Expression of Interest (EOI) from Eligible Contract Research Organizations (CROs)

TO

Plan and perform detailed non-rodent pharmacokinetic/pharmacodynamic (PK/PD) and toxicity studies using Disarib

EoI No: BC/SCR/EOI(1)-2024

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Department of Biochemistry, Division of Biological Sciences, Indian Institute of Science (IISc), Bangalore – 560 012

080 2293 2674

https://biochem.iisc.ac.in/

CONTENTS

BACKGROUND

The Indian Institute of Science (IISc), established in 1909 in Bangalore, is one of India's premier institutions for research and education. Known for its pioneering work in scientific and technological fields, IISc has consistently pushed the boundaries of knowledge through cutting-edge research and innovation. Its reputation for academic excellence is supported by a strong foundation of rigorous programs, world-class faculty, and advanced research infrastructure. With a diverse and vibrant student community, IISc has played a pivotal role in shaping India's scientific landscape and continues to be a symbol of the nation's dedication to progress and intellectual growth.

The Dept. of Biochemistry at the Indian Institute of Science (IISc) has a rich legacy of groundbreaking research and academic excellence since its establishment in the year 1921. Over the years, it has made significant contributions to the fields of molecular biology, genetic engineering, and metabolic biochemistry, making seminal discoveries, and some of them translated for the advancement of health sciences. This underscores IISc's relentless role in translating research into practical, life-saving medical treatments.

We, therefore, are pleased to invite Expression of Interest (EOI) from eligible vendors with demonstrated expertise in preclinical studies to collaborate on advancing Disarib (a small molecule Bcl-2 inhibitor) through critical stages of drug development, ensuring compliance with regulatory standards and the highest scientific rigor. As background, Disarib, first identified by researchers at the IISc (SCR Lab) as a potential anti-cancer agent, selectively targets and inhibits Bcl-2 and promotes apoptosis, making it an effective candidate for cancer treatment. Preclinical studies (rodent studies) have shown its effectiveness in inducing cancer cell death, without significantly affecting normal cells (Iyer et al., 2016; Raveendran et al., 2024; Sharma et al., 2020, 2021; Vartak et al., 2016, 2017)

We are committed to a fair and transparent selection process that ensures a level playing field for all interested vendors. This EoI document provides detailed information about the scope of work, eligibility criteria, evaluation methodology, and submission guidelines.

We encourage all eligible vendors to submit their EoI and participate in this exciting opportunity to work with our organization.

ELIGIBILITY CRITERIA

- The vendor must be accredited by relevant regulatory authorities (e.g., OECD GLP, AAALAC) and demonstrate a clear understanding of the regulatory requirements for non-rodent preclinical studies.
- The vendor should have state-of-the-art facilities and equipment required for conducting PK/PD and toxicity studies in non-rodent species.
- The vendor must employ a qualified and experienced team of scientists, including toxicologists, pharmacologists, and bioanalytical experts, with a track record of delivering similar studies within the agreed timelines and budgets.
- They should have executed ≥ 10 projects of a similar nature that has been deployed in a large academic campus and should attach a copy of the purchase order/work completion certificate from clients as proof.

SCOPE OF WORK

The selected Contract Research Organization (CRO) will be responsible for conducting preclinical non-rodent Pharmacokinetic/Pharmacodynamic (PK/PD) and toxicity studies for our novel Bcl-2 specific inhibitor, Disarib, targeted against cancers prevalent in the Indian subcontinent.

These preclinical studies are critical to determining the safety, efficacy, and dosing parameters necessary for advancing Disarib into clinical trials. By gaining a comprehensive understanding of Disarib's ADME (Absorption, Distribution, Metabolism, and Excretion) characteristics, pharmacological impact, and potential toxicities, we aim to establish a solid foundation for future regulatory submissions and clinical development, ultimately contributing to the development of effective cancer therapies.

PROJECT DETAILS

S.No.	STUDY DETAILS
1	Metabolic study with rabbit plasma – Bridging study
2	7-day Dose range finding/MTD in Rabbit
3	28-Day Toxicity Study in Rabbit with 14-day Recovery with TK
4	MDV in HPLC for dose formulation analysis

- **GLP - Disarib - Metabolic Stability Study with Rabbit Plasma – Bridging Study:**

To assess the metabolic stability of the test compound in rabbit plasma and determine its rate of degradation/metabolism over time. This helps predict the compound's in vivo stability, aiding in cross-species comparison and drug development decisions.

The study report should typically include a summary of the experimental setup, a table with time points and concentration data, half-life and clearance rate calculations, and a discussion of the findings, especially focusing on the comparison with other species.

