

**Request for Proposal**

**2017 Asahi Kasei Pharma Open Innovation Competition Program**

**Overview**

Asahi Kasei Pharma believes “locomotive syndrome” to be a serious problem that needs to be urgently addressed in our aging society. For this reason, we dedicate our research and development efforts toward developing new drugs that help patients worldwide who are suffering from chronic pain, metabolic bone diseases, or rheumatoid arthritis. We are a leader in the field of these disorders and have thus far developed the synthetic calcitonin derivative Elcitonin®, the human parathyroid hormone preparation Teribone®, and the immunosuppressant Bredinin®. In the future, we will continue in our efforts to generate a steady flow of new innovative drugs. To achieve this, we aim to build a larger pipeline of new drug candidates through collaboration with our research partners and further strengthen our drug development capabilities in the areas of orthopedics and musculoskeletal disorders.

**Areas of Interest and Specific Research Needs and Topics**

1. **New drug candidates and drug development technologies in the core research fields of Asahi Kasei Pharma**

Chronic Pain

< Drug Candidates >

1.1 New drug-target molecules or drug candidates in the field of pain management.

* Target diseases: Neuropathic pain, psychogenic pain, and osteoarthritic knee pain.
* Provide an in vivo efficacy. (In vivo studies with relevant knockout mice are also acceptable.)
* Out of scope for this program: Drug-target molecules and drug candidates that directly act on opioid receptors or inflammatory pathways (e.g., COX)**.**

< Drug Development Technologies >

1.2 Omics-based identification of molecular targets or biomarkers for pain drug discovery.

* Study populations: Patients with pain, elderly individuals, and/or patients with central nervous system disorders accompanied by pain.
* Analytical techniques: Proteomics, metabolomics, and/or genomics.
* Your proposal can be focused on molecular targets only, biomarkers only, or both.

1.3 Biomarkers that correlate with pain scores in humans or in animal models of pain.

* Preferred biomarkers are those that can be assayed in samples collected in a less invasive manner. Examples of these samples are blood, synovial fluid, urine, and tears.

1.4 Identification and functional characterization of new drug-target molecules localized to specialized cells (including both neuronal and non-neuronal cells) that are involved in the onset and maintenance of pain.

* Cells to be investigated, e.g., interneurons, astrocytes, etc.

1.5 New and innovative technologies for pain assessment.

* Pain measurement tools that can be used, or adapted for use, in humans.
* Pain measurement tools utilizing pain indices that enable the assessment of emotional experiences.
* Animal models or any other test systems that mimic patients' hyporesponsiveness to known analgesics (such as pregabalin).
* Proposed measures should be able to differentiate between pain and baseline conditions both in vitro and in vivo.

1.6 New animal models of pain that can recapitulate more aspects of human pain perception than conventional models.

* Non-rodent models of pain.
* Models of diabetic neuropathy (excluding STZ-induced models). Type 2 diabetes models will receive high priority.
* New osteoarthritis pain models (excluding conventional MIA-, MT-, and DMM-induced models).
* Animal pain models and bioassay systems for high-throughput screening studies.
* Ideal models are those that can be established easily and quickly.
* Pain assays should be highly reproducible through the use of objective indices.
* Translational animal models for the study of human pain conditions.

1.7 Technologies to differentiate human iPS cells into dorsal root ganglia (DRG), dorsal-horn (DH) neurons, or glial cells (microglia or astrocytes).

* Differentiated cells should possess the functional characteristics of their corresponding primary cultures. The characteristics include expression patterns of marker genes, profiles of cellular responsiveness, and activities of reference compounds.
* Proposed technologies should allow for the robust and reproducible production of these cells for in vitro screening in multiwell (> 96) plates.

1.8 Phenotypic assay systems utilizing neuronal (e.g., DRG or DH neurons) or glial (e.g., microglia or astrocytes) cells.

* Proposed systems should mimic clinically-relevant chronic pain conditions. Assay systems for inflammatory pain (that involve, for example, NSAIDs, COX2, and prostaglandins) are outside the scope of this program announcement.
* Proposed systems should be suitable for in vitro medium-throughput screening performed in multiwell (> 96) format.
* When neuronal cells are incorporated into phenotypic assays, one of the following co-culture systems must be used to maintain the cells: 1) DRG – DH, or 2) DRG/DH – glia.

