



Igniting Innovation: Science in Space to Cure Disease on Earth

ISS National Lab Research Announcement (NLRA) 2024-9

Instructions to Offerors

Center for Advancement of Science in Space™

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End Date of Step 1A: Concept Summary submission period: September 26, 2024

End Date of Step 1B: Technology Roadmap*: December 10, 2024

Due Date for Step 2: Full Proposal submission*: March 31, 2025

(* by invitation only)

Note: For any updates regarding submission deadlines, please visit www.issnationallab.org/research-on-the-iss/solicitations. For general questions related to this research announcement, please email info@issnationallab.org.

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I. SUMMARY

Since 2000, the International Space Station (ISS) has enabled humans to live and work in space, supporting research and technology development that is not possible anywhere on Earth. Since its designation in 2005, the ISS National Laboratory[®] has expanded access to this orbiting laboratory to research communities from U.S. academic institutions, government agencies, and the private sector. ISS National Lab-sponsored research seeks scientific discovery and technology advancement on the ISS that directly benefits humanity by increasing fundamental knowledge, scientific application, education outreach, workforce development, and demand creation for sustainable, scalable innovation and production in low Earth orbit (LEO).

As managers of this national laboratory in partnership with NASA, the Center for the Advancement of Science in Space[™] (CASIS[™]) awards access to funding and resources on the ISS via competitive grant solicitations to support non-exploration science and technology development as well as science, technology, engineering, and mathematics (STEM) education initiatives from U.S.-based institutions.

As a U.S. taxpayer-funded organization, CASIS only contracts with U.S. Persons¹. Submitted proposals must comply with all U.S. Export Administration Regulations (EAR) and International Traffic in Arms Regulations (ITAR). This document will assist offerors in the development of concepts and proposals to leverage the ISS National Lab for applied research and technology development and demonstration.

II. DESCRIPTION OF RESEARCH

The 2024 Igniting Innovation ISS National Lab Research Announcement (NLRA) seeks to accelerate the translation of scientific discovery enabled by microgravity research into health solutions on Earth. By focusing ISS National Lab resources on targeted projects that leverage collaborations, this solicitation aims to improve existing and develop new technologies that bring value to our nation and promise to create a robust, sustainable, and scalable low Earth orbit (LEO) economy for terrestrial benefit. For this NLRA, we are particularly interested in use-inspired, transformational research and technology development (R&D) that accelerates therapeutic development. We seek projects that utilize microgravity and the unique space environment to address challenges that hinder the progress in preventing, diagnosing, and treating some of the most significant diseases of our time, such as cancer. Similarly, advanced therapies for cardiovascular, immune, muscle and bone, and neurodegenerative diseases face obstacles that thwart scientific advancements and the translation of research findings into clinical applications. These challenges frequently overlap and share common elements, despite the complexity and variability of mechanisms within and among these diseases. Many of these challenges can be mitigated using accelerated disease models in microgravity. This NLRA also aims to foster collaborations between academia, industry, and government to tackle complex challenges and develop innovative, commercially viable products and technologies for disease prevention, diagnosis, and treatment to improve medical outcomes on Earth.

¹ U.S. Person - a natural person who is a lawful permanent resident as defined in 8 U.S.C. 1101(a)(20) or who is a protected individual as defined by 8 U.S.C. 1324b(a)(3). It also means any corporation, business association, partnership, society, trust, or any other entity, organization or group that is incorporated to do business in the U.S. It also includes any governmental (federal, state or local), entity.

Topics of particular interest for this NLRA include, but are not limited to, the following:

1. Enhanced Models to Study Disease Mechanisms

The etiology (mechanistic cause or set of causes) of any disease is often complex because of the interplay of multiple factors that typically result in multiple changes in function, each associated with an underlying pathophysiology. The prevention, diagnosis, and treatment of many diseases like cancer, neurodegeneration, diabetes, cardiovascular disease, and chronic obstructive pulmonary diseases (COPD) is difficult because of this complexity. Challenges include unraveling the intricate dynamics of disease onset and progression, developing accurate models, and identifying effective therapeutic targets unique to the disease. Improved cell-based models leveraging advances in microphysiological systems like tissue chips or organ(s)-on-a-chip and organoids promise to deepen our understanding of disease mechanisms and are essential for developing personalized therapies.