- **GLP - 7-day MTD study of Disarib in Rabbits by oral (gavage) route**

GLP Status	Non-GLP
Guideline	NDCT Rules, 2019
Objective	The objective of this study is to determine the maximum tolerated dose of Disarib after 7-day administration by Oral (gavage) route to New Zealand White rabbits.
Test System	New Zealand White rabbits
Age	3-6 months
Route	Oral (gavage)
No. of Dose levels	3 dose levels + 1 vehicle control
Dose formulation analysis	No dose formulation analysis. Formulations will be prepared afresh and administered immediately
Dosing regimen	Dosing once daily for 7-days necropsy on day 8

Mortality / morbidity	Twice Daily
Daily Clinical signs	At least once daily, or more frequently based on the requirement
Body Weight	Days 1, 4 & 7 (fasting body weight on day 8)
Feed consumption	1-4, 4-7
Clinical pathology	At termination – haematology, coagulation, clinical chemistry & urinalysis (standard list of parameters)
Gross Necropsy	At termination
Histopathology	On gross changes

- **GLP - 28-Day Repeat Dose toxicity study of Disarib by Oral (gavage) route in Rabbits with 14-Day Recovery and TK**

GLP Status	GLP
Guideline	NDCT Rules, 2019
Objective	The objective of this study is to determine the toxicity potential of the Disarib following 28-day administration by Oral (gavage) route to New Zealand White rabbits with 14-Day Recovery. This study is designed to provide information on major toxic effects, kinetics, target organs, and an estimate of No Observed Adverse Effect Level (NOAEL) and to check delayed effects (if any) during recovery period
Test System	New Zealand White rabbits
Age	3-6 months
No. of Dose levels	3 dose levels + 1 vehicle control
Route	Oral (gavage)
Dose formulation analysis	Twice (during day 1 and week 4): single analyte. Method validation at testing facility
Dosing regimen	Dosing once daily for 28 days and main group necropsy on day 29 and recovery group necropsy on day 43
Ophthalmology	Pre-dose and at termination
Mortality / morbidity	Twice Daily
Daily Clinical signs	At least once daily, or more frequently based on the requirement
Detailed clinical sign	Once in every week
Body Weight	Once weekly
Feed consumption	Once weekly
Clinical pathology	At termination – haematology, coagulation, clinical chemistry & urinalysis (standard list of parameters)
Gross Necropsy	At termination

Organ collection, weighing & preservation	Standard tissue list as per NDCTR 2019
Histopathology	From preserved organs of control & high dose main groups; and target organs from lower dose groups and recovery groups
Blood collection for TK	Blood will be collected from main group on days 1 & 28 from 3 rabbits/time point from ear vein/artery and plasma will be separated and stored frozen until analysis TK parameters will be analyzed using WinNonlin software and presented in report

- **GLP Method development and validation for Dose Formulation Analysis by HPLC**

To develop and validate an HPLC method for the quantitative analysis of dose formulations, ensuring accuracy, precision, specificity, and reproducibility. Toxicokinetic analysis (MDV, LCMS, and 300 sample analysis)

DELIVERABLES

The vendor is expected to deliver the results within a specific timeline of 6 months from the date of initiation of the project including, progress reports provided on a monthly basis to ensure transparency and track milestones.

SELECTION CRITERIA

The shortlisting of CROs will be done by a committee set up by Competent Authority, IISc. The criteria for evaluation would be:

S.No.	Criteria
1.	**Experience**
1.1.	Number of years in providing preclinical services
1.2.	GLP and AAALAC accreditation
1.3.	Past Assignments-experience in dealing with similar projects listed under Project Details
2.	**Technical Aspects**
2.1.	Expertise and experience of key personnel
2.2.	Quality of past projects relevant to the current project listed under Project Details
3.	**Quotation**
3.1.	Evaluation will be based on the bids submitted by the shortlisted vendors.
3.2.	Final selection will not only be based on the overall cost of the project, but also by considering the cost of

	resources per month and the total effort required within the appropriate time unit, such as weeks or months.

This comprehensive evaluation will ensure that the total cost for delivering the scoped phase of the project can be accurately calculated. Therefore, vendors are expected to provide the project efforts and associated costs for resources required. This will enable a fair and transparent evaluation process, leading to the selection of a vendor who can provide the best value for money while meeting the necessary project requirements.

Documents Required for Validating Eligibility Criteria

- Certificate of incorporation or registration of the company.
- Certificate of Good Laboratory Practices (GLP) Compliance.
- PAN (Permanent Account Number) card of the company.
- GST (Goods and Services Tax) registration of certificate.
- References or testimonials from previous clients or projects.
- Technical proposal outlining the experimental blueprint for performing preclinical studies, including details of the methodology, number of animals, and bioanalytical equipments to be used.
- Financial proposal specifying the cost of the project, including a breakdown of the costs as per the objectives of the project.

How to Submit the EoI

EoI with all enclosures should be emailed to sathees@iisc.ac.in or posted to Dept. of Biochemistry, Division of Biological Sciences, Sir CV Raman Road, Bengaluru – 560012 on or before **11 am** on **13.11.2024**.

Late submissions will not be considered.

There will be a clarification meeting arranged on ------ at ---- am/pm in the Dept. of Biochemistry committee room.

IISc reserved the right to reject any/or all the EoIs without assigning any reasons whatsoever.

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Annexure I

Self-Declaration Format

Ref. No.: Date:

To,

The Chair,

Dept. of Biochemistry, Indian Institute of Science

With reference to my/our expression of interest to IISc, it is hereby declared that I/ (name of firm) was not declared ineligible for corrupt & fraudulent practices either indefinitely or for a particular period by any Govt or other agency.

I/ (name of firm) also declare that there are no contractual restrictions or legal disqualifications or other obligations which will prohibit from me/us entering this bid and each and every one of the statement and particulars contained herein are correct.

Signature of the Applicant

Date:

Place:

Seal