Program Solicitation

Biological Technologies Office (BTO)

Generative Optogenetics (GO)

DARPA-PS-26-10

December 19, 2025

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PROGRAM SOLICITATION OVERVIEW INFORMATION

- **Federal Agency Name** – Defense Advanced Research Projects Agency (DARPA), Biological Technologies Office (BTO)
- **Funding Opportunity Title** – Generative Optogenetics
- **Announcement Type** – Initial Announcement
- **Funding Opportunity Number** – DARPA-PS-26-10
- **Dates**
  - Posting Date: December 19, 2025
  - Proposer Workshop: January 7, 2026
  - Questions Due Date: January 12, 2026 by 5:00 PM, Eastern Time (ET)
  - Abstracts Due Date and Time: January 16, 2026 by 5:00 PM (ET)
  - Oral Presentations Due Date and Time: By Government request, estimated 29 days after Abstract submission

The Defense Advanced Research Projects Agency (DARPA) is soliciting innovative concepts to design a protein complex that can be expressed *in vivo* (i.e., in a living cell) and responds to optical signals to synthesize a corresponding DNA or RNA sequence. This technology should enable massless transfer of genetic information to cells expressing the protein complex via a template-free mechanism that incorporates nucleotide bases in response to specific optical signals (e.g., different wavelengths of light). The GO program is focused on two main Research Objectives (ROs): (1) achieving the core capability of synthesizing DNA/RNA directly in living cells using optical signals, and (2) developing error mitigation methods that ensure high-fidelity nucleic acid synthesis. The acquisition process for GO will proceed through a two-stage process, starting with (1) written abstracts which will inform invitations to brief (2) an Oral Proposal Package (OPP) at DARPA.

- **Multiple awards are anticipated.**
- **Total Funding -** Phase 1 fixed price awards of $1.7M or $1.99M depending on RO selected. DARPA anticipates multiple awards for Phase 2.
- **Types of instruments that may be awarded** – Other Transaction (OT) for Prototype agreements
- **Agency Contact**

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- **Attachments**

  A: Abstract Summary Slide Template
  B: Abstract Template
  C: Model Other Transaction (OT) Streamlined, Fixed
  D: Cost Spreadsheet Template
  E. Representations and Certifications
  F: GO CUI Guide

PROGRAM SOLICITATION

Defense Advanced Research Projects Agency (DARPA)

Generative Optogenetics (GO)

1. Program Information

1.1. Background

Synthetic DNA and RNA are essential molecules for technologies that address critical global and national security challenges related to resilient supply chains, advanced materials manufacturing, agriculture, and human health. However, traditional methods for the *de novo* synthesis of DNA and RNA sequences are constrained by the size and complexity of the desired oligonucleotides, limited scalability, and environmental concerns. Current methods for nucleic acid synthesis fall into two categories: catalyzed by proteins (i.e., enzymatic) or synthetic chemistry. Naturally, cells replicate copies of their genomes and produce RNA via enzymatic processes, achieving remarkable speed and accuracy with error rates as low as 1 in 10^{10}. This fidelity is driven by mechanisms such as template-directed polymerization, proofreading freshly synthesized nucleic acids, and DNA mismatch repair. However, none of these processes are capable of *de novo* synthesis because they all require a nucleic acid template.

For template-free production of nucleic acids, chemical phosphoramidite synthesis is the gold standard. Considering the entirety of the phosphoramidite process, DNA and RNA synthesis rates can take 20–45 min per base with an error rate of 0.01 per base. Phosphoramidite synthesis is constrained by sequence length (200 bp for DNA, 40 b for RNA) and requires extensive downstream processing to make nucleic acids biologically compatible. Recent advancements in cell-free enzymatic synthesis have improved *de novo* synthesis rates to 1.3–10 minutes per base, with error rates ranging from 0.01 to 0.2 per base. However, enzymatic methods remain limited by fragment size and centralized production, requiring additional steps for assembly and delivery into cells. Furthermore, while approximately 70% of human protein-coding RNAs are ≤3 kb in length, current state-of-the-art methods cannot achieve single-shot synthesis of such sequences. Instead, substantial downstream efforts are required to assemble shorter fragments into longer protein-coding sequences, a process that must occur outside the cell. This process can take anywhere between 10 days to over a month. **No existing technology enables massless information transfer to relay genetic instructions to living cells. All current approaches require some mechanism predicated on moving matter that encodes the genetic information, typically DNA or RNA nucleic acids, across biological barriers like a cell wall/membrane.**

Generative Optogenetics (GO) program aims to create a molecular machine that can be expressed in living cells and provide a mechanism for transducing genetic information transmitted masslessly via optical signals into the nucleic acid sequences (DNA and/or RNA), which are the native information storage for all known life. Such a capability will create a direct interface between computers used to design genetic sequences and living cells that operate on those sequences. Technology developed on GO will enable precise influence over cellular behavior by facilitating genetic programing with single-cell spatial resolution, temporal precision to deliver different messages to a cell sequentially, and remote, scalable dissemination of genetic instructions.

At its core, GO addresses the high-risk challenge of developing a novel, open-ended genetic control platform that functions *in vivo* (i.e., within a living cell) to accelerate the transmittal of genes to living systems. If successful, this technology is anticipated to unlock a foundational capability with ramifications for medicine, agriculture, and manufacturing, while diminishing reliance on brittle supply networks that become untenable for long distance operations, like extended human spaceflight. GO is solely focused on building a proof-of-concept to address this high-risk challenge, but performers that meet the program's ambitious goals will pave the way for broadly transformative applications.

1.2. Acquisition strategy

Abstract submission deadline is anticipated to be January 16, 2026, 5:00PM (Eastern Time). Abstracts will be reviewed by the Government; if selected, the proposer will be asked to brief an Oral Presentation Package

(OPP). OPPs will be reviewed by the Government, and if selected, they may result in a Phase 1 award of an Other Transaction (OT) for Prototype (P) and eligibility to participate in future Phases of the program. As the GO acquisition strategy moves forward from abstracts to OPPs and finally to the Concept Design Review (CoDR) in Phase 1, DARPA expects that each team's approach to developing an optically controlled, template-free system for synthesizing nucleic acid sequences within living cells will solidify, and consequently, the performer teams' composition will become more finalized.

This PS encourages solutions from all responsible sources capable of satisfying the Government's needs, including large and small businesses, *nontraditional defense contractors* as defined in 10 U.S.C. § 3014, and *research institutions* as defined in 15 U.S.C. § 638.

To facilitate this objective, the Government will use the following acquisition process for GO:

1.2.1. Abstracts

Through the forthcoming program solicitation, the Government will require proposers to submit 5-page Abstracts as the first step in the acquisition process. The Government will review all submitted Abstracts to gain a high-level understanding of each proposing team's strategy to develop a prototype molecular machine capable of functioning in a living cell to transduce genetic information encoded in optical signals into protein-coding nucleic acid sequences. Predicated on the review of submitted abstracts for their technical comprehension and ability, the Government will decide to invite a subset of proposing teams to submit and brief OPPs in an Oral Presentation.

1.2.2. Oral Presentations

Upon the Government's request, proposers will have the opportunity to submit and present their OPP to the DARPA program team. The Government will evaluate all OPPs from teams whose abstracts were selected in the first stage of the acquisition process. Oral presentations of the OPP are required, and these will afford the Government an opportunity to ask clarifying questions of the briefing teams. The OPP, including the briefing, will provide the detailed information needed for Phase 1 selection decisions, requiring significantly more detail than the Abstracts. The Government anticipates that teams selected on the basis of the OPP will be given fixed-price OT-P awards to address Phase 1 goals/metrics over a 12-month period of performance.

While awards made following the OPP will be for Phase 1 only, the content of the OPP should describe each team's overall plan to develop their molecular machine, including planned Phase 2 effort, with particular emphasis placed on how the proposed Phase 1 effort will de-risk and refine the strategy for Phase 2. It is not expected that Phase 2 plans will be finalized at this time, but proposing teams should articulate a reasonably detailed draft, including a design and test plan for their proposed mechanism of transducing genetic information transmitted masslessly via optical signals into nucleic acid sequences. The draft Phase 2 plan should align to the goals of the program for demonstrating this transduction mechanism in a living cell. Based on this draft plan for Phase 2, the OPP must describe a set of clear, finalized Phase 1 tasks, and it must justify how these tasks will de-risk and inform the finalization of the Phase 2 plan by month 9 after award.

1.2.3. Phase 1 (12 months)

Performers will refine and de-risk their work plan for Phase 2. The revised work plan will be provided to DARPA in a written form (i.e. a Task Description Document, TDD, that may be included in the OT agreement) as well as in an oral presentation. All Phase 1 performers will present their final revised Phase 2 plans during the CoDR, scheduled approximately ~9 months after the Phase 1 agreement award.

1.2.4. Phase 2 (30 months)

This phase DARPA may be negotiated Phase 2 using the existing OT agreement from Phase 1. Performers advancing to this phase will execute their technical plan for developing a prototype molecular machine capable of functioning in a living cell to transduce genetic information encoded in optical signals into protein coding nucleic acid sequences.

1.3. Program Description/Scope

1.3.1. Overall Scope of the GO Program

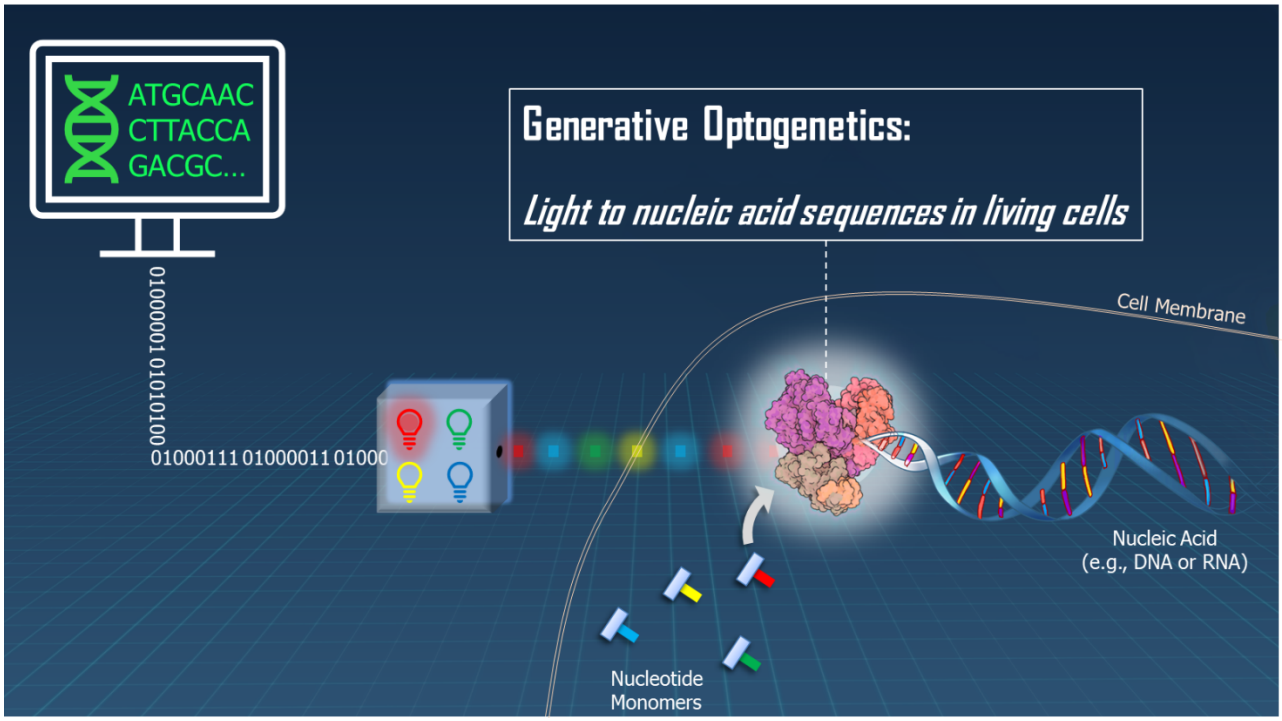

Figure 1. Overview of the GO program. The goal of the program aims to create a protein complex that is expressed within living cells, which converts optical signals (e.g., light pulses) into nucleic acid sequences that the cell can process using its natural transcription and translation mechanisms.

