**MULTI-ARMING AND REGULATORY DIAL GENE CIRCUITS TO ADDRESS KEY DISEASE CHALLENGES IN HCC**

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**Abstract:**

Multi-Arming and Regulator Dial Gene Circuits to Address Key Disease Challenges in HCC

**Background:** Tumor microenvironment (TME) is the driving force for tumor growth, therapy resistance, and metastasis. Genetic and epigenetic alterations activate complex signaling pathways that promote tumor growth, proliferation, and survival. Therefore, developing novel therapeutic strategies that simultaneously target multiple aspects of the tumor microenvironment is crucial.

**Senti-301 Aims to Safely Overcome the Immunosuppressive Tumor Microenvironment for Patients with R/R HCC**

**Senti-301 Multi-Arming Approach is Designed to Attack Cancer in Multiple Complementary Ways**

**SENTI-301 Ensures Regulated ON/OFF Control**

**SENTI-301 Enables Optimal Targeting Strategy Using Senti’s Synthetic Biology Platform**

**Vector 1: Expression and In Vitro Functional Analysis of Top Constructs**

**GPC3 CAR in Vivo Antitumor Function**

**HCC intraperitoneal (IP) Xenograft Model**

**Regulator Dial Enables ON/OFF/ON Regulation of IL-12 In Vivo**

**Study Design**

**Senti Bio’s Regulator Dial Enables Physician Real-Time Control of Protein Expression In Vivo to Improve Efficacy and Reduce Side Effects**

**Regulated cIL-12**

**HCC Median survival (days)**

**SEN1-301 Gene Circuits Expression in NK Cells**

**Summary**

**SEN1-301** is an all-inclusive platform of NK cell therapies with regulator dial gene circuits designed to deliver existing molecules of proven immunomodulatory activity for the solid tumor microenvironment.

**SEN1-301** provides a potentially improved, safe and more efficacious therapeutic option for patients with HCC.

**SEN1-301** is a drug-like small molecule platform for NK cell therapies with regulator dial gene circuits designed to deliver existing molecules of proven immunomodulatory activity for the solid tumor microenvironment.

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