixed dose of 75mg q4 weekly in combination with durvalumab 1500 mg q4 weekly
- Settings of interest – biomarker-driven and translational investigations and studies that provide potential for understanding tremelimumab

Acalabrutinib (BTK inhibitor)

Project representatives: Edwin.Clark@astrazeneca.com
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- Development stage – Phase III, with ongoing trials in MCL, CLL, FL, r/r DLBCL, WM
- Availability – open to expressions of interest. Proposals will be prioritised based on scientific merit and fit with the core development program
- Settings of interest
  - Combinations with novel agents, including chemo-free combinations, based on scientific hypotheses
  - Define molecular signatures and patient subtypes
  - New tumor models (hematologic malignancies) for acalabrutinib
  - Biomarker/pathway discovery using primary human samples
  - Model directed MRD or tumor/microenvironment interactions
  - Mechanistic studies of BTK biology
  - Address resistance mechanisms