The DARPA GO program aims to develop a protein complex, referred to here as a nucleic acid compiler (NAC), that can be expressed within living cells to allow an end user to program genetic instructions into those cells, template-free, using nothing but light to transfer the genetic information to the cells (Figure 1). The central challenge of developing the NAC involves integrating protein domains / subunits for precise optical responsiveness (i.e., optogenetic domains), substrate binding, and enzymatic activity into a functional complex of proteins (i.e., a holoenzyme). While many of these domains have precedence as either engineered or naturally occurring proteins, the challenge lies in developing the interoperability and seamless integration of these domains into a functional holoenzyme, the NAC. Advances in computational design, which allow for accurate prediction of protein structures and binding interactions, are essential for optimizing substrate binding sites, allosteric interactions, and domain integration. These computational tools are crucial for designing the NAC to respond rapidly and predictably to optical signals, enabling the synthesis of long, accurate nucleic acid sequences that can precisely alter cellular function as intended. Moreover, expression of the NAC itself must not be deleterious to host cell function or viability.

To develop the NAC, the GO program consists of two Research Objectives (ROs):

1.3.2. Research Objective 1 (RO1): *De Novo* Synthesis

All GO performers MUST address RO1, which focuses on developing the core capability of the NAC for template-free DNA or RNA synthesis, where optical inputs precisely dictate the sequence of the nucleic acid produced by the NAC in a living cell. A NAC can be designed using a variety of architectures, ranging from extremes of a single, monolithic protein comprised of multiple domains to multi-unit complex (Figure 2). To accomplish this, performers will need to solve three critical challenges: achieving multiplexed optogenetic control, ensuring stability and the precise polymerization of the NAC-nucleic acid sequences, and successfully integrating the molecular components into the NAC.

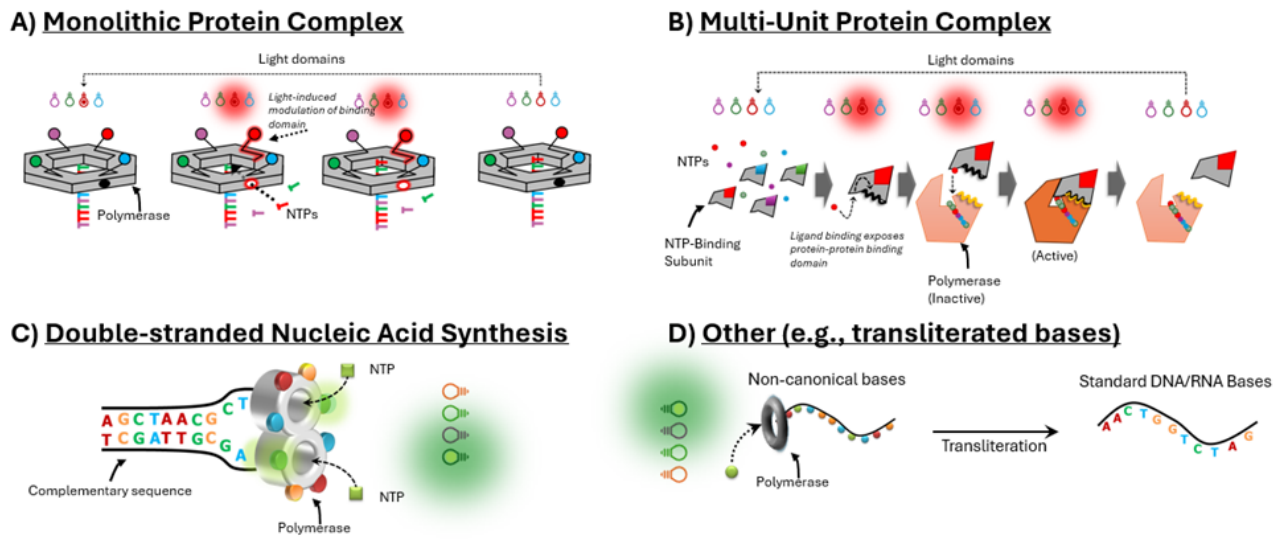

Figure 2. A non-exhaustive subset of possible high-level designs for a NAC.

1.3.2.1. Multiplexed Optogenetics

Achieving distinct multiplexed optical programming of the NAC presents a significant challenge, as it requires precise engineering of multiple protein domains capable of responding to distinct wavelengths of light. Currently optogenetic systems have been demonstrated to support up to three distinguishable wavelengths (red, green, and blue) within a cell, but expanding this capability is essential for enabling the NAC to incorporate nucleotides with high precision. This expansion may involve optimizing existing optogenetic domains or developing new ones with improved photophysical properties, such as enhanced spectral separation, faster on/off kinetics, and reduced phototoxicity. By leveraging photons as massless information carriers, these optogenetic domains must facilitate precise molecular motion and interaction, ensuring accurate nucleotide incorporation and enzymatic activity. Computational protein design tools and directed evolution approaches offer potential strategies to overcome these limitations, enabling the multiplexed optical control required for the NAC to function effectively.

1.3.2.2. Stable and Precise Polymerization

The NAC must achieve precise polymerization, including initiating synthesis, maintaining processivity to stabilize elongating nucleic acid sequences, and efficiently releasing the synthesized strand to meet program metrics for length and accuracy. The NAC design may need to include strategies to address the challenge of selectively binding the correct nucleotide substrate at the correct time from the mixture of these substrates that exists within the cellular environment. Overcoming this challenge will be necessary for the NAC to achieve desired sequence accuracy metrics for the GO program. Additionally, the stability of the complex formed between the NAC and the nucleic acid sequence it is synthesizing must be sufficient to avoid unwanted dissociations that will result in truncated sequences. Similarly, NACs that synthesize single-stranded nucleic acids will need to overcome issues associated with secondary structures (e.g., hairpin loops) in the DNA/RNA molecule that could interfere with continued synthesis. Achieving stable NAC-based nucleic acid synthesis may necessitate designs that incorporate accessory subunits/domains to improve processivity by holding on to the newly synthesized strand and/or single-stranded binding proteins/domains that hinder the formation of problematic secondary structure in DNA/RNA molecules. Finally, the performers will need to resolve the challenge of releasing synthesized sequences, which may involve strategies such as natural termination signals or engineering inducible cleavage mechanisms.

1.3.2.3. Integration of Molecular Components

A fully functional NAC must integrate optogenetic, substrate binding, catalytic, and other domains into a cohesive holoenzyme capable of precise and predictable operation. This integration presents significant

challenges, as the domains must interact seamlessly to ensure accurate nucleotide incorporation and overall system functionality. For example, optogenetic domains may need to regulate substrate binding to ensure that nucleotide incorporation into the DNA or RNA sequence aligns precisely with the optical illumination pattern. Similarly, designs involving protein subunit binding must coordinate these interactions with substrate binding domains to maintain synchronization and fidelity. Addressing these challenges may involve strategies such as identifying domains that interact effectively to control the NAC, ensuring synchronous activation and deactivation of multiple NACs within a living cell, and optimizing domain interfaces for efficient communication. Potential approaches include leveraging computational tools to map allosteric pathways, modeling molecular motion to predict domain interactions, and employing high-throughput empirical methods to refine and validate integration strategies.

1.3.3. Research Objective 2 (RO2): Error Mitigation

OPTIONAL, GO performers may elect to address RO2 in addition to RO1. Note that GO performers shall not pursue RO2 without addressing RO1. RO2 addresses the challenge of achieving high-fidelity synthesis in NACs by incorporating mechanisms to detect and filter out sequence errors. Some applications of GO technology will necessitate NACs capable of synthesizing longer sequences, and it is anticipated that increasing the length of the sequence will increase the likelihood it contains errors. To this end, RO2 aims to investigate the tradeoffs involved in designing a NAC with enhanced error detection capabilities to meet stricter error tolerance requirements, including how these design choices impact overall NAC performance. There are several potential approaches to address RO2 (Figure 3), an example includes developing double-stranded synthesis methods that incorporate components such as mismatch-binding proteins (e.g., MutS homologs). These proteins can either flag errors for downstream correction or be engineered to degrade faulty sequences, ensuring that only high-fidelity nucleic acid strands are retained. Other strategies may include utilizing base editors to identify nucleotide incorporation errors or synthesizing palindromic sequences that fold onto themselves to increase error detection. RO2 provides an opportunity to explore innovative solutions to error mitigation while considering the tradeoffs in performance, complexity, and scalability inherent to these approaches.

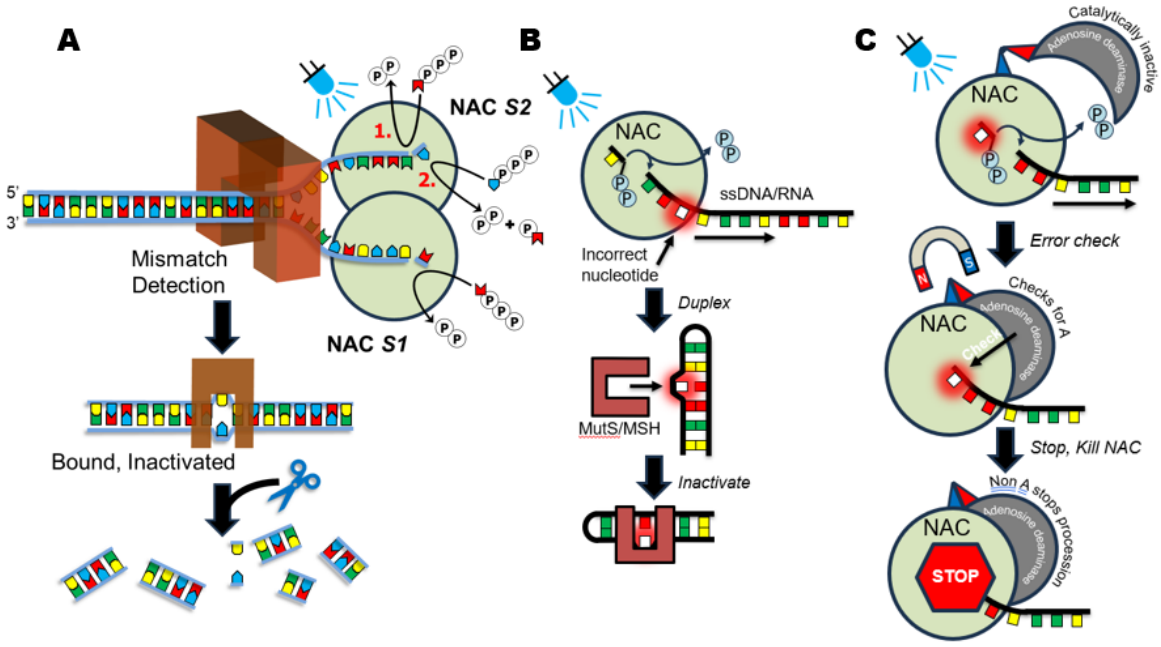

Figure 3. Notional non-exhaustive and non-mutually exclusive set of mechanisms for introducing error detection and mitigation to a NAC design. A, NACs synthesizing double-stranded molecules could include mechanisms based on base-pair mismatch detection; B, palindromic nucleotide sequences could be interleaved with mismatch detection inspired mechanisms; C, iterative toggling between a 'write' and 'error recognition' mode. Proposals should clearly explain their approach along with its relative strengths and weaknesses.

1.3.4. Program Constraints / Out of Scope

To ensure alignment with program objectives, certain approaches are deemed out of scope. Specifically, the program will not support bioprospecting to identify or characterize wholly new domains or proteins from natural systems, nor exploratory work focused on phenomenological or mechanistic characterization of novel proteins that respond to light or other physical signals. Additionally, approaches requiring *in vitro* synthesis steps, such as lysis and ligation/annealing of smaller oligonucleotides, are excluded, as are designs seeking to create entire systems that operate in-parallel to the central dogma. While synthesis of nucleic acid sequences built from non-canonical bases is permissible, these sequences must be converted into canonical DNA/RNA for transcription or translation by the host cell's existing enzymes. While GO performers may work in most common cell chassis including yeast, bacteria, plants, immortalized mammalian cell lines (e.g., HEK293, CHO, etc), or human induced pluripotent stem cells (iPSCs), the development of the NAC in embryonic stem cells (ESCs) is explicitly prohibited. No genes that are export-controlled or restricted for biosafety reasons will be within scope. Furthermore, substantial hardware development, including novel optical systems or sequencing platforms, is unnecessary for success on GO and is therefore excluded. Tasks to develop or discover completely novel mechanisms for error mitigation or physical signal modalities are also out of scope, though additional physical signal modalities beyond optical signals may be considered if scientifically justified and plausible within a transitional use case. All human subjects research and animal subjects research is explicitly out of scope for GO.