2. Population and Disease Heterogeneity

Population and disease heterogeneity pose significant obstacles to drug discovery. Variability in genetic and demographic factors, such as age and sex, leads to markedly different responses to treatments across individuals when using human cells. Researchers must use models that represent diversity and include underrepresented ethnic groups. Additionally, the inherent heterogeneity of diseases themselves must be considered. Conditions such as cancer, neurodegeneration, COPD, diabetes, and cardiovascular diseases are multifactorial and complex, characterized by genetic and phenotypic diversity.

3. Drug Screening and Development

Innovative research approaches and advanced technologies for identifying and preclinically assessing drug candidates are needed to accelerate the development of new, more effective therapeutics and improve patient outcomes. The microgravity environment enables high-throughput drug screening in three-dimensional cell cultures and tissue models that more accurately simulate the human body's conditions, significantly bolstering the ability to advance drug screening and development. Additionally, the development of sensitive and specific diagnostic biomarkers is critical for the early detection and effective management of clinical conditions, which often lack reliable early indicators.

4. Drug Delivery

The therapeutic landscape, especially in oncology and respiratory therapy, faces challenges ranging from effective drug delivery to side effects management. Advanced technologies aim to enable precise drug targeting to minimize adverse effects and systemic exposure. In cancer treatment, delivering drugs without affecting healthy tissues is challenging. Innovations like nanotechnology and targeted therapies are vital for enhancing treatment precision. However, the absence of well-defined biomarkers complicates treatment selection, and the toxicity of treatments like chemotherapy necessitates balancing efficacy with side effects. These issues highlight the need for ongoing innovation in drug delivery and biomarker discovery to improve treatment outcomes.

5. Drug Resistance and Toxicity

Drug resistance poses significant challenges in treating diseases like cancer, diabetes, and COPD. In oncology, cancer cells can become resistant due to genetic mutations or changes in signaling pathways, decreasing drug efficacy. Similarly, in diabetes, prolonged use of medications often leads to insulin resistance and beta-cell failure. For COPD, continuous corticosteroid and bronchodilator use can result in tolerance, reducing effectiveness. Additionally, the toxicity of cancer treatments like chemotherapy requires careful management to balance efficacy and side effects. These issues highlight the need for

innovative strategies to develop more effective and sustainable treatments.

Proposals must demonstrate the necessity of using the ISS, including a statement describing how the scientific goals benefit uniquely from space. Proposals should review existing space-based research to enhance experimental design, aiming for novel and impactful results. Technical objectives should focus on advancing development or demonstration in space, targeting a technology readiness level (TRL) increase from TRL 4 to TRL 6 or higher. Proposals must outline milestones, provide timelines for product advancement, and include support letters from commercial partners to confirm feasibility or commercial interest.

ISS National Lab Implementation Partners, Facilities, and Capabilities

Offerors should be familiar with the capabilities of flight hardware for in-orbit studies that are relevant to their proposed scientific and technical objectives. Multiple facilities and services for research and technology development are available on the ISS. Facilities and services may be provided by NASA or by ISS National Lab [Implementation Partners](#). Existing flight hardware can be referenced on NASA's [Space Station Research Explorer website](#). Additional information is also provided in NASA's [ISS Researcher's Guide Series](#). The ISS National Lab partners with a variety of Implementation Partners—organizations that provide research, engineering, and technical services and, in some cases, operate and maintain commercial payload facilities on the ISS—to support and facilitate flight projects. For details about these providers and their specific hardware and services, visit our [Implementation Partner database](#). Where applicable, the ISS National Lab encourages communication between offerors and Implementation Partners prior to the submission of a Step 1A: Concept Summary to ensure receipt of accurate and current information required for budget and schedule estimates. If requested, the ISS National Lab can facilitate contact between Implementation Partners and offerors. Proposals to utilize facilities owned and operated solely by international partners on the ISS will not be considered for this research announcement. While it is not necessary to finalize the choice of Implementation Partner before submitting a Step 1A: Concept Summary, we strongly encourage offerors to select an Implementation Partner prior to submission of their Step 1B: Technology Roadmap.