Rheumatoid Arthritis and Other Autoimmune Diseases

< Drug Candidates >

2.1 Drug candidates for rheumatoid arthritis and other autoimmune diseases.

* New drug candidates (samall molecule compounds, peptides, antibodies, or proteins) must be in the preclinical stages of development.
* Priority will be given to proposals that present a unique concept or aim to identify a new mechanism of action for a drug molecule.
* Drug candidates those have demonstrated efficacy in vivo (with animal models) are preferred.

# Bone/cartilage tissue repair and regeneration

< Drug Candidates >

3.1 Potential drug molecules (such as small molecule compounds, peptides, antibodies, or proteins) that can promote bone/cartilage tissue repair and regeneration (e.g., bone fracture, bone defect, bone fusion).

* Provide efficacy data produced by cell-based or animal studies.

< Drug Development Technologies >

3.2 Cell-based assays, animal models, biomarkers, or imaging technologies that can facilitate the translation of preclinical findings to clinical outcomes in the field of bone/cartilage regenerative medicine.

1. **New technologies aimed at addressing the challenges in drug discovery and development at Asahi Kasei Pharma**

Drug Development Core Technologies

4.1 Protein expression and purification systems that can produce stable membrane proteins (especially ion channels) suitable for structural analysis.

4.2 New technologies for 3D structural analysis of proteins (including membrane proteins) that are not readily amenable to conventional techniques such as X-ray crystallography or NMR. The desired resolution is approximately 3 Å.

4.3 Co-crystallization approaches for improving physicochemical properties of active pharmaceutical ingredients.

* Proposed approaches must have a great potential for large-scale production, possibly yielding on the order of kilograms.

4.4 Model systems for predicting human oral absorption of salts/co-crystals of poorly water-soluble drugs.

4.5 Microreaction technologies for small-scale (≤ 1 mg) organic synthesis.

* The quality of the final compounds synthesized by proposed technologies must be similar to or higher than that of conventional products.
* Ideal technologies should be able to perform multiple reactions in parallel.

4.6 New solvents for extracting organic compounds.

* These solvents should be heavier than water, highly effective in dissolving organic compounds, affordable (< US $150/500 mL), and non-halogenated.

4.7 Identification of novel disease indications for secreted frizzled-related protein 1 (SFRP1) inhibitors.

Prediction of Pharmacokinetics and Toxicity

5.1 In vitro tests for predicting neurotoxicity. Specifically, proposed tests should be able to evaluate the following adverse effects on the central nervous system: memory impairment, convulsive seizures and/or feeding activity. Assay systems specific to other central nervous system side effects will also be considered.

5.2 Non-clinicalexperimental models for the quantitative prediction of metabolite exposures in humans.

5.3 Cutting-edge modeling and simulation technologies for accurately predicting human pharmacokinetics and pharmacodynamics of therapeutic agents for pain or autoimmune diseases.

5.4 Simulation methods for predicting local concentrations and plasma kinetics of therapeutic agents following topical administration of their sustained-release preparations.

Manufacturing Technologies

6.1 Technologies enabling long-term storage of drugs in aqueous solutions that can be directly administered by hypodermic syringe. Drugs must retain ≥ 95% of their initial activities after three months of storage at room temperature.

(Applications proposing to use the following approaches will not be considered.)

* Lyophilization. (Drugs must be stored in aqueous solutions.)
* Methodologies that compromise drugs’ physical properties and prevent their subcutaneous injection.
* Covalent modification of drugs.

6.2 Sustained-release delivery technologies and/or functional pharmaceutical additives for subcutaneous formulations of therapeutic agents (peptides, proteins, or intermediate-molecular-weight compounds).

* The duration of controlled release must be four weeks or longer.
* PLGA microsphere-based release technologies are excluded from this solicitation.

6.3 Technologies for the needle-free delivery of peptides or proteins.

**Award amounts(research grant) and Collaboration Period**

Award amounts will be determined individually for each application and will not exceed a maximum of US $50,000 for one year.

The collaboration period is generally limited to one year. However, based on demonstrated project success, funding for an additional one-year period may be granted.

**Application Guidelines**

Applicants must submit proposals using the designated forms.

* Proposals must not include any proprietary, confidential, or privileged information.

**Submission Information**

* **How to apply?**

Applicants are required to submit the entire proposal as an attachment via email to the address shown below:

drug-seeds@om.asahi-kasei.co.jp

Open Innovation Program

Attn: Program Administrator

Request for Proposals

Asahi Kasei Pharma Corporation

* **Submission Deadline**

Friday, December 22, 2017, 12:00 (Greenwich Mean Time)

* **Contact Information**

If you have any questions regarding this program announcement, please direct them to the email address shown above.