1.3.5. Program Structure

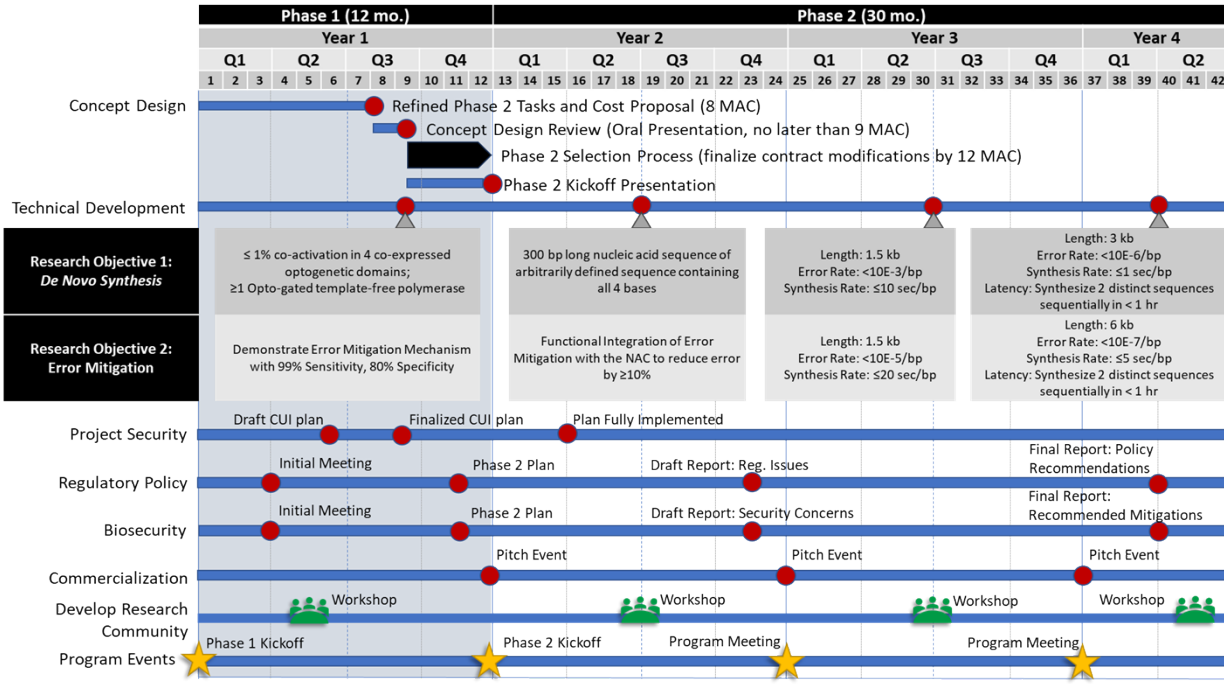

Figure 4. The GO program structure.

The GO Program will proceed across two phases spanning a total period of performance of 42 months. Phase 1 (12 months) focuses on refining molecular components and de-risking integration strategies, while Phase 2 (30 months) focuses on integration and demonstration of the NAC platform *in vivo*.

1.3.5.1. Phase 1 (12 months)

During Phase 1, performers will focus on refining and demonstrating the critical molecular components necessary for a functional NAC, including optogenetic domains, enzymatic polymerization, and error mitigation mechanisms. This phase is structured to culminate in a month 9 technical milestone (section 1.3.7),

providing teams with an opportunity to de-risk their technical approach before advancing to the more complex integration work required in Phase 2. Phase 1 also allows teams to address any capability gaps identified through their progress and make adjustments to their approach. For example, experimental results from Phase 1 may reveal the need for additional expertise or resources, which can be addressed by reorganizing the team, such as adding a Co-PI or sub-awardee for Phase 2. This expertise could come from other Phase 1 participants or external collaborators. The final three months of Phase 1 will focus on the initial integration of technologies into a prototype NAC.

1.3.5.2. Concept Design Review (CoDR; month 9)

Performers must present a refined Phase 2 plan during a CoDR at month 9, including any planned restructuring of their team. The CoDR serves as a critical down-selection point, requiring performers to present compelling technical plans supported by demonstrable progress in Phase 1 to de-risk those plans. At the CoDR, performers will need to communicate a project plan, including any changes in teaming, to establish confidence that the technical work is achievable within the required timeframe for the program. Key technical and project risks will be evaluated to ensure that only the most viable and impactful approaches are selected to advance, contributing to the overall success of the program. The presentation and accompanying written material on the performer's concept at the design review will include a refined Phase 2 strategy, complete work plan and cost proposal for the revised Phase 2 work plan, a Science and Technology Protection Implementation Plan for safeguarding program components, and a data rights plan (section 1.3.6).

1.3.5.3. Phase 2 (30 months)

Phase 2 focuses on integration of the components developed in Phase 1 to create a functional NAC and ultimately demonstrate functionality within a living cell. The first major technical milestone in Phase 2 (month 19) requires performers to demonstrate their NAC design either cell-free (*in vitro*) or *in vivo*. However, by the second milestone (month 31) all demonstrations for both RO1 and RO2 must be completed within a living cell, showcasing the full functionality of the NAC platform. Components of research conducted in Phase 2 will be categorized as controlled unclassified information (CUI) since a functional NAC will have similar metrics to export controlled synthesizers.

1.3.5.4. Additional program events

Program Workshops*:*

Phase 1: To support the development of a research community around GO technology and to facilitate team refinement during Phase 1, the program incorporates a DARPA-sponsored workshop scheduled for month 5. All Phase 1 performers will be required to present their research at this event, which will also be open to relevant research communities beyond GO performers. The workshop will serve as a platform for performers to identify talent to augment their teams and foster discussions on barriers to adoption and ethical development of GO technology. DARPA will determine attendees, but Phase 1 performers will provide statements of interest/disinterest regarding abstracts submitted by non-performers to inform whether their presentations align with GO program goals.

Phase 2: Workshops will continue annually in Phase 2 to accelerate GO technology adoption and expand its impact. These events will showcase performer progress and remain open to the broader community to help address challenges and identify organizations with critical capabilities. While team restructuring becomes more challenging in Phase 2, the month 19 workshop will support this process. Performers will be expected to continue providing feedback to DARPA in the form statements of interest/disinterest on research synopsis submitted by the broader community regarding their interest in proposed presentations. Workshops in months 31 and 41 will increasingly emphasize commercial and research applications of GO technology, focusing on transitioning fundamental advancements beyond the program's scope.

Pitch Events:

Technologies emerging from GO will have an enormous range of potential applications, likely necessitating

the commercial transition from the program. Beginning in Phase 1, performers will develop commercialization strategies with the guidance of the Independent Commercialization and Consulting Group (ICCG; Section 1.5.3). Performers will be expected to attend commercialization workshops that begin in Phase 1 and present their business hypotheses at "Pitch Events" starting in Phase 2. These workshops and Pitch Events will be hosted by the ICCG throughout the program and GO performers will be expected to progressively revise their commercialization strategy. Importantly, the ICCG workshops and Pitch Events are a program-wide resource to aid technical performers in developing ideas and strategies to commercialize the technology they develop on GO.

1.3.6. Program Security

Phase 1: Will be conducted as unclassified fundamental research, allowing teams the flexibility to de-risk and refine their technical approaches. However, performers must submit a draft Phase 2 CUI S&T PIP by month 6, with a finalized version due by month 9. This plan must include a timeline for acquiring CUI-compliant systems and equipment, data protection requirements, and other security measures.

Phase 2: Will require performers to implement the S&T PIP to safeguard all information, materials, and processes generated during the program, particularly the DNA sequence of the NAC. Performers are subject to controls outlined in the program-specific CUI guide, which provides a framework for identifying, protecting, and marking CUI in accordance with DoD policies and security classification guides. The scope of protection includes all aspects of NAC sequence development, design, optimization, and integration into living cells, with strict prohibitions on public disclosure or publication of the NAC sequence.

Throughout the program performers are encouraged to publish findings, however, all publications, external engagements, and investor discussions must be coordinated with DARPA and the Program Security Officer (PSO) to ensure compliance with CUI guidelines and export control regulations. Additionally, all publications must be submitted to DARPA's Public Release Center (DISTAR) for review and approval prior to public dissemination.

All individuals accessing CUI information must complete approved training and ensure that sensitive information is safeguarded on systems compliant with NIST 800-171 standards. This security strategy balances the need for commercialization with the protection of sensitive information, ensuring the program's success. A detailed CUI guide is provided as an attachment to this solicitation and further described in section 5.2.

1.3.7. Program Metrics

Table 1. GO program metrics and milestone by RO.

	Research Objectives	
Program Milestones:	**RO1: De Novo Synthesis**	**RO 1 + 2: Error Mitigation**
Phase 1: Month 9 Advancement Criteria	In vitro demonstrate: • ≤ 1% co-activation in 4 co-expressed optogenetic domains • ≥1 Opto-gated template-free polymerase	In vitro demonstrate: • ≤ 1% co-activation in 4 co-expressed optogenetic domains • ≥1 Opto-gated template-free polymerase In vitro demonstrate: error mitigation mechanism with 99% sensitivity, 80% specificity
Phase 2: Month 19 Milestone	In vitro or in vivo demonstrate: • 300 bp long nucleic acid sequence of arbitrarily defined sequence containing all 4 bases	In vitro or in vivo demonstrate: • 300 bp long nucleic acid sequence of arbitrarily defined sequence containing all 4 bases In vitro: functional integration of error mitigation with the NAC to reduce error by ≥10%
Phase 2: Month 31 Milestone	In vivo demonstrate: • Length: 1.5 kb • Error Rate: <10E-3/bp • Synthesis Rate: ≤10 sec/bp	In vivo demonstrate: • Length: 1.5 kb • Error Rate: <10E-5/bp • Synthesis Rate: ≤20 sec/bp
Phase 2: Final Metric	In vivo demonstrate: • Length: 3 kb • Error Rate: <10E-6/bp • Synthesis Rate: ≤1 sec/bp • Latency: Synthesize 2 distinct sequences sequentially with < 1 hr between the 1st and 2nd sequence	In vivo demonstrate: • Length: 6 kb • Error Rate: <10E-7/bp • Synthesis Rate: ≤5 sec/bp • Latency: Synthesize 2 distinct sequences sequentially with < 1 hr between the 1st and 2nd sequence

The GO program contains four major technical milestones spread across the two program phases, and each of these milestones are associated with a set of quantitative metrics (Table 1) designed to assess technical progress on the program. Ultimate success on the program involves meeting or exceeding the final metrics in Phase 2 via NAC design that functions in a living cell (i.e., *in vivo*) to synthesize nucleic acids template-free. Of note, the metrics listed in Table 1 represent the minimal set of metrics used to define success on the program, and these DARPA-defined metrics are system-level requirements that are generally agnostic to performer-specific approaches. Proposing teams are strongly encouraged to include additional quantitative metrics to characterize success reflective of specific aspects of their unique NAC design. Similarly, DARPA reserves the right to include additional metrics to awards on a per team basis as necessary to manage risks unique to individual teams' different technical strategies for designing a NAC.

1.3.7.1. Phase 1 metrics

In Phase 1, RO1 focuses on de-risking the integration of NAC components and demonstrating critical capabilities. By month 9, all performers must demonstrate optogenetic domains capable of responding to at least four distinct wavelengths of light with minimal (≤ 1%) co-activation. Meeting this milestone will establish the minimal amount of confidence required to advance teams to Phase 2 because co-expression of multiple optogenetic domains will be required to enable precise incorporation of each nucleotide base into a nucleic acid sequence. Additionally, performers must show that these optogenetic domains can be integrated into a polymerase to control its function. This integration is essential to show that the optogenetic domains can regulate nucleotide incorporation in response to optical signals, which is a critical step in de-risking the development of the NAC for Phase 2.