Research Objectives and Priorities

The NLRA aims to accelerate scientific discovery, foster collaboration, and develop new technologies to benefit our nation and drive a robust, sustainable, and scalable LEO economy for terrestrial applications. This NLRA mainly focuses on R&D that advances cancer research and therapeutic development by leveraging microgravity or the space environment. However, proposals addressing other diseases that benefit from microgravity will also be considered. Key areas of interest include:

Automation and Standardization of Crystallization Processes

- **Objective:** Develop automation and standardization techniques for crystallizing small and large molecules in microgravity, including protein crystal growth for biologics.
- **Goal:** Improve protein structural unit definition, target site identification, drug resistance prediction, and the production, processing, and purification of active pharmaceutical ingredients (APIs) for terrestrial use.

Accelerated Human Disease and Cancer Tumor Models in Microgravity

- **Objective:** Develop and validate tumor models in microgravity that demonstrate improved

clinical relevance.

- **Goal:** Create bioengineered solutions to increase statistical sample size, accurately represent human population diversity, and enable iterative experimental trials in orbit.
- **Specific Areas of Interest:**
 - Patient-derived organoids from cancers such as ovarian, pancreatic, head, and neck to study drug response and resistance.
 - Micro-physiological systems (MPS) mimic the tumor microenvironment, including cells, extracellular matrix, immune components, and organ-on-a-chip models (brain, pancreas, lung, heart) to understand disease interactions and develop immunotherapies.

Significant Obstacles to Consider in MPS Development

- **Complexity and Standardization:** Challenges in replicating the intricate structure and function of human organs and tissues in vitro and the need for standardized protocols for reproducibility.
- **Scalability and Manufacturability:** Difficulties in scaling up MPS production for widespread research and industry use and the high costs associated with developing and manufacturing these systems.
- **Integration and Readout:** Integrating MPS with existing laboratory equipment and workflows and developing reliable, non-invasive methods to monitor cellular responses.
- **Biological Relevance and Validation:** Ensuring MPS accurately recapitulate human physiology and disease and validating models against in vivo human data.

Developing and Validating Accelerated Disease Models in Microgravity

- **Objective:** Use 3D tissue chips and organoid model systems to understand disease onset and progression in response to the spaceflight environment.
- **Goal:** Explore how these models can aid in developing novel therapeutics and drug delivery vectors for drug discovery and preclinical trials.

Early Disease Detection and Target Specificity

- **Objective:** Investigate in-space production applications (InSPA) for micro- and nanoparticle polymers.
- **Goal:** Use these particles for early disease detection, precision drug delivery, and developing "smart material" therapeutics, such as Janus nanoparticles.

Novel Approaches to Increase Clinical Relevance

- **Objective:** Leverage in-space biomanufacturing to develop computational and non-computational approaches that increase statistical significance and clinical relevance.
- **Goal:** Facilitate the development of population and personalized medicine through technological advancements.

The ISS National Lab offers R&D opportunities in LEO to advance scientific knowledge and foster value creation in economic, educational, scientific, and technical domains. By addressing a transformative national research goal defined by a technology roadmap, awardees will be expected to discuss how their project will foster education, training, and engagement opportunities to develop and inspire the next generation of researchers and professionals in biomedical research. By integrating educational outreach efforts, the ISS National Lab seeks to contribute to the growth of the workforce and encourage broader participation in cancer research and related fields. Each proposal must include a description of how the

dimensions of IDEA, including outreach, talent development, and workforce diversity, are to be addressed in the assembly of teams to execute the proposed R&D goals. Proposals must also describe how the proposed IDEA activities are key for mission success and will contribute to workforce development.

