**AB928, a Novel Dual Adenosine Receptor Antagonist, Combined With Chemotherapy or AB122 (anti-PD-1) in Patients With Advanced Tumors: Preliminary Results From Ongoing Phase I Studies**

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**Dose Expansion**

**Change From Baseline (%)**

**Figure 1.** Adenosine Pathway

**Safety and Tolerability**

**Table 1.** List of AB928 Combination Studies in Ongoing Subjects

**Table 2.** Summary of Treatment Emergent Adverse Events (TEAEs) in AB928 Dose Escalation

**Trial Design**

Across the AB928 combination studies, tumor biopsies were obtained at screening or as archival (w/n 6 months) tissue. On‐treatment biopsies were collected around Day 43, if medically feasible. The example below illustrates the planned biomarker characterization of all participants.

**Results**

Demographics and Patient Characterization

As of 17 May 2019 (data cut-off), a total of 26 participants have been treated with AB928 combination therapy in studies AB928‐002, AB928‐003, AB928‐005. A total of 26 participants have been treated with AB928 combination therapy in at least one on‐treatment biopsy (including both screening and on‐treatment biopsies).

**Figure 2.** Study Scheme

**Figure 3.** PK/PD in Oncology Subjects is Comparable to That Seen in Healthy Volunteers

**Figure 4:** Changes in tumor diameters at screening (A), tumor shrinking at screening (B), shrinkage (C), and efficacy (D) in advanced tumor types with traditionally low response rates and disease stabilization in advanced tumor types with traditionally low response rates.

**Figure 5:** PK/PD correlations are shown from efficacy analyses (A) and safety analyses (B). Data from screening and on‐treatment biopsies are evaluated at 100% accuracy (0.1% false discovery rate).

**Figure 6:** TCR clarity in screening and on‐treatment biopsies by Leica Full TCR + CD3 signature represent unique T cell clonotypes identified within the bulk population. Clonotypes representing less than 2% of the population are identified in the ingenuity sets. Analysis of the on‐treatment biopsies indicates clonal expansion of specific cell clonotypes.

**Figure 7:** This subject has remained on treatment for 47 weeks with stable disease. NGS characterization of the CD3 signature was performed in the on‐treatment biopsy and is shown.

**Conclusions**

- Early escalation of AB928 in combination with chemotherapy or AB122 demonstrates a favorable safety profile.
- AB928 PK/PD biomarkers can help identify responders and non‐responders.
- Preliminary biomarker characterization illustrates increased CD8 (T cell infiltrate) in the neoadjuvant setting and increased T cell cytolytic activity and T cell clonotypes in PD1/PD1+ tumors.
- Further analysis of biomarkers in combination with AB122 demonstrates tumor response and disease stabilization in advanced tumor types with traditionally low response rates.

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**Methods**

- Three global phase II/III disease‐specific platform studies are underway: the safety, efficacy, PK, PD, and clinical activity of AB928 in combination with chemotherapy (platinumbased or targeted agents) (AB928‐002).
- Eligible patients have advanced solid tumors, an ECOG performance status of 0‐1, and adequate tumor tissue or have received w/in 6 months of prior therapy.
- AB928 was administered every 21 days, starting at 1 mg on day 1 and increasing every 21 days up to 4 mg on day 15 with the intent to define the RP2D for each combination of chemotherapy (platinumbased or targeted agents) (AB928‐002).
- Safety assessments include identification of adverse events (AEs) and dose limiting toxicities (DLTs) as well as adverse events (AEs) and dose limiting toxicities (DLTs).
- Clinical laboratory parameters, safety assessments, and AE assessments are performed at screening and on‐treatment (day 43) biopsies.
- All participants will be monitored at least on a monthly basis for an additional 12 months after completion of the treatment.
- Blood samples will be collected to describe the PK profile and the clinical activity of AB928.
- Biomarker evaluations include gene sequence and expression, protein quantification, and T cell profiling before and after treatment with AB928 combinations.
- Clinical activity will be determined per RECIST v 1.1 or appropriate response criteria in tumor‐specific disease‐progression cohorts.

**Figure 6.** TCR clarity in screening and on‐treatment biopsies by Leica Full TCR + CD3 signature represents unique T cell clonotypes identified within the bulk population. Clonotypes representing less than 2% of the population are pulled in the ingenuity sets. Analysis of the on‐treatment biopsies indicates clonal expansion of specific cell clonotypes.

**Figure 7.** This subject has remained on treatment for 47 weeks with stable disease. NGS characterization of the CD3 signature was performed in the on‐treatment biopsy and is shown.

**Evidence of Immune Engagement in a Subject With a CD73 High, PD-L1 Low, TMB Low, Ovarian Carcinoma**

The inhibition of A2a receptor mediated effects by AB928 was determined in blood samples from all AB928 studies by the decreased phosphorylation of CREB (pCREB) following AB928 dosing. The overall AB928 related AEs were reported across the studies.

**Figure 8:** Changes in tumor diameters at screening (A), tumor shrinking at screening (B), shrinkage (C), and efficacy (D) in advanced tumor types with traditionally low response rates.

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**Figure 3:** PK/PD in Oncology Subjects is Comparable to That Seen in Healthy Volunteers

**Figure 4:** Dose Escalation (n=12‐18): Safety analyses are based upon all participants who received at least 1 dose of AB928. The overall AB928 related AEs were reported across the studies.

**Table 4.** AB928‐related ≥ Grade 3 Adverse Event Profile by Treatment Group

**Table 5.** Summary of Treatment Emergent Adverse Events (TEAEs) in AB928 Dose Escalation

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**Figure 7:** This subject has remained on treatment for 42 weeks with stable disease. NGS characterization of the CD3 signature was performed in the on‐treatment biopsy and is shown.

**Figure 8:** Changes in tumor diameters at screening (A), tumor shrinking at screening (B), shrinkage (C), and efficacy (D) in advanced tumor types with traditionally low response rates.