Performers pursuing RO2 must meet the RO1 metrics, and they must also demonstrate a mechanism for error detection that is highly sensitive. When multiple NACs are expressed in a single cell, less specific error detection mechanisms may mistakenly label correct sequences as errors, reducing the yield of sequences per cell. The metrics for RO2 are established under the assumption that over assessing errors will limit yield of sequences per cell, if error containing sequences are filtered out of the population. However, the hindrance on yield could be overcome by increasing the expression level of NAC proteins in the cellular chassis. Thus, RO2 metrics at this milestone are established to bias development toward highly sensitive approaches. All Phase 1 must be achieved using *in vitro* (cell-free) preparation, with optional *in vivo* results for additional validation. The final three months of Phase 1 will focus on initial integration of technologies into a prototype NAC and preparation for Phase 2.

1.3.7.2. Phase 2 metrics

Phase 2 builds on Phase 1 progress and focuses on developing a fully functional NAC capable of synthesizing nucleic acid sequences *in vivo*. By the month-19 milestone, RO1 performers must demonstrate a NAC capable of integrating four optogenetic domains to regulate nucleotide incorporation into a 300-mer oligonucleotide. RO2 performers must additionally show a 10% relative reduction in error compared to designs without error mitigation mechanisms. For RO1, the month-19 milestone can be achieved through either *in vitro* or *in vivo* experiments; however, RO2 performers must demonstrate error reduction metrics using *in vitro* data.

Metrics for the months 31 and 41 milestones require performers to demonstrate synthesis of longer nucleic acid sequences (up to 6 kb for RO2) with significantly reduced error rates. RO2 metrics supersede RO1 metrics at these milestones, with relaxed synthesis rate requirements to accommodate error mitigation mechanisms. All month 31 and 41 milestone data must come exclusively from *in vivo* experiments. A key attribute of GO systems is their ability to achieve short-latency sequential transmission of multiple genetic sequences to living cells. As part of the month 41 milestone, all GO performers must demonstrate the capability to write two distinct nucleic acid sequences to the same cell or population of cells, with less than 1 hour required to reset the system between write events. Error rate metrics for the months 31 and 41 milestones represent absolute maximum error rates but do not prescribe sequence-specific error rates. Performers will be required to characterize sequence-specific error rates, particularly for sequences known to be problematic for *de novo* synthesis technologies, such as those with high GC content. Additional guidance and a common set of test

sequences will be provided by DARPA in Phase 1 ahead of the CoDR, allowing performers to refine their approaches to address sequence-specific challenges *in vivo*.

1.3.8. Program Milestones & Deliverables

A detailed breakdown of tasks, deliverables and reporting requirements are presented in Table 2. In addition to the milestones listed below, performers will be expected to provide monthly and quarterly status updates to DARPA, including technical and financial summary reports.

Table 2. GO Milestones and Deliverables.

Phase 1 (12 mo.)		
Month	**Milestone**	**Deliverables/Exit Criteria**
1	Phase 1 Kickoff	Slides detailing the Phase 1 project plan and summarizing the initial plan for Phase 2.
5	Workshop #1	Approximately 8 weeks (40 working days) prior to the workshop, provide interest/disinterest feedback on research synopses submitted by the broader community to DARPA. At least 3 weeks (15 working days) prior to the workshop, performers will submit slides to DISTAR and provide them to DARPA: Present at a DARPA-hosted workshop slides including details of their technical plan highlighting risks and potential gaps in approach/design to help identify potential organizations not selected for Phase 1 that may possess critical technologies to support their technical plan.
6	There is No Milestone Associated with this Deliverable	Submit a Phase 2 CUI S&T PIP, to include a timeline for acquiring CUI compliant equipment/systems, data requirements, etc.
8	There is No Milestone Associated with this Deliverable	Revised Phase 2 Task Description Document (TDD) for pursuing either RO1 or RO2. Cost Proposal for Phase 2. Slides for refined Phase 2 plan that include details for all experimental components, timeline for development, expected costs for Phase 2, potential risks and mitigation strategies, team capabilities, and notional transition plan for commercialization. Highlighting any changes from initial proposal.
9	Technical Milestone #1	Technical report on molecular components developed for NAC design assembly, focused on performer-specific RO metrics. Note: Performers selecting RO2 must also demonstrate RO1 metrics. RO1 & RO2: Demonstrate *in vitro* ≤ 1% co-activation in 4 co-expressed optogenetic domains and construct ≥ 1 Opto-gated template-free polymerase RO2 only: Demonstrate *in vitro* error mitigation mechanisms with 99% sensitivity and 80% specificity

	Concept Design Review (CoDR)	Present slides for refined Phase 2 plan and review TDD and Cost Proposal with DARPA. Finalize CUI S&T PIP and get approval from DARPA.

No Later Than 12	Phase 1 Final report	All performers: Phase 1 final report. For performers selected to advance to Phase 2, all agreements and sub-agreements required for Phase 2 work are fully executed. For performers selected to advance to Phase 2, briefing slides for Phase 2 Kickoff (at least 1 week in advance of meeting) and a draft pitch deck for the Pitch Event.
Phase 2 (30 mo.)		
Month	**Milestone**	**Deliverable/Exit Criteria**
13	Phase 2 Kickoff and Pitch Event #1	Kickoff presentation of detailed technical plan, including preliminary data generated in Phase 1. Pitch deck slides; Present a business hypothesis for *in vivo* de novo nucleic acid synthesis capabilities that could be commercialized, either by venture creation or integration into an existing business; identify a value proposition for a NAC that addresses a market need.
15	There is No Milestone Associated with this Deliverable	Fully execute CUI S&T PIP.
19	Technical Milestone #2	Technical report on NAC assembly and initial performance, focused on performer-specific RO metrics. Note: Performers selecting RO2 must also demonstrate RO1 metrics. Performers addressing RO1 should include justification of assay choice (e.g. *in vitro* vs *in vivo*). RO1: Demonstrate *in vitro* or *in vivo* synthesis of >300 bp-long nucleic acid sequence of arbitrarily defined sequences containing all four bases. RO2: Demonstrate *in vitro* functional integration of error mitigation with the NAC to reduce error by 10%
	Workshop #2	Approximately 8 weeks (40 working days) prior to the workshop, provide interest/disinterest feedback on research synopsis submitted by the broader community. At least 3 weeks (15 working days) prior to the workshop, performers will submit slides to DISTAR and provide them to DARPA: Present at a DARPA-hosted workshop that communicates technical progress and current challenges.
25	Program Meeting	Slides; Technical presentation on performer specific ROs.
	Pitch Event #2	Pitch deck slides; Present a refined business hypothesis and value proposition for a NAC platform, including target market sizing and segmentation, possibilities for a minimum viable product, analysis of alternative approaches, and evaluation of partnership needs for advanced technology development.

31	Technical Milestone #3	Technical report on *in vivo* functionality of the NAC, focused on performer-specific ROs. RO1: Demonstrate synthesis of 1.5 kb-long nucleic acid sequence with an error rate less than $1x10^{-3}$ / bp and a synthesis rate less than or equal to 10 sec / bp. RO2: Demonstrate synthesis of 1.5 kb-long nucleic acid sequence with an error rate less than $1x10^{-5}$ / bp and a synthesis rate less than or equal to 20 sec / bp.
	Workshop #3	Approximately 8 weeks (40 working days) prior to the workshop, provide interest/disinterest feedback on research synopses submitted by the broader community to DARPA. At least 3 weeks (15 working days) prior to the workshop, performers will submit slides to DISTAR and provide them to DARPA: Present at a DARPA-hosted workshop that communicates technical progress and current challenges.
37	Program Meeting	Slides; Technical presentation on performer-specific ROs.
	Pitch Event #3	Pitch deck slides; Present a polished pitch showcasing developed NAC technology to investors that includes a specific ask for follow-on investment (e.g. raise estimate needed) or identifies a transition partner that would enable commercialization.
41	Technical Milestone #4	Technical report on *in vivo* functionality of the NAC, focused on performer-specific ROs. RO1: Demonstrate synthesis of 3 kb-long nucleic acid sequence with an error rate less than $1x10^{-6}$ / bp and a synthesis rate less than or equal to 1 sec / bp. Synthesize two distinct sequences sequentially with < 1 hr between the 1st and 2nd sequence. RO2: Demonstrate synthesis of 6 kb-long nucleic acid sequence with an error rate less than $1x10^{-7}$ / bp and a synthesis rate less than or equal to 2 sec / bp. Synthesize two distinct sequences sequentially with < 1 hr between the 1st and 2nd sequence.
	Workshop #4	Approximately 8 weeks (40 working days) prior to the workshop, provide interest/disinterest feedback on research synopses submitted by the broader community to DARPA. At least 3 weeks (15 working days) prior to the workshop, performers will submit slides to DISTAR and provide them to DARPA; Present developed GO technology at a DARPA-hosted workshop aimed at aligning commercialization strategies with regulatory and national security considerations.
42	Final Report	Final report: content will include (but is not limited to) a detailed and comprehensive summary of approaches, data from all relevant milestones and metrics, limitations of technical solutions, and potential future directions.

1.4. Technical Guidelines for Proposals

As discussed in section 1.2 above, DARPA's staged acquisition approach for the GO program enables agile management and control of technical risks. With each stage (i.e. abstracts, OPPs, Phase 1), DARPA expects technical approaches and team composition to evolve and solidify. 2.1 belowThis section discusses specific content required for preparing abstracts and/or OPPs in the context of the GO program's technical goals and milestones, while section 2.1 below provides procedural guidance. In addition to these sections, Appendix A

provides a preparation checklist addressing all solicitation requirements.

Abstracts are required to provide high-level descriptions of proposed NAC designs and Phase 1 technical plans that will enable DARPA to assess whether the innovation and feasibility of the proposed ideas merit additional discussion in the OPPs. By contrast, OPPs must include detailed Phase 1 plans and justify these plans in the context of Phase 2 goals to make it clear how Phase 1 work will aid in the refinement and finalization of the Phase 2 by the CoDR at month 9. The Oral Presentation itself affords the Government with an opportunity for deeper discussion with a proposing team about their proposed approach to develop a NAC. Both abstracts and OPPs must clearly describe how their proposed approach addresses each of the challenges associated with RO1 and RO2, if applicable, detailed in sections 1.3.1 – 1.3.3 above. In their OPP, proposing teams must discuss any approach-specific challenges requiring resolution on the Phase 1 as part of their justification for the proposed Phase 1 work. Proposing teams may pursue multiple approaches for risk mitigation, but they must clearly describe their primary NAC development strategy and prioritize any additional approaches. Approach-specific challenges identified should be accompanied by a detailed risk mitigation strategy provided in the OPP that is in alignment with meeting program metrics on schedule.