All proposals seeking to leverage the ISS National Lab must require and justify use of the ISS to conduct the proposed research. As such, proposals must include a statement defining how the scientific aims will benefit from execution in space and why the proposed investigation can only be performed in space. In addition, offerors are strongly encouraged to explore the literature for prior space-based R&D that may help improve their experimental design and deliver novel, high-impact results. Proposals must define technical objectives beyond basic concept validation and instead focus on seeking maturity through development and/or demonstration in the space environment. Desirable flight experiments will raise the technology readiness level (TRL) from 4 or higher to 6 or higher (see Appendix A for a description of TRL) and must describe milestones and the projected timeline to advance a product toward a viable market offering. The ISS National Lab strongly recommends obtaining and submitting letters of support from commercial partners and/or potential users of new technologies or products to demonstrate feasibility or commercial interest when applicable.

This NLRA employs a multi-step proposal process. It involves a concept submission and evaluation in Step 1A, an invited technology roadmap submission and evaluation in Step 1B, and an invited full proposal submission and evaluation in Step 2. If a proposal is selected for award, all phases of the project will include a gated review before each subsequent phase is approved. Therefore, all phases must be proposed in sequential order without overlapping phases. The gate reviews will assess progress toward achieving the objectives for each phase, as defined in the technology roadmap included in the proposal, and to evaluate the results from each flight opportunity. This multi-phased approach allows for careful selection, monitoring, and review of projects throughout their phases, ensuring that the proposed research aligns with the objectives and approach set forth in the proposal and the objectives of the ISS National Lab.

III. SUBMISSION AND SELECTION PROCESS

This research announcement will follow a multi-step proposal submission process as described above. What follows is additional detail on each step of the process.

Step 1A: Concept Summary Submission

- Concept summaries must be submitted electronically using the concept summary portal (a link to the portal is provided on the research announcement webpage). Offerors must complete all sections of the online concept summary form and attach requested documents.
- No concepts will be accepted after the Step 1: Concept Summary close date for a given cycle. Offerors may revise and resubmit the concept within the same cycle if received by the Step 1: Concept Summary close date.
- Concepts will be evaluated based on scientific and technical merit, business and economic merit, operational feasibility, and compliance with the research announcement.
- Concepts approved based on Step 1A: Concept Summary evaluation will proceed to Step 1B: Technology Roadmap by invitation only.
- Offerors not invited to submit a Step 1B: Technology Roadmap will receive feedback.

Step 1B: Technology Roadmap Submission

- Technology roadmaps must comply with the template and instructions provided on the research announcement webpage and online submission page.
- Submissions will consist of a technology roadmap narrative and a timeline Gantt chart breaking down the intended phases of the proposed project.
- Technology roadmaps will be evaluated in accordance with the criteria identified in the template and instructions.
- Feedback that CASIS provided to the offeror during the Step 1A: Concept Summary submission notification must be addressed in the Step 1B submission.
- No technology roadmaps will be accepted after the Step 1B: Technology Roadmap close date, listed on the research announcement webpage.
- Technology roadmaps approved based on Step 1B: Technology Roadmap evaluations will proceed to Step 2: Full Proposal by invitation only.
- Offerors not invited to submit a Step 2: Full Proposal will receive feedback.

Step 2: Full Proposal Submission

- The process for developing Step 2: Full Proposals is outlined in greater detail within the Proposal Instructions available on the research announcement webpage.
- Full proposals will be evaluated in accordance with proposal evaluation documents provided as attachments.
- At the end of Step 2: Full Proposal, the proposals recommended for selection will be presented for final determination to the CASIS chief executive officer, who is the selecting official.

Further details and requirements on Step 1A: Concept Summary, Step 1B: Technology Roadmap, and Step 2: Full Proposal submission, including instructions and templates, can be found in the Proposal Instructions document available on the research announcement webpage.

Award Information

CASIS may award a funded or unfunded agreement for a selected proposal. All awarded proposals will receive ISS National Lab sponsorship of ISS resource utilization, payload launch to the ISS, in-orbit ISS crew time, data return, and payload return, if required. Grant funding is not available for efforts that are solely ground-based efforts.

Funds Availability: The obligation of CASIS to make an award is contingent upon the availability of funds from which payment can be made. The number of grants awarded and the amount of grant funding for each award will depend on the number of meritorious applications received and favorably reviewed.

