REQUEST #2334005

Partners for Antibody-Drug Conjugate (ADC) Technology

RESPONSE DUE DATE: April 21, 2017

Opportunity:
Antibody derivatization and ADC joint research & development

The following are expected to be achieved within 1-3 years:
1) Antibody humanization & antibody-drug conjugation
2) Verification of in vivo activity in mouse models
3) Initiation of preclinical study of drug-conjugated antibody

Financials
Details to be negotiated based on the contents of the proposal and the stage of research and development.

REQUEST FOR PROPOSAL DESCRIPTION

NineSigma, representing Daiichi Sankyo Co., Ltd. (http://www.daiichisankyo.com/), seeks business partners possessing cancer-targeting antibodies to which the antibody-drug conjugate (ADC) technology developed by Daiichi Sankyo can be applied. Business partners wishing to use the ADC technology are also being sought.

Daiichi Sankyo has established a platform to deliver innovative ADCs and is developing an internal ADC pipeline portfolio, including DS-8201a, an ADC which is comprised of an anti-HER2 antibody attached by a peptide linker to a very potent topoisomerase-1 inhibitor. In non-clinical (in vivo) pharmacological studies and clinical trials, DS-8201a exhibited clearly higher anti-tumor effects than the marketed ADC (T-DM1), and it was granted Fast Track designation (expedited review) by the FDA for the treatment of HER2-positive unresectable and/or metastatic breast cancer.

Daiichi Sankyo is aiming to use their proprietary ADC technology to continually create new drugs that address unmet medical needs in the cancer area. They have therefore issued this open request to academic institutions and companies with promising antibody seeds that meet the criteria for making a safe and effective ADC.

POTENTIAL PARTNERS

Two potential types of partnerships are envisioned depending on different roles and responsibilities for development:

1) Academic institutions and companies possessing a cancer-targeting antibody to which ADC technology can be applied
Out-licensing proposals regarding the antibody are anticipated from academic institutions and companies that possess antibodies which meet the necessary requirements and that wish to have Daiichi Sankyo perform antibody-drug conjugation and the associated research and development.

2) Academic institutions and companies that aspire to conduct joint ADC research and development applying Daiichi Sankyo’s ADC technology
Proposals are anticipated from academic institutions and companies that possess or are developing cancer-targeting antibodies which meet the necessary requirements and that wish to conduct joint ADC research and development applying Daiichi Sankyo’s ADC technology.
Requirements for Proposed Antibodies

The proposed antibody must be an already selected lead antibody capable of fulfilling the following requirements (mouse and rat antibodies also acceptable).

- Antibody which targets membrane proteins (ligand-targeting antibodies are not accepted)
- Any type of cancer may be targeted
- Tumor - selective expression of the target antigen, with no or minimal normal tissue presence, as typically demonstrated by IHC.
- Demonstrated cell surface presentation of the antigen by FACS.
- Demonstrated internalization of the antigen-antibody complex after binding.

**DAIICHI SANKYO'S ADC TECHNOLOGY**

The ADC technology introduced herein is characterized by the following features.

- **Highly Novel Payload**
  The payload of Daiichi Sankyo's ADC technology is a novel topoisomerase-1 inhibitor, DXd, exhibiting approximately 10 times more Topo-1 inhibitory activity than SN-38, the active metabolite of irinotecan.\(^1\),\(^2\)

Fig. 1. Mechanism of Action of Payload

- **High Biostability & Mitigated Side Effects**
  The ADC applying Daiichi Sankyo’s technology has a low aggregation rate even when eight payloads per one antibody are loaded\(^1\) and shows high stability in the bloodstream.\(^2\) Moreover, free drug dissipates quickly. The good safety profile of the payload was verified in non-clinical studies with cynomolgus monkeys.\(^2\)

- **Highly Effective**
  Contribution of bystander killing effect of the payload in Daiichi Sankyo’s ADC technology, not only antigen-positive cancer cells on which the ADC acts, but also adjacent antigen-negative cancer cells are killed.\(^3\)

Fig. 2. Pharmacokinetics of DS-8201a in Cynomolgus Monkeys\(^2\)

Fig. 3. Bystander Killing Effect

Since a high number of drugs loaded also have the bystander effect, the ADC has been verified to exhibit potent anti-tumor activity against heterogeneous tumors and tumors that show low antigen expression.\(^2\),\(^3\)
**Fig. 4.** In vivo evaluation in mice with HER2 heterogeneous tumors generated by inoculating the mixture of HER2-positive cell line (NCI-N87) and HER2-negative cell line (MDA-MB-468-luc). Luciferase activity of each mouse was measured to detect HER2-negative tumors after ADC treatment.