As described in sections 1.3.1 – 1.3.2 and Figure 2 above, any NAC design addressing program metrics is acceptable, provided:

1. The resulting NAC can function inside a living cell to synthesize nucleic acid sequences with light (i.e., an optical signal) as the sole source of information encoding the nucleic acid sequence. Abstracts and OPPs must discuss how this could be achieved with their proposed NAC design.
2. The resulting system (i.e., the cell engineered to express the NAC) does not require any exogenous substrates (e.g., engineered, non-canonical nucleotides) beyond H, C, N, O, S and P containing molecules that are typically included in standard broth or media. However, cell lines may be engineered to synthesize substrates for the NAC, if these are not produced by the cell's native metabolism. Abstracts must state any metabolic engineering requirements, and OPPs must detail these strategies.
3. The NAC and/or resulting cellular system incorporates plausible, synchronous activation/deactivation strategies for population-level control of optical signal transduction by NACs expressed inside a cell. Abstracts should provide a high-level overview of the team's approach and discuss how it will support both synchronous initiation of NAC-based transduction and deactivate to eliminate unwanted transduction. OPPs must discuss notional mechanisms and any Phase 1 work necessary to de-risk or revise the approach. Proposers are strongly encouraged to consider mechanisms that will facilitate overall security of the resulting system by pursuing approaches that minimize inadvertent (i.e. non-specific) activation of the NAC.
4. The NAC is designed for *in vivo* single-shot synthesis of long, coding nucleic acid sequences capable of modulating cellular function via translation into functional proteins that results in quantifiable effect on the cell (e.g., expression of a reporter, secretion of a molecule, cell division, differentiation, etc). Approaches requiring *in vitro* steps to obtain the desired sequence (e.g., oligonucleotide synthesis within cells followed by lysis and ligation/annealing *in vitro*) are out of scope for GO. Abstracts and OPPs must be clear that their NAC design is capable of *in vivo* single-shot synthesis, and OPPs must discuss a notional Phase 2 plan for how they intend to test the ability of NAC-derived sequences to affect cellular function.
5. Genetic messages produced by the NAC must intersect with the cell's natural machinery for producing RNA and/or protein. Thus, approaches seeking to design entire systems that operate in parallel to the central dogma are out of scope. However, approaches using non-canonical bases may be permissible if abstracts and OPPs provide: 1) plausible, known means of engineering host cells to synthesize all required non-canonical bases and 2) a known mechanism for transliterating these bases into a canonical DNA or RNA sequence. Proposers taking this approach must provide clear evidence as part of their OPP for the feasibility of the metabolic pathways and transliteration mechanism, and this

evidence must include proof that the enzymatic machinery to perform these functions is known.

Both abstracts and OPPs must provide a clear conceptual mechanism for the final NAC they aim to develop in Phase 2 and articulate necessary Phase 1 de-risking plans. All submissions must specify whether they intend to develop a NAC that will synthesize RNA or DNA, single-stranded or double-stranded molecules, utilize canonical nucleotides (ATP, GTP, etc) or non-canonical molecules, etc. Both abstracts and OPPs should clearly describe the approach to synchronize initiation and termination of synthesis across a population of NACs expressed within a living cell, and they should discuss the primary cell line that the team intends to use for the NAC. The choice of cell line should be justified both scientifically and in terms of a notional use case (i.e., commercial transition or clinical translation that could follow successful development of the NAC on the GO program). The OPP should discuss any additional cell lines required for development or risk mitigation strategies. If different cell lines are proposed for Phase 1 development compared to the final Phase 2 design, the OPP should explain its relevance and how it will yield insights that de-risk development for Phase 2 work.

Proposals submitted for RO2 must also address RO1. Proposals responding solely to RO2 will be deemed non-compliant with this PS, and they will be excluded from review. RO2 proposals must be explicit in their intent to respond to both ROs in their abstract and OPP. Additionally, RO2 proposals must clearly describe their primary approach to error mitigation along with any supporting strategies. If RO2 teams propose a combinatorial strategy for error mitigation that combines several mechanisms to reduce error rates, their abstracts must clearly indicate this intent, and their OPP should include an experimental plan to evaluate both the combined mechanism and individual components in isolation. Ideally, these proposals will also include Phase 1 work plans to simplify (i.e., down-select) error mitigation mechanisms for integration in Phase 2. Proposals are not required to make their technical approach to RO2 severable from their RO1; however, all submissions should clarify whether or not, and to what extent, their RO2 approach is separable from their RO1. All submissions must distinguish which elements of proposed Phase 1 work address RO1 and which address RO2.

Abstracts should discuss alternative strategies to de-risk and revise NAC development plans for Phase 2, whereas OPPs must include a detailed risk analysis and mitigation plan for Phase 1. Additional guidance on the risk analysis and mitigation plan will be provided to teams after they submit their abstracts. While it is anticipated that only a subset of Phase 1 teams will move on to Phase 2, proposals in response to this solicitation should include plans to use the last three months of Phase 1 in preparation for Phase 2. This plan for the last three months of Phase 1 should be reflected in the error mitigation plans included in the OPP.

Overall, proposing teams should justify the feasibility of their proposed NAC design and development approach using as much prior art as possible. This prior art includes evidence related to the constituent protein domains intended for integration into their NAC as well as computational, rational, and empirical methods for achieving novel functions through domain integration. Preliminary data on the NAC itself is not required in abstracts of OPPs. While it would be welcomed during the review process, the program is structured to support precisely this work during Phase 1, culminating in CoDR. Teams are encouraged to propose studies that go beyond Phase 1 metrics and are necessary to de-risk and refine their NAC design by month 9, in time for the CoDR. For example, additional experiments needed to demonstrate interoperability of NAC components developed in Phase 1 are strongly encouraged to provide confidence that these components can be effectively integrated in the Phase 2. However, proposed Phase 1 work should exclude extraneous or tangential tasks that do not directly inform Phase 2 plans.

OPPs should also include a discussion of any additional metrics specific to the proposed Phase 1 approach. The metrics included in this PS represent the minimal set applicable to all GO performers. DARPA reserves the right to add additional metrics to awards for Phase 1 on a per team basis, based on the Government's review of each team's proposed approach. Additional metrics for Phase 2 will be discussed in the CoDR and are not required in abstracts or OPPs.

Due to the flexibility teams have in designing their NACs and the wide variety of cell lines they may use for development and demonstration, it is not feasible to prescribe a single set of assays to meet program metrics. While *in vivo* (i.e., in a living cell) demonstrations of NAC functionality are required for milestones in months

31 and 40, the month 9 milestone in Phase 1 mandates *in vitro* (i.e., cell-free) demonstrations. Additional *in vivo* experiments that further de-risk Phase 2 approaches during Phase 1 are permitted but not required. OPPs should enumerate all *in vitro* approaches for demonstrating co-activation of optogenetic domains, opto-gated polymerases, and initial nucleic acid synthesis in highly controlled environments appropriate to meet Phase 1 metrics. Similarly, any additional Phase 1 *in vivo* assays must be listed and prioritized for de-risking Phase 2 work. OPPs must include descriptions of all assays, but detailed methods (i.e., to the level of a peer-reviewed journal) should be avoided. The description of assays must include all relevant control groups, and specifically, OPPs responding to RO2 must include appropriate controls that lack error mitigation mechanism(s).

As discussed in section 1.3.51.3.5.4 above, the GO program will include workshops for the broader research community and commercialization pitch events. OPPs must include a statement confirming the proposing team's intent to provide statements of interest/disinterest on research synopses submitted by workshop registrants who are not part of GO program performer teams. OPPs must also include plans to attend and participate in the Phase 1 workshop. Proposing teams are ***not*** expected to have a fully developed commercialization strategy prior to the start of the program, and resources to develop pitch decks, IP strategies, and funding strategies will be provided by ICCG. While the pitch events do not begin until Phase 2, all proposers are strongly encouraged to identify named personnel as the commercialization lead in their OPP, who will interact with the ICCG to develop pitch materials. The commercialization lead may hold another role on the team (e.g., a CO-I); however, they may not be the Principle Investigator (PI) or Project Manager (PM). If the commercialization lead cannot be identified before submitting the OPP, then teams must include a clear plan to identify this individual before month 5 when the first commercialization training is scheduled to occur alongside the Phase 1 workshop. All teams are required to include a dedicated PM, and this person should be named in the OPP. Similarly, the OPP should name a security lead who will interact with DARPA Program Security Representatives to develop and implement security plans for Phase 2.

1.5. Advisory and Working Groups

The GO program will include three specialized working groups for Biosecurity, Regulatory Policy, and Commercialization. Together, these working groups aim to ensure the responsible development, regulation, and commercialization of GO technologies. Over the course of the GO program, performers will be afforded multiple opportunities to interact with the Biosecurity, Regulatory Policy, and Commercialization working groups.

The Government will be soliciting for the working groups separately via a Special Notice attached to the BTO Office-Wide BAA. **Any proposals received in response to this solicitation that are seeking to participate in the working groups will be deemed non-conforming and will not be considered for review.** To avoid organizational conflicts of interest on the GO program, institutions that submit proposals to both the solicitation for the working groups and this program solicitation (i.e., as a technical performer) must provide DARPA with a clear mitigation plan to implement appropriate firewalls between the technical performer team and the team providing program-level support via the working group. In the event that DARPA were to make awards to an organization submitting separate proposals to act as both a technical performer and establish a working group, the same individual(s) cannot be included as named personnel on both awards.

1.5.1. Biosecurity Working Group (BSWG)

The Biosecurity Working Group (BSWG) will be led by a contracted, nonpartisan, third-party to perform a comprehensive analysis of risks, to include international relations, jurisdictional, and cultural differences in biotechnology assessment. It will also develop policy recommendations against accidental and intentional misuse of GO technologies. The BSWG will interface with other aspects of industrial policy, including export control, to evaluate security and safety measures for GO. It will balance the risk of overprotection, which could limit the benefits of widespread use, against the risk of under-protection, which could lead to misuse or misappropriation by adversarial nations, undermining U.S. interests and security. The BSWG will also undertake a preliminary assessment of the cybersecurity risks associated with the development of devices incorporating on GO technology, to include software and hardware. Outputs from the BSWG may contribute

to inform DARPA's decision making on the overall security posture for the GO program.

1.5.2. Regulatory Policy Working Group (RPWG)

Current regulatory frameworks are not equipped to address the implications of reprogrammable, decentralized, and *in situ* manufacturing of biological molecules, creating a high barrier to technology transition. A Regulatory Policy Working Group will be established, comprised of individuals both from relevant government agencies and from academic and non-government legal settings. The RPWG's mandate will be to identify concerns, develop clear, forward-looking regulatory policy guidelines, and inform technology developers and investors on specific demonstrations needed to navigate regulatory pathways within the Coordinated Framework for the Regulation of Biotechnology Products.

1.5.3. Independent Commercialization and Consulting Group (ICCG)

Proposing teams should plan to interact with the ICCG, which will be led by a contracted third-party to perform research and disseminate results on markets, business cases, and finance pathways required to support commercial/industrial transition of technologies developed on the GO program. The working group will consist of investment professionals, entrepreneurs, and consultants with relevant backgrounds and expertise germane to the GO program and the specific makeup of performers that DARPA awarded under the program. As described in section 1.3.5.4 above, the ICCG will coordinate periodic "pitch events" where GO performers brief professionals in finance on their technical progress and on how that progress supports a notional business case. In turn, the ICCG will provide feedback to GO performers on refinements to their strategy and pitch that are predicated on their knowledge of market trends and opportunities. GO proposals should include plans to attend and prepare for these "pitch events", including establishing any necessary agreements with the ICCG (e.g. non-disclosure agreements, NDAs) in advance of "pitch events". While foreground data and IP generated on the GO program will be provided to DARPA with unlimited rights for government use, including sharing key relevant information with working groups supporting the program, proposers should plan to establish non-disclosure agreements with ICCG members if it is necessary to discuss background IP or data with them. Proposals must include milestones relevant to establishing these agreements to allow for transparent discussions with the ICCG at all events. DARPA is not responsible for negotiating these agreements because these terms must be agreed upon between the two parties exchanging information; however, DARPA will facilitate introductions between entities that will be present at these events.

2. PS AUTHORITY

This PS may result in the award of an Other Transaction (OT) for Prototype (OT-P) agreement, which can include not only commercially-available technologies fueled by commercial or strategic investment, but also concept demonstrations, pilots, and agile development activities that can incrementally improve commercial technologies, existing Government-owned capabilities, and/or concepts for broad defense and/or public application(s). The Government reserves the right to award an OT for Prototypes under 10 U.S.C. § 4022, or make no award at all. In all cases, the Government agreements officer shall have sole discretion to negotiate all agreement terms and conditions with selected offerors. The OT agreement will not require cost sharing unless the offeror is a traditional defense contractor who is not working with a non-traditional defense contractor participating in the program to a significant extent.