Funding for this Research Announcement: The total funding allocated by CASIS and the NASA Biological and Physical Sciences division for this research announcement is \$4 million, with an expectation to make two to three awards. Funding may be allocated to support all aspects of the project, including project management, hardware development, and/or Implementation Partner mission integration costs. We are seeking proposals that have funds provided by the offeror or a funding partner that match or exceed the funds requested through this solicitation. Offerors must provide commitment letters for all matching funds in their proposal (please see Proposal Instructions Criteria D-5 for details). CASIS reserves the right to refuse award of grant funding if no meritorious offers are received.

Indirect Cost Rates Policy: CASIS will allow any previously approved federal indirect cost rate that has

been negotiated between the grantee and a U.S. government agency. If no such rate has been negotiated with a U.S. government agency, CASIS shall apply a *de minimis* indirect rate of ten percent (10%) for those seeking indirect costs in a grant award. Also, CASIS will allow a grantee to voluntarily waive indirect costs or charge less than the full *de minimis* indirect cost rate should they choose to do so.

All proposal submissions seeking funding from CASIS are subject to this policy. All grantees are required to provide satisfactory written evidence in or accompanying their proposal submission of a previously approved federal indirect rate. Such evidence shall demonstrate the existence of an approved federally recognized indirect cost rate negotiated between the grantee and a U.S. government agency. In the absence of this evidence, CASIS will apply the *de minimis* indirect cost rate stated above.

Notice of Award: For selected proposals, a CASIS official will contact the principal investigator named in the proposal. Offerors have the right to be informed of the major factor(s) that led to the acceptance or rejection of their proposal.

Period of Performance: It is anticipated that the period of performance for all phases of a project will be no longer than three years from the date of award.

CASIS assumes no liability (including bid and proposal costs) for cancelling this NLRA or for any entity's failure to receive notice of cancellation.

IV. PROPOSAL PREPARATION AND CONTENT

Before submitting a Step 1A: Concept Summary, offerors are encouraged to identify and begin working with an Implementation Partner—organizations that work with the ISS National Lab to provide services related to payload development. There are two ways to identify an Implementation Partner:

- Visit www.issnationallab.org/implementation-partners to browse, select, and contact an Implementation Partner.
- Email the ISS National Lab Payload Operations team at Ops@ISSNationalLab.org for guidance.

Failure to work with an Implementation Partner before finalizing and submitting a Step 1B: Technology Roadmap could limit the potential for advancement to the full proposal phase, as Implementation Partners have knowledge and experience vital to the successful development of a roadmap.

Offerors are strongly encouraged to talk with an Implementation Partner about any aspects of their experiment that they deem significant beyond their standard description.

Before finalizing full proposals, offerors are strongly encouraged to consult with the ISS National Lab Payload Operations team for feedback regarding feasibility and compliance with flight requirements and capabilities. Please reference NLRA 2024-9 in the subject line and email ops@issnationallab.org. Please note that submitted questions and answers may be posted on the ISS National Lab website.

Offeror Qualifications

Proposals must be submitted by a Principal Investigator or an authorized official of the proposing organization. In addition, any business entity or institution capable of executing the proposed research may submit a proposal. However, CASIS will **ONLY** consider proposals from U.S. Persons (business and individual) as defined above. Regardless of who submits the proposal, all individuals listed as either the Principal Investigator or Co-Principal Investigator must be U.S. persons. In addition, the Principal Investigator's CV must demonstrate relevant expertise necessary to lead the investigation.

V. PROPOSAL EVALUATION AND SELECTION

Proposals will be evaluated under the ISS National Lab's review and selection criteria for its technology development and demonstration line of business. The proposal evaluation factors are scientific and technical merit, business and economic merit, funding and resource commitment, implementation and commercialization feasibility, and operations and ISS utilization. Each factor is numerically weighted and scored. Project cost is not scored but is a factor in the final selection. All submitted proposals must express a commercial purpose or intent. Proposals that are determined to better fit other CASIS research announcements will be redirected to those areas.

Please note that CASIS will not accept or consider proposals submitted by NASA or NASA civil servants.

