

Unique Features of GeminiMab ADC Platform

Syndivia's GeminiMab ADC platform is the first to enable site-specific conjugation at the hinge-region heavy-heavy upper disulfide bond of native IgG1 antibodies. This technology offers unprecedented simplicity and scope in creating efficient and well-tolerated antibody-drug conjugates (ADCs). The platform allows for optimal drug-to-antibody ratios (DAR) of payloads or payload combinations, including unique DAR1, DAR1+1, DAR2, DAR4, and DAR6 configurations, which are not achievable with traditional methods.

The GeminiMab technology ensures (Fig. 1):

- Natural concealment of the payload, reducing hydrophobicity and immunogenicity without additional modifications.
- Preservation of the native glycosylation profile and antibody integrity, maintaining flexibility and ensuring a covalent bond across all antibody chains.
- An enzyme-free process that results in stable linkages, making it directly applicable to native antibodies without the need for antibody engineering.

Preclinical studies show enhanced tumor penetration and superior efficacy of the resulting conjugates.

Lead Asset: Targeting PSMA with SDV2102

Syndivia's lead asset, SDV2102, is a DAR1 ADC targeting Prostate-Specific Membrane Antigen (PSMA) for metastatic castration-resistant prostate cancer (mCRPC). This asset features a proprietary anti-PSMA antibody (XT42) with improved tumor penetration and high internalization levels. The XT42 antibody targets a novel PSMA epitope and is conjugated to MMAE, a tubulin binder, via GeminiMab technology with a stable linker.

SDV2102 demonstrated superior pharmacokinetics, stability (Fig. 2), efficacy (Fig. 3), and tolerability (Fig. 4) profiles compared to traditional ADCs. The DAR1 format allows for high dosing, with an estimated dose in human clinical trials of 10 mg/kg and a therapeutic index of 38.4.

Ongoing Series A Fundraising

Syndivia's development strategy focuses on expanding the GeminiMab platform to include up to five additional ADC targets (TF, Trop2, B7H3, and two undisclosed targets) while conducting Phase 1/2a clinical trials to assess the safety and efficacy of the lead asset, SDV2102, thereby validating clinical proof of concept for the GeminiMab ADC platform.

With a financial requirement of **€40 million**, Syndivia is positioned to address unmet clinical needs in mCRPC and explore additional oncology indications using its advanced GeminiMab ADC Platform.

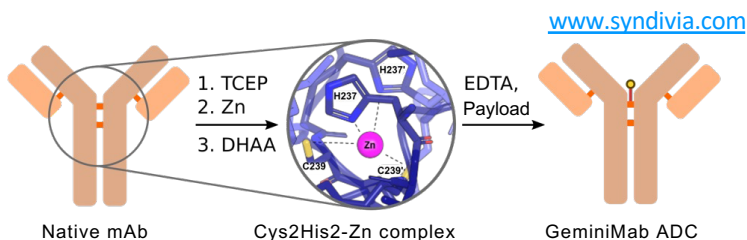


Fig. 1. GeminiMab conjugation workflow. Proximal His237 in the interchain-reduced native mAb lead to the formation of the key Cys2His2-Zn complex, protecting the Cys239 (upper heavy-heavy disulfide) from oxidation with DHAA. Subsequent site-specific conjugation with a payload yields GeminiMab ADC.

Pharmacokinetics (PK) of SDV2102 and Plasma Stability of its Linker

SDV2102 is well-tolerated (no signs of adverse effects) and maintains favourable PK properties of XT42 in Sprague Dawley Rats.
A dual-handle conjugation GeminiMab format provided promising plasma stability.

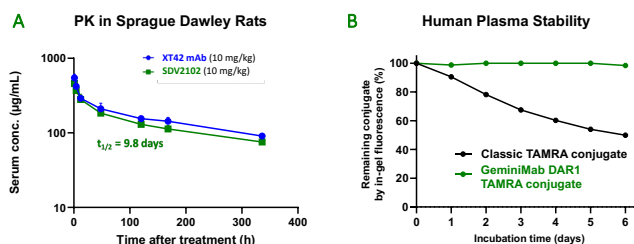


Fig. 2. (A) Evaluation of the stability and clearance of SDV2102 in SD rats ($n=3/\text{group}$) dosed IV once at 10 mg/kg. Plasma samples were analyzed by ELISA using anti-human secondary IgG. (B) Ex vivo human plasma stability study at 37 °C of a GeminiMab DAR1 conjugate and the classic Cys-conjugated ADC.

In Vivo Efficacy of SDV2102 in CDX and PDX models

SDV2102 demonstrated a significantly stronger anti-tumor effect in PSMA-positive CDX models compared to classic DAR4 ADCs (XT42 and J591), and a low MED of 2.5 mg/kg (single dose) was observed. SDV2102 achieved 10/10 complete responses in low- to mid-range PSMA-expressing PDX models.

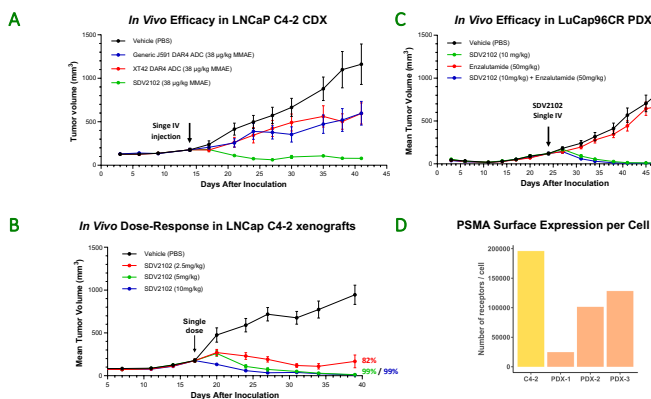


Fig. 3. (A) In vivo antitumor efficacy in SCID mice ($n=10/\text{group}$) xenografted with C4-2 prostate cancer cells. Single IV dose administration when tumors reached 178 mm³. (B) In vivo dose-response study in C4-2 xenografts showing MED of 2.5 mg/kg. (C) In vivo antitumor efficacy in SCID mice ($n=10/\text{group}$) xenografted with LuCap96CR PDX. Single IV dose administration when tumors reached 120 mm³. (D) Quantification of PSMA membrane expression on cells isolated from three LuCap96CR PDX using XT42 mAb and Human IgG Calibrator. C4-2 cell line was included as a representative control of a known high-expressing cell line.

Evaluation of SDV2102 Tolerability and its Therapeutic Index (TI)

Toxicology in non-human primates (NHP). Evaluated parameters included mortality, clinical signs, food consumption, body weight, ophthalmology, body temperature, hematology, coagulation, clinical chemistry, urinalysis, organ weights, and macroscopic tissue examinations.

ADC	MED (in mice)	MTD (in NHP)	TI (mg/m ² basis)
SDV2102	2.5 mg/kg 7.5 mg/m ²	24 mg/kg 288 mg/m ²	38.4

Fig. 4. Evaluation of SDV2102 therapeutic index by measuring the minimum efficacious dose (MED) in mice and the maximum tolerated dose (MTD) in non-human primates. The therapeutic index (TI) is calculated as the ratio of two equivalent human doses.