2.1. PS Procedure

In response to this solicitation offerors are asked to submit a 5-page abstract as described in Section 4.2. This process allows DARPA to ascertain (1) whether the proposers understand the key challenges of the GO program, and (2) whether they can execute a proposed concept. Specific evaluation criteria used to make the assessment can be found in Section 4.3. If DARPA finds that both conditions are met, it may request the offeror submit an Oral Proposal Package (OPP) as described in Section 4.4, and participate in an oral presentation to DARPA, where the proposed technical solution will be evaluated. Specific evaluation criteria used to make the assessment can be found in Section 4.5. After the Oral Presentations, DARPA will decide as to which offerors may be awarded an OT for Prototypes agreement for Phase 1 of the program and provide

instruction on the development of the Phase 2 proposal. The Government will not pay offerors responding to this PS for the costs associated with Abstract submissions or Oral Presentations.

DARPA will use the following process to facilitate the GO source selection:

a. **Proposer Workshop:** The Program Manager will hold a Proposer Workshop on January 7, 2026, where they will briefly describe the program and its goals and solicit questions from the audience in real time. In-person participation in the Proposer Workshop is highly encouraged, as it serves as a valuable opportunity to discuss ideas and enables collaborations among experts and organization. Additionally, the DARPA Contracts Management Office will discuss the award mechanism (OT-P). Thus, it is encouraged that proposing teams bring a representative from entities' grants/contract office to be involved in the discussion.

   Participation in the Proposer Workshop is optional and is not a requirement for proposers seeking to submit an abstract. Additional details about the Proposer Workshop are provided in Special Notice DARPA-SN-26-19 separate from this PS and can be accessed here (https://sam.gov/opp/f71088b5a7d147ec8d9b7e8edc304c81/view). Furthermore, DARPA will post several videos explaining the program technical approach, acquisition, and security, and these videos will be made available on the registration website for the Proposer's Workshop (https://events.sa-meetings.com/website/91848/).

b. **Program Solicitation Questions and Answers (Q&A) (Informational Only):** DARPA will host a Q&A session during the GO Proposer Workshop and will post a consolidated Q&A document. The Q&A document will be available online at http://www.darpa.mil/work-with-us/opportunities. Following the Proposer Workshop, questions can be sent to GO@darpa.mil. DARPA will respond to any relevant and/or PS clarification question(s) prior to the final abstract due date and post consolidated Q&As at the DARPA Opportunities page (http://www.darpa.mil/work-with-us/opportunities).

c. **Abstracts (Required)**: Abstracts shall be submitted as specified in Section 4.2 of this PS. The Government will review all submitted abstracts for technical comprehension and ability (see Section 4.3). This process allows DARPA to ascertain (1) whether the proposers understand the key challenges of the GO program and (2) whether they can execute a proposed concept. Specific evaluation criteria used to make the assessment can be found in Section 4.3. Selected proposers will be invited to provide an OPP and participate in an in-person oral presentation (see Section 4.4) to the Government. Note that *proposers must submit an abstract(s) in response to this solicitation to be considered for participation in the GO program. Proposers will not be invited to submit an OPP, provide an oral presentation, or be included in any further progression of the program without participating in the abstract phase of the solicitation.*

d. **Oral Proposal Package (OPP)/Oral Presentation (Required if selected)**: Oral presentations are anticipated to take place approximately two weeks after notification of your selection. OPP content and format is detailed in Section 4.4, however the final requirements, to include templates, submittal instructions for OPPs, and proposed presentation dates for oral presentations will be provided in the invitation to submit an OPP and participate in an oral presentation. The Government will review all OPPs (see Section 4.5), which will not be made public or provided to other proposers. For Phase 1, proposers must propose an OT for Prototype with fixed payable milestones. (Note – Milestones represent a completed event. Milestone schedule is based on key observable events in the critical path to accomplish program objectives. Payments are issued upon the successful completion of observable technical events. Fixed payable milestones are directly linked to the achievement of specific milestone defined in the milestone plan. A Schedule of Milestones and Payments is included as a tab in Attachment D.)

e. **Phase 1 (12 months):** DARPA will review OPPs and oral presentations to determine which proposed solutions sufficiently meet the evaluation criteria stated in Section 4.5. Upon favorable review, and

subject to the availability of funds, the Government may award an OT for Prototype under 10 U.S.C. § 4022 with fixed, payable milestones for Phase 1 selectees. The awards will support the refinement and demonstration of critical molecular components required for a NAC, including optogenetic domains, enzymatic polymerization, and mechanism for error mitigation. Phase 1 awards will have a 12-month period-of-performance, with funding amounts of $1.7M for RO1 or $1.99M for RO1 +RO2 combined. DARPA plans to issue proposal instructions for Phase 2 to successful Phase 1 performers at month 9 of Phase 1. Phase 2 work may be an add to the Phase 1 OTs, but DARPA reserves the right to negotiate the OT-P.

3. ELIGIBILITY INFORMATION

3.1. Eligible Applicants

3.1.1. Federally Funded Research and Development Centers (FFRDCs) and Government Entities

3.1.1.1. FFRDCs

FFRDCs are subject to applicable direct competition limitations and cannot propose to this PS in any capacity unless they meet the following conditions: (1) FFRDCs must clearly demonstrate, with specific details, that the proposed work, expertise, and facilities are not otherwise available from the private sector, and (2) FFRDCs must provide a letter on official letterhead from their sponsoring organization citing the specific authority establishing their eligibility to propose to Government solicitations and compete with industry, and their compliance with the associated FFRDC sponsor agreement's terms and conditions. This information is required for FFRDCs proposing to be awardees or subawardees. FFRDC proposals that do not include these elements may be deemed non-conforming and removed from consideration.

FFRDCs proposing as prime awardees must be able to accept an OT for Prototype agreement as the award instrument. FFRDCs that can only be funded through their existing sponsor contracts should not submit an abstract directly to this PS.

3.1.1.2. Government Entities

Government Entities (e.g., Government/National laboratories, military educational institutions, etc.) are subject to applicable direct competition limitations. Government entities must clearly demonstrate that the work is not otherwise available from the private sector and provide written documentation citing the specific statutory authority and contractual authority, if relevant, establishing their ability to propose to Government solicitations and compete with industry. This information is required for Government Entities invited to submit OPPs as either awardees or subawardees.

Government Entities submitting abstracts as prime awardees must be able to accept an OT for Prototype agreement as the award instrument. Government Entities that can only be funded through their existing sponsor contracts should not submit abstracts directly to this PS.

3.1.1.3. Authority and Eligibility

At the present time, DARPA does not consider 15 U.S.C. § 3710a to be sufficient legal authority to show eligibility. While 10 U.S.C. § 4892 (formerly 10 U.S.C. § 2539b) may be the appropriate statutory starting point for some entities, specific supporting regulatory guidance, together with evidence of agency approval, will still be required to fully establish eligibility. DARPA will consider FFRDC and Government entity eligibility submissions on a case-by-case basis; however, the burden to prove eligibility for all team members rests solely with the proposer.

3.1.2. Other Applicants

Non-U.S. organizations and/or individuals may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances.

3.2. Organizational Conflicts of Interest (OCI)

Without prior approval or a waiver from the DARPA Deputy Director, a contractor cannot simultaneously provide scientific, engineering, technical assistance (SETA), advisory and assistance services (A&AS), or similar support and also be a technical performer. As part of the OPP, all members of the proposed team (including any potential sub-awardees or consultants) must affirm whether they (their organizations and individual team members) are providing SETA or similar support to any DARPA office(s) through an active award or subaward. All facts relevant to the existence or potential existence of Organizational Conflicts of Interest (OCI) must be disclosed in the Administrative and National Policy Requirements document, should the proposer be invited to submit an OPP.

If SETA, A&AS, or similar support is being or was provided to any DARPA office(s), the OPP must include in the Administrative and National Policy Requirements document:

- The name of the DARPA office receiving the support;
- The prime contract number;
- Identification of proposed team member (subawardees, consultant) providing the support;
- OCI mitigation plan.

Under this section of the OPP, the proposer is responsible for providing this disclosure with each OPP submitted. The disclosure must include the proposer's OCI status, and as applicable, proposed team member's OCI mitigation plan. The OCI mitigation plan must include a description of the actions the proposer has taken, or intends to take, to avoid, neutralize, or mitigate such conflict, prevent the existence of conflicting roles that might bias the proposer's judgment, and prevent the proposer from having unfair competitive advantage. Prior to the start of OPP evaluations, the Government will assess potential conflicts of interest based on the OPPs submitted. DARPA will promptly notify the proposer if any appear to exist. The Government assessment does NOT affect, offset, or mitigate the proposer's responsibility to give full notice and planned mitigation for all potential organizational conflicts.

If, in the sole opinion of the Government after full consideration of the circumstances, a proposal fails to fully disclose potential conflicts of interest and/or any identified conflict situation cannot be effectively mitigated, the OPP will be rejected without technical evaluation and withdrawn from further consideration for award.

If a prospective proposer believes a conflict of interest exists or may exist (whether organizational or otherwise) or has questions on what constitutes a conflict of interest, the proposer should send his/her contact information and a summary of the potential conflict via the specific email address identified in this PS before time and effort are expended in preparing an OPP and mitigation plan.

4. GUIDELINES FOR ABSTRACTS, ORAL PRESENTATIONS, AND PROPOSALS

4.1. General Guidelines

a. Do not include elaborate brochures or marketing materials; only include information relevant to the submission requirements or evaluation criteria.

b. Use of a diagram(s) or figure(s) to depict the essence of the proposed solution is permitted.

c. All Abstracts, Oral Presentations, and Proposals shall be unclassified.

d. Offerors are responsible for clearly identifying proprietary information. Submissions containing proprietary information must have the cover page and each page containing such information clearly marked with a label such as "Proprietary" or "Company Proprietary." NOTE: "Confidential" is a classification marking used to control the dissemination of U.S. Government

National Security Information as dictated in Executive Order 13526 and should not be used to identify proprietary business information.

e. Questions can be sent to GO@darpa.mil by January 12, 2026 5:00 PM (ET).

f. Send Abstracts to GO@darpa.mil by January 16, 2026 5:00 PM (ET). Files containing Controlled Unclassified Information (CUI) must be encrypted when sending over the Internet.

g. Submissions sent through other mediums, channels, or after the prescribed PS deadline will not be considered, reviewed, nor evaluated.

h. Offerors providing Abstracts that are not invited to an Oral Presentation will be notified in writing as soon as practicable.

i. Abstracts and oral presentations should inherently address all of the Heilmeier questions as described here: https://www.darpa.mil/work-with-us/heilmeier-catechism

j. Proposers are encouraged to review "Appendix A: Checklist" to ensure their proposal conforms to the GO solicitation.

4.2. Abstract Content

Abstracts should not exceed five (5) single-sided 8.5" by 11" written pages using 12-point Times New Roman font with 1" margins all around. Abstract contents are described below in Table 3:

Table 3. GO Abstract Content

Section Headings	Required Content
Abstract Summary Slide	See Attachment A: Abstract Summary Slide template.
Title Page (Excluded from 5-page limit)	See Attachment B: Abstract Template Proposer Name Title Date E-Mail Addresses Phone Numbers and Addresses for Technical Point of Contact and Administrative Point of Contact. The proposer should include a statement that no persons on the proposer's team works for DARPA as Scientific Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS), or similar support services, as DARPA has a policy prohibiting such individuals/organizations from working as a technical performer.
Executive Summary (No more than 1 page and is counted towards the 5-page limit)	Provide a summary of your technical approach and execution strategy to address the goals of their proposal to GO program. The goal is for the proposer to demonstrate clear understanding of this program's purpose and goals. This summary shall be specific to the proposer's own technical approach and not simply restate the program goals listed in this Program Solicitation. The summary should also include a statement of anticipated rough order-of-magnitude (ROM) costs for Phase 2.