The proposal review is guided by an overall assessment of expected project impact upon successful completion of proposed objectives. CASIS has overall responsibility for conducting and facilitating reviews, presenting information for final determination, and ensuring compliance with CASIS-defined processes. For further information on the proposal evaluation and selection, including the relative importance of each evaluation factor, refer to the ISS National Lab Proposal Evaluator Instructions in the information package linked to the NLRA 2024-9 research announcement webpage.

VI. CONTRACTING

Offerors will be required to enter into either a User Agreement (unfunded or Implementation Partner costs only) or Grant Agreement (funding granted to proposing organization to cover other costs, not only Implementation Partners) with CASIS, at the sole discretion of CASIS. CASIS is required contractually by the NASA Cooperative Agreement and by United States federal law, rules, and regulations to flow down various contractual terms and conditions to any award recipient. These terms and conditions, which are included in both CASIS Grant Agreements and CASIS User Agreements (regulated in part by the Federal Acquisition Regulations (FAR), 48 C.F.R., as well as by NASA-specific rules, regulations, and policies), are non-negotiable. If invited to submit a full proposal, offerors will be required to agree and accept these non-negotiable flow-down terms and conditions by completing and returning a cover page and a supplemental sheet during the proposal submission stage. Offerors that do not accept or fail to comply with these terms and conditions will not be considered for award, and may be rejected, at CASIS' sole discretion, for non-compliance with any other terms and conditions. If the Proposing Organization will be unable to agree to these terms and conditions and requires any changes, they must attach an addendum to their proposal entitled "Requested Revisions to Terms and Conditions" identifying the proposed change(s) and including clear and detailed reasoning for each requested change. The addendum must follow the format guidelines of the proposal and be submitted as a separate document attached as an addendum to the proposal submission (excluded from page count). There is a checkbox on the proposal cover page template and the online proposal submission form to indicate this request. Failure to reach an agreement on requested revisions prior to the CASIS project selection date (typically

60 days after proposal submission) may result in the rejection of this proposal with CASIS retaining the sole right to select the next favorable proposal. Additionally, if the offeror's organization intends to work with any collaborators, the offeror must contract with those collaborators and include the CASIS flow-down clauses. These terms and conditions from the NASA Cooperative Agreement will apply to all Grant Agreements and User Agreements. The User Agreement and Grant Agreement templates are provided as part of the Step 2: Full Proposal zipped documents made available to offerors via the ISS National Lab web page for this research announcement.

Appendix A: Technology Readiness Level Descriptions

Actual system “flight proven” through successful mission operations	TRL 9	<p>COMMERCIALIZATION</p> <ul style="list-style-type: none"> ▪ Product manufacturing ▪ Product sales <ul style="list-style-type: none"> • Roll out for real-world application/deployment <hr/> <p>TRIALS/SCALE-UP</p> <ul style="list-style-type: none"> ▪ Regulatory approval/certification ▪ Business analysis ▪ Market testing <ul style="list-style-type: none"> • Testing on subjects/commercial target ▪ Manufacturing development/scale-up <hr/> <p>DESIGN/PRODUCT REFINEMENT</p> <ul style="list-style-type: none"> ▪ New Applications, Product Improvements, and Line Extensions (NAPILEX; existing products) ▪ Product development/testing in advanced models ▪ Production development/optimization ▪ Product design/market research ▪ Business/market definition <hr/> <p>DISCOVERY/BASIC RESEARCH</p> <ul style="list-style-type: none"> ▪ Testing in validated early models (optimization to candidate) ▪ Science development (model development/market understanding) <hr style="border-top: 1px dashed black;"/> <ul style="list-style-type: none"> ▪ Fundamental research <ul style="list-style-type: none"> • Research leading to understanding of natural phenomena • Screening and testing in basic models to identify the target
Actual system completed and “flight qualified” through test and demonstration (ground or space)	TRL 8	
System prototype demonstration in a space environment	TRL 7	
System/subsystem model or prototype demonstration in a relevant environment (ground or space)	TRL 6	
Component and/or breadboard validation in a relevant environment	TRL 5	
Component and/or breadboard validation in a laboratory environment	TRL 4	
Analytical and experimental critical function and/or characteristic proof-of-concept	TRL 3	
Technology concept and/or application formulated	TRL 2	
Basic principles observed and reported	TRL 1	