OMNIA-1, a Phase I/II study of ANV419, an IL-2R-βγ targeted antibody-IL-2 fusion protein, as monotherapy or in combination with anti-PD-1 or anti-CTLA-4 antibodies, in patients with advanced melanoma

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Background

- Significant advancements, including development of immune checkpoint inhibitors and targeted therapies have transformed outcomes for patients with unresectable or metastatic melanoma
- Patients who do not respond or who progress while receiving these regimens have limited options
- Recombinant IL-2 (aldesleukin) has demonstrated single agent anti-tumor efficacy and durable responses in approximately 10% of patients and is approved for the treatment of metastatic melanoma, but its use is limited due to safety/efficacy concerns, and logistic constraints
- ANV419 is a fusion protein of IL-2 and anti-IL-2 monoclonal antibody ANV419, designed to selectively activate cytotoxic T cells and NK cells and avoid a suppressive tumor response while minimizing toxicities

Figure 1.

OMNIA-1 is an open label, randomized, parallel arm, Phase 1/2 adaptive study to evaluate the efficacy and safety of ANV419 as a monotherapy and in combination with pembrolizumab or ipilimumab in patients with previously treated unresectable or metastatic melanoma. There will be up to 3 separate parts in this study:

**Part 1:** Monotherapy dose expansion (N = 30)
- Patients are randomized to receive ANV419 108 µg/kg or 243 µg/kg every 2 weeks
- If Part 1 is successful, part 2 will be opened

**Part 2:** Combination dose finding (N = 50)
- Patients will be randomized to receive ANV419 in combination with pembrolizumab or ipilimumab every 3 weeks using the approved doses of pembrolizumab and ipilimumab
- Dose escalation will be guided by BOIN using a DLT observation period of 3 weeks

**Part 3:** Combination dose expansion (N = 50)
- Part 3 will evaluate the safety and efficacy of ANV419 in combination with pembrolizumab or ipilimumab using a Simon 2-stage design

Duration of treatment
- ANV419 +/- pembrolizumab: up to 12 months in absence of progression/unacceptable toxicity
- ANV419 + ipilimumab up to 4 cycles, followed by ANV419 monotherapy (Q2W) up to 12 months in absence of progression/unacceptable toxicity

Key eligibility criteria

- ≥ 18 years of age
- Histologically confirmed Stage 3 (unresectable) or Stage 4 (metastatic) cutaneous melanoma (uveal/ocular and mucosal excluded)
- Progressed on or following at least 1 line of standard care immunotherapy
- Patients with BRAF mutant disease must have received prior BRAF/MEK inhibitors
- IF CNS involvement, no active disease and no carcinomatous meningitis
- Measurable disease per RECIST criteria
- ECOG performance status of 0 or 1

*As per protocol V.3, other criteria also apply

**Study objectives and endpoints**

**Objective**
To assess the efficacy and safety of ANV419 single agent or in combination with pembrolizumab or ipilimumab in patients with unresectable or metastatic cutaneous melanoma

**Primary Endpoints**
- Objective Response Rate of ANV419 single agent (Part 1) and in combination (Part 3) by RECIST 1.1
- Safety/tolerability and RP2D determination of ANV419 in combination (Part 2)

**Secondary Endpoints**
- ORR, DCR, PFS and OS
- Pharmacokinetics (PK) and Pharmacodynamics (PD)
- Immunogenicity
- QoL

**Exploratory Endpoints**
- Changes in tumor microenvironment before and after ANV419

Participating countries

Part 1 ongoing in the USA, France, Spain, Germany and Italy

First patient dosed in Dec 2022

Preliminary monotherapy efficacy expected by Q1/2024

Thank you to all sites and patients in this study

Reference

Research Sponsor: ANAVEON AG, Basel, Switzerland

ClinicalTrials.gov Identifier: NCT05578872