Proposed Technical Approach (No more than 2 pages and is counted towards the 5-page limit)	Provide a summary of the following: • Your technical vision to achieve the goals of this program • Approach during Phase 1/Plan for Phase 2 tasks • Overall approach to meet the goals and milestones of Phase 1 • Outlines specific tasks to meet the milestones of Phase 1 • Presentation of, not just reference to, unpublished data that establishes technical feasibility of Phase 1 work
Technology Challenges (No longer than 1.5 page and counted towards the 5-page limit)	This section should identify specific technical challenges associated with the proposed approach. The proposer should include what they think the primary risks are to successful development in the GO program and the envisioned mitigations for those risks.
Technical Expertise (No more than 0.5 page and is counted towards the 5-page limit)	Detail why the proposer believes their team can be successful at achieving program goals, if selected to participate in GO. The proposer may include experience, organizational capabilities, team members' qualifications, or anything else that demonstrates competence in designing and building run-time reprogrammable biomanufacturing platforms.
References (References are not included in the 5-page limit)	Provide a list of citations, references, or end notes. The reference list must include 1-2 sentences per citation regarding the relevance of the cited reference for the proposal. Proposers should also annotate their perception of the relative importance of cited research for the proposed work (***critical; **important; *informative)

4.3. Abstracts – Process and Basis of Evaluation

Abstract evaluation criteria are listed in order of importance. Individual Abstracts will be evaluated against the evaluation criteria described in Table 4 below:

Table 4. Review Criteria for Proposal Abstracts

Evaluation Criteria	Required Content
Technical Comprehension	The proposed technical understanding accurately reflects GO goals, and key technical challenges and risks are identified.
Technical Ability	The proposer's team and organization are capable of developing molecular components required for NAC including: optogenetic domains, opto-gated polymerases, and error mitigation mechanisms, and the proposers convey a plausible strategy to design, build, test, and refine such a platform.
Past Performance	The proposers demonstrate an ability, if selected, to achieve the goals of the GO program. Of particular interest and aspects to consider including would be, but are not limited to, highlighting key personnel who will work on the program, providing examples of past performance or projects in this technical domain.

Abstracts will be evaluated by DARPA using the evaluation criteria listed above in descending order of importance and the Evaluation Board Chair (EBC) Memorandum.

DARPA will use the evaluation criteria to assess similarities, differences, strengths, and weaknesses of the

competing abstracts and, ultimately, use that assessment to offer select proposers the opportunity to proceed to Oral Presentations. The Government will endeavor to complete the evaluation of Abstracts within 10 business days of the closing of the submittal period. As stated above, offerors are required to submit an Abstract for evaluation by DARPA to minimize effort and reduce the potential expense of preparing an unsuccessful proposal. DARPA will respond to the 5-page Abstract with a statement as to whether DARPA is interested in seeing an Oral Presentation. If DARPA is not interested in an Oral Presentation, it will state this in written communication to the offeror. Upon review of Abstracts, the Government may elect to invite all, some, or none of the offerors to Oral Presentations. *Only Abstract offerors invited by DARPA to participate in Oral Presentations are eligible to provide one.*

4.4. Oral Presentations Content

Specific instructions for the Oral Proposal Package (including content submission guidelines), in addition to oral presentation details, will be provided in the invitation letter. Oral Proposal Packages must include:

a. **Title Page** – Proposer Name, Title, Date, Point of Contact (POC) Name, E-Mail Address, Phone, and Address. (The title page does not need to be briefed, and it may be included as the first slide in the deck for the oral presentation). The title page must also include the following:

   - A statement that no people on the proposer's team works for DARPA as a SETA, A&AS, or similar support services on an active contract or subcontract (including those awarded through DARPA agents); or list which offices the proposer supports and identify the prime contract numbers. DARPA policy prohibits supporting contractor individuals and entities from concurrently working as research and development performers, unless potential organizational conflicts of interest are identified, eliminated, or appropriately mitigated, and granted a waiver.
   - A statement that identifies and substantiates which of the following condition(s) are met to permit use of OTs for Prototypes in accordance with 10 U.S.C. § 4022(d)(1): (A) There is at least one nontraditional defense contractor or nonprofit research institution participating to a significant extent in the prototype project; (B) All significant participants in the transaction other than the Federal Government are small businesses (15 U.S.C. § 638) or nontraditional defense contractors; (C) At least one third of the total cost of the prototype project is to be paid out of funds provided by sources other than the Federal Government; or (D) The senior procurement executive for the agency determines in writing that exceptional circumstances justify the use of a transaction that provides for innovative business arrangements or structures that would not be feasible or appropriate under a contract, or would provide an opportunity to expand the defense supply base in a manner that would not be practical or feasible under a contract.

b. **Task Description Document (TDD) –** will be provided to the proposers at a later date.

c. **Detailed cost spreadsheet for Phase 1** – proposals that are only responding to RO1 must budget for $1.7M; proposals responding to both RO1 and RO2 must budget for $1.99M (see Attachment D). Complete cost information must be provided for Phase 1, and additionally, all teams must complete the budget estimation table for Phase 2 ('PHASE 2 BET' tab in Attachment D)

d. **Schedule of Milestones and Payments** – see 'Milestone Schedule' tab in Attachment D.

e. **Completed Representations and Certifications** – see Attachment E.

f. **Oral Presentation Slides –** Refer to the information in Table 5. This table will also be provided with the invitation letter. Please note, these oral presentations will be in-person only in Arlington, VA at a location to be determined. No virtual presentations will be allowed.

Table 5 Oral Presentation – Expected Details

Requirement	Description
Duration	• 60 minutes (45 minutes for presentation, 15 minutes for questions)
Executive Summary (intended for review in advance of briefing; not required to be briefed)	• 8 slides (recommended); 15 slides (max) • Technical approach overview • Facilities and personnel qualification
Oral Presentation (Required to be briefed)	• 25 slides (recommended); 30 slides (max) • Detailed GO technical approach (no animations) • Detailed risks and mitigation plan • Description of facilities available to execute proposed work • Budget estimation table for Phase 2 ('PHASE 2 BET' tab in Attachment D) • Teaming/subcontractors, including plans for establishing agreements and/or subcontracts during Phase 1 that are germane to program execution in Phase 2 • Data Rights and Intellectual Property; between the government and the proposing team, and within the proposing team • Notional commercialization strategy: business model canvas (1 slide; template will be provided to teams following submission of abstracts)

In addition to the above-required areas, the Government may request the proposer provide clarifying information in addition to the Oral Proposal Package. Submission instructions, due date for submitting the Oral Proposal Package, date and time of Oral Presentation will be provided with the invitation. Any questions asked by proposers must be submitted to GO@darpa.mil.

4.5. Oral Presentations – Process and Basis of Evaluation

1. The Government intends for Oral Presentations to be done in-person; the Government reserves the right to record the presentations. The Government will evaluate information provided in the content submission (documentation), the Oral Presentation, and Q&A session as basis for evaluation. Oral Presentations will be evaluated by the GO Program Manager with support from a panel composed of Government subject matter experts (SMEs).

Oral presentation evaluation criteria are listed in

Table 6 in descending order of importance. Individual presentations will be evaluated against the evaluation criteria described below. The government will provide final evaluation criteria in the oral presentation invitation.

Table 6 Review Criteria for OPPs

Evaluation Criteria	Required Content
Technical Approach	The proposed technical approach is reasonable, feasible, and innovative. The approach demonstrates an innovative yet feasible approach to address the identified technical risks and challenges and meet program metrics.
Relevant Qualifications	Personnel and/or company experience and qualifications are accurate, relevant, and demonstrate the ability of the proposer to meet the technical goals of the program.
Budget	The proposed costs reflect the guidance in the Program Solicitation for RO1 proposals ($1.7M) and proposals responding to both RO1 and RO2 ($1.99M). Estimated ROM for Phase 2.
Data Rights	The extent to which data assertions allow the Government to realize the objectives and progression of the GO program. The Government will require Unlimited Rights for foreground IP and data developed under this program.

3. After completing evaluation of Oral Presentations, DARPA will either: 1) make a 12-month award for Phase 1 of the program; or 2) inform the offeror that its proposed concept/technology/solution is not of continued interest to the Government and they are no longer considered for participation in the program.

5. AWARDS

5.1. General Guidelines

1. Upon favorable review of the proposal and subject to the availability of funds, the Government will award an OT for Prototypes agreement for Phase 1.

The Agreements Officer reserves the right to negotiate directly with the offeror on the terms and conditions prior to execution of the resulting OT agreement, including payment terms, and will execute the agreement on behalf of the Government. A copy of the draft OT agreement is attached to this PS for review. In order to speed up negotiations, offerors selected for oral presentations will be required to either attest to compliance of all OT agreement articles or note those they take exception to. Be advised, only a Government Agreements Officer has the authority to enter into, or modify, a binding agreement on behalf of the United States Government.

In order to receive an award:

a. Offerors must have a Unique Identity ID number and must register in the System for Award Management (SAM). Offerors are advised to commence SAM registration upon notification of entry to Phase 1 of the competition.

b. Offerors must also register in the prescribed Government invoicing system (Wide Area Workflow: https://wawf.eb.mil/xhtml/unauth/registration/notice.xhtml). DARPA Contracts Management Office (CMO) personnel will provide assistance to those offerors from whom a proposal is requested.

c. Offerors must be determined to be responsible by the Agreements Officer and must not be suspended or debarred from award by the Federal Government nor be prohibited by Presidential Executive Order and/or law from receiving an award.

d. Being asked to submit a proposal does not guarantee that an offeror will receive an award. The

Government reserves the right not to make an award.

5.2. Controlled Unclassified Information (CUI) and (CTI) on Non-DoD Information Systems

In accordance with the Controlled Unclassified Information (CUI) guidance for GO, detailed NAC related information and integrated error mitigation process when demonstrated in vivo will be controlled at the CUI level. DARPA anticipates that GO will also produce unclassified, fundamental research which will be required to be reviewed and approved by DARPA prior to public release. The program-specific CUI Guide provides additional details on GO's CUI controls and is published with this solicitation as Attachment F. Proposers must describe credible approaches to complying with GO's CUI guide. Performers will need to operate at the CUI level in accordance with the GO's CUI Guide and DODI 5200.48. This includes providing a list of prospective individual researchers and their citizenship who will have access to CUI. Individuals with access to CUI must complete CUI training, agree to safeguard all CUI data, and submit manuscripts for review to DARPA prior to publications. Performers will be responsible for ensuring their systems and research adhere to CUI standards (NIST 800-171) including but not limited to data analysis, storage, networking and data transfer, cloud, high-performance-computing (HPC), and document systems. Performers may provide their own CUI-certified systems, including laptops, desktops, cloud, HPC, etc. Proposers' Price Volume may include IT asset requests, provided requests are NIST 800-171 compliant. Solutions may include but are not limited to FedRAMP certified cloud services, local servers, etc. Proposed approaches must meet this requirement.

5.3. Representations and Certifications

All offerors are required to submit DARPA-specific representations and certifications for Prototype OT awards in order to be eligible to receive an OT award. See http://www.darpa.mil/work-with-us/reps-certs for further information on required representations and certifications for Prototype OT awards.

5.4. Competition Sensitive Information

DARPA policy is to treat all submissions as competition sensitive, and to disclose their contents only for the purpose of evaluation. Restrictive notices notwithstanding, during the evaluation process, submissions may be handled by support contractors for administrative purposes and/or to assist with technical evaluation. All DARPA support contractors performing this role are expressly prohibited from performing DARPA sponsored technical research and are bound by appropriate nondisclosure agreements. Input on technical aspects of the proposals may be solicited by DARPA from non-Government consultants/experts who are strictly bound by the appropriate non-disclosure requirements.