**Fig. 5.** In vivo evaluation using patient-derived tumor xenograft (PDX) mouse models (left: PDX with high HER2 expression; right: PDX with low HER2 expression).

- **DS-8201a Clinical Trial Results (Phase I)**
  Preliminary overall efficacy results from 20 evaluable patients demonstrated an objective response rate of 35% (seven partial responses) and disease control rate of 90%, including 12 patients previously treated with T-DM1 and five patients with HER2 low expression (IHC2+/FISH or IHC 1+). Furthermore, in a subanalysis of the group of 12 evaluable HER2+ breast cancer patients previously treated with T-DM1, the objective response rate was 42% with a disease control rate of 92%.

- **Applicability to Other Antibodies**
  Daiichi Sankyo’s ADC technology has also been applied to antibodies against other targets, such as CD30, CD33, CD70, and B7-H3, and confirmed their efficacy in vitro and in vivo, suggesting that Daiichi Sankyo’s ADC technology is widely applicable to a diverse number of antibodies. A Phase 1 clinical trial for anti-HER3 ADC (U3-1402), applying Daiichi Sankyo’s ADC technology, is also currently being conducted.

**References**


4) Tamura-K et al. Abstract 4548 (LBA17), ESMO 2016


ANTICIPATED PROJECT PHASES OR PROJECT PLAN

Applicants are required to submit their proposals through NineSights in accordance with the attached Proposal Template. Daiichi Sankyo will conduct the primary evaluation of the proposals based on “Response evaluation” (see right) and will directly initiate contact with applicants of interest. Daiichi Sankyo will, as needed, enter into non-disclosure agreements and material transfer agreements with applicants they have directly contacted.

In the event that promising proposals are obtained, Daiichi Sankyo will discuss licensing agreements, contract research agreements, and/or joint research agreements separately with the applicants.

ITEMS TO BE INCLUDED IN THE PROPOSAL

Applicants will use the Proposal Template which is linked to the “attachments” shown at the bottom of the link <REQ2334005> and proposals should include the following information:

- The type of cancer targeted
- Overview of the cancer-targeting antibody (mechanism of action, principles, superiority over other approaches, etc.)
- Practical examples (pharmacology, safety, toxicity, pharmacokinetics, etc.)
- Current stage of research and development
- Future research/development plans
- Status of intellectual property related to the proposed technology
- Past research achievements (or achievements/scale of business pertaining to antibody drugs)
- Desired collaboration style with the client

SUBMITTING A RESPONSE

All proposals should be submitted online at NineSights, the NineSigma open innovation community, according to the instructions in the Proposal Template. Supplemental files may be submitted in addition to the proposal document.

For assistance, please contact the Solution Provider Help Desk (PhD2@ninesigma.com).

REQUEST GUIDELINES

Non-Confidential Disclosure

By submitting a response you represent that the response does not and will not be deemed to contain any confidential information of any kind whatsoever.

Response Evaluation

NineSigma’s client will evaluate the responses using the following criteria:

- Overall scientific and technical merit of the proposed approach
- Approach to proof of concept or performance
- Potential for proprietary position (i.e., is the technology novel or protectable)
- Economic potential of concept
- Applicants’ capabilities and related experience
- Realism of the proposed plan and cost estimates
- Ability of the applicants organization and related performance

Response Selection

By submitting a response, you acknowledge that NineSigma’s client reserves the sole and absolute right and discretion to select for award all, some, or none of the responses received for this announcement. NineSigma’s client also may choose to select only specific tasks within a proposal for award. NineSigma’s client has the sole and absolute discretion to determine all award amounts. NineSigma will contact applicants with highly responsive proposals for next steps, or the client may contact applicants directly.