5.5. Intellectual Property / Data Rights

The GO program seeks to develop foundational technology that will be enormously disruptive to existing approaches for introducing genetic instructions to living cells. Much of the initial impact of GO technology is anticipated to be in greatly accelerating research and development throughout any industry that relies at least in part on biotechnology. However, outside of its use as a research tool, DARPA expects intellectual property developed on GO to transition to commercial applications, some of which will have dual-use for the military. DARPA seeks to protect its investment of public funds in GO technology without unduly decreasing the value of the foreground IP that GO performers create with those public funds. To achieve this balance, DARPA intends to retain unlimited rights for all foreground subject inventions and data, which affords DARPA the ability to sublicense this IP to a third party for any purpose, including commercialization. Importantly, to protect the value of the IP, in the assertion of unlimited rights included in awards made under GO, DARPA intends to include a Right of First Refusal (ROFR) for the purposes of commercialization, where DARPA must obtain a ROFR from the IP owner before DARPA may sublicense the IP to a third party that aims to commercialize it. Critically, should the IP owner sell the IP to another party, DARPA would still be bound to seek a ROFR from the new owner before sublicensing the IP for the purpose of commercialization. The ROFR does not apply when DARPA exercises its unlimited rights for government purposes such as providing

program data or deliverable to other organizations for the purpose of executing work on a government contract or program. Proposers are directed to review the specific language included Articles VI and VII in Model Other Transaction Agreement (Attachment C) attached to this Program Solicitation. For convenience, relevant clauses pertaining to subject inventions and data rights are included below:

- Subject invention: DARPA shall have a perpetual, paid in-full, non-exclusive, transferable, irrevocable license to practice, or have practiced for or on behalf of the United States, any Subject Invention throughout the world for any purpose or for any commercialization purpose. For purposes of this clause, commercialization means the development, manufacture, practice, or operation of a subject invention such that its benefits are made available to the public on reasonable terms, including through the manufacture, sale, distribution, or other commercial use of products or services embodying the invention. Prior to DARPA granting a commercial license to any third party, DARPA will provide a Right of First Refusal on the Subject Invention to the Performer to undertake commercialization on substantially the same reasonable terms. The Right of First Refusal shall be continuous and transferable should the Performer sell the Subject Invention. If the Performer declines to exercise its Right of First Refusal, the Performer shall, per Article VI.C. of the Model OT for Prototype Agreement, convey to DARPA the title or rights necessary for DARPA to grant the proposed commercial license on substantially the same reasonable terms. DARPA shall request only those rights required to effectuate such license, and title shall not otherwise transfer.
- Data: DARPA has unlimited rights under this Agreement to the Subject Data. Prior to DARPA providing any Subject Data to a third party for commercialization purposes, not defense purposes, DARPA will provide the Performer a Right of First Refusal to undertake commercialization on substantially the same reasonable terms. The Right of First Refusal shall be continuous and transferable should the Performer sell the Subject Data. For purposes of this clause, commercialization means the development, manufacture, practice, or operation of Subject Data such that its benefits are made available to the public on reasonable terms, including through the manufacture, sale, distribution, or other commercial use of products or services embodying the Subject Data.

5.6. Procurement Integrity Act (PIA)

All awards under this PS shall be treated as Federal Agency procurements for purposes of 41 U.S.C. Chapter 21. Accordingly, the PS competitive solicitation process and awards made thereof must adhere to the ethical standards required by the PIA.

5.7. Fundamental Research Risk-Based Security Review Program (FRRBS)

DARPA's Fundamental Research Risk-Based Security Review Process (formerly CFIP, now FRR-BS a.k.a. "FERBS") is an adaptive risk management security program designed to help protect the critical technology and performer intellectual property associated with DARPA's research projects by identifying the possible vectors of undue foreign influence. DARPA will create risk assessments of all proposed senior/key personnel selected for negotiation of a fundamental research award. The DARPA risk assessment process will be conducted separately from the DARPA scientific review process and adjudicated prior to final award. For additional information on this process, please visit Proposer Instructions: Other Transactions.

6. PS DEFINITIONS

"Data" refers to recorded information, regardless of form or method of recording, which includes but is not limited to, technical data, software, mask works and trade secrets. The term does not include financial, administrative, cost, pricing or management information and does not include inventions.**"Nontraditional Defense Contractor"** is defined in 10 U.S.C. § 3014 as an entity that is not currently performing and has not performed, for at least the one-year period preceding the solicitation of sources by the DoD for the procurement or transaction, any contract or subcontract for the DoD that is subject to full coverage under the cost accounting standards prescribed pursuant to 41 U.S.C. § 1502 and the regulations implementing such section. This

includes all small business concerns under the criteria and size standards in 15 U.S.C. § 632 and 13 C.F.R. Part 121.

"Other Transaction" refers to the type of OT that may be awarded as a result of this PS. This type of OT is authorized by 10 U.S.C. § 4022 for prototype projects directly relevant to enhancing the mission effectiveness of military personnel and the supporting platforms, systems, components, or materials proposed to be acquired or developed by the DoD, or for theimprovement of platforms, systems, components, or materials in use by the armed forces.

"Prototype Project" is described in the DoD Other Transactions Guide (Version 1, Nov. 2018) issued by the Office of the Under Secretary of Defense for Acquisition and Sustainment: https://www.dau.edu/guidebooks/Shared%20Documents/Other%20Transactions%20(OT)%20Guide.pdf.

"Small Business Concerns" is defined in the Small Business Act (15 U.S.C. § 632).

"Unlimited Rights" are rights to use, duplicate, release, or disclose, Data, in whole or in part, in any manner and for any purposes whatsoever, and to have or permit others to do so.

7. Appendix A: Checklist

DARPA encourages the use of this checklist to ensure that your proposal conforms to the GO program solicitation. This checklist is for your own use only, do not submit it with the proposal and cost documents. For the purposes of this checklist, the term "proposal" refers to either the abstract or the oral presentation.

This checklist does not represent evaluation criteria that DARPA will use to review proposals received in response to the GO PS. These evaluation criteria are listed and described in Sections 3.3 & 3.5 of the GO PS. Rather, this checklist is only included as a tool to help respondents ensure their proposals conform to the GO PS. Conforming proposals address all aspects of the PS, and this table calls attention to all instances where "must", "should", "shall", and "encouraged to" language is used.

Technical approach and execution strategy	Abstract	OPP
All Proposals must address RO1		
Provide clear, high-level conceptional mechanisms for the final proposed NAC designs enabling the evaluation for innovation, feasibility, and potential of the proposed ideas to meet program goals.	X	X
Provide high-level descriptions of proposed NAC designs and Phase 1 technical plans.	X	
Provide comprehensive Phase 1 plans that demonstrate how the proposed work will address Phase 2 objectives.		X
Clearly states whether the planned NAC design is intended to synthesize DNA, RNA, and single- vs. double-stranded molecules, and utilize canonical nucleotides (ATP, GTP, etc) or non-canonical molecules, etc.	X	X
Describes how they will develop the core capability of the NAC for template-free DNA or RNA synthesis such that optical inputs dictate the sequence of nucleic acids produced by the NAC.	X	X
Describes how proposed approach addresses each of the challenges associated with RO1 and RO2, if applicable, detailed in sections 1.3.1 – 1.3.3 in the PS	X	X
Includes a detailed risk analysis and mitigation plan for Phase 1. Discuss any approach-specific challenges requiring resolution on Phase 1 as part of the justification, approach-specific challenges identified should be accompanied by a detailed risk mitigation strategy		X
A clear conceptual mechanism for the final NAC that is aimed to be developed in Phase 2 is provided and Phase 1 de-risking plans are articulated.	X	X
Proposal justifies the feasibility of their proposed NAC design and development approach using prior art, such as evidence related to constituent protein domains intended for integration, and/or computational, rational, and empirical methods for achieving novel functions through domain integration.	X	X
The proposed NAC design can function inside a living cell to synthesize nucleic acid sequences with light as the sole source of information.	X	X
The proposed NAC design does not require any exogeneous substrates beyond H, C, N, O, S, and P containing molecules typically included in media or produced by the cell.	X	X
If cell lines require engineering to synthesize substrates for the NAC, this is stated.	X	
Metabolic engineering strategies are detailed.		X

High-level overview of team's approach to synchronously activate/deactivate a population of NACs expressed inside a cell and discussion of how it will support both synchronous initiation of NAC-based transduction and deactivate to eliminate unwanted transduction is included.	X	
Notional mechanisms and any Phase 1 work necessary to de-risk of revise the approach to synchronously activate/deactivate a population of NACs is discussed.		X
Proposal considers mechanisms that will facilitate overall security of the resulting system.		X
The proposed NAC is designed for *in vivo* single-shot synthesis of long, coding nucleic acid sequences capable of modulating cellular function.	X	X
A notional Phase 2 plan describing how teams intend to test the ability of NAC-derived sequences to affect cellular function is included.		X
Genetic messages produced by the NAC are designed to intersect with the cell's natural machinery for producing RNA and/or protein.	X	X
If the proposed approach utilizes non-canonical bases, the proposal also includes a mechanism to convert these sequences into canonical DNA/RNA for transcription or translation by the host cell's existing enzymes and provides clear evidence that the transliteration mechanism and enzymatic machinery to perform this mechanism are known.	X	X
If the proposed approach utilizes non-canonical bases, clear evidence is provided to justify the feasibility of the metabolic pathways and transliteration mechanism, including proof that the enzymatic machinery to perform these functions is known.		X
Approach to synchronize initiation and termination of synthesis across a population of NACs expressed within a living cell is clearly described.	X	X
Describe the primary cell line planned for NAC implementation, justify both scientifically and notional use case.	X	X
Discuss any additional cell lines required for development or risk mitigation strategies, explain their relevance and how it will yield insights that de-risks NAC development.		X
Proposal includes any additional studies that go beyond those needed to meet Phase 1 metrics and can be justified as necessary to de-risk and refine their NAC design by month 9.		X
Discussion of any additional metrics specific to the proposed Phase 1 approach is included.		X
All *in vitro* approaches for demonstrating co-activation of optogenetic domains, opto-gated polymerases, and initial nucleic acid synthesis in highly controlled environments appropriate to meet Phase 1 metrics are enumerated.		X
Any additional Phase 1 *in vivo* assays are listed and prioritized for de-risking Phase 2 work.		X
Proposal includes descriptions of all assays, including all relevant control groups.		X
Proposals addressing RO2		
Proposal **does not** solely address RO2, proposals must be explicit in their intent to respond to both ROs.	X	X

Clearly describe primary approach to error mitigation along with any supporting strategies.	X	X
Proposal clearly indicates which elements of the approach pertain to the base NAC (RO1) and which elements represent additional error mitigation mechanisms (RO2).	X	X
If combinatorial strategy for error mitigation that combines several mechanisms to reduce error rates is of interest, this intent is clearly indicated.	X	
If multiple error mechanisms are proposed, an experimental plan to evaluate both the combined mechanism and individual components in isolation is included.		X
Approaches that make RO2 severable from RO1 clarify whether or not, and to what extent, the RO2 approach is separable from the RO1 approach.	X	X
Appropriate controls that lack error mitigation mechanisms are included.		X
Out of Scope		
Proposal **does not** incorporate approaches such as bioprospecting to identify and characterize new domains or proteins from natural systems		
Proposal **does not** include exploratory work focused on phenomenological or mechanistic characterization of novel proteins that respond to light or other physical signals.		
Proposal **does not** involve substantial development of novel optical systems or sequencing platforms.		
Proposed design approach **does not** involve systems that operate in parallel to the central dogma.		
Proposal **does not** include tasks to develop or discover completely novel mechanisms for error mitigation or physical signal modalities.		
Proposal **does not** involve development of the NAC in embryonic stem cells.		
Proposal **does not** involve sequences that would be export controlled or restricted for biosafety reasons.		
Approach **does not** require additional *in vitro* synthesis steps, such as lysis and ligation/annealing of oligonucleotides.		
Proposal **does not** include human subjects research or animal subjects research.		
Costs and Budget		
A statement of anticipated rough order-of-magnitude (ROM) costs for Phase 2 is included.	X	
A budget estimation table for Phase 2 is included		X
Detailed cost spreadsheet for Phase 1 is provided. RO1 performers budget $1.7M and performers responding to both RO1 and RO2 budget $1.99M		X
Tasks and costs associated with large expenses (i.e. laboratory equipment) are rigorously justified.		X
Data Rights, Intellectual Property & Security		
Proposal includes plan to include a Science and Technology Protection Implementation Plan (S&T PIP).		X
Proposal includes plan to comply with CUI guidelines and export control regulations.		X
Data Rights and Intellectual Property; between the government and the proposing team, and within the proposing team are included.		X

Proposal is in acknowledgement that DARPA maintains unlimited rights for all foreground subject inventions and data		X
Team and Capabilities		
The appropriateness of the team's capabilities and expertise relative to the technical plan for Phase 1 are clearly articulated.	X	X
Any additional capabilities needed to execute in Phase 2 are highlighted.		X
A plan is provided for identifying and onboarding the required expertise needed for Phase 2 work to be executed during Phase 1.		X
Named personnel are identified as the commercialization lead, or a clear plan to identify this individual before month 5 is included.		X
The team includes a dedicated PM.		X
The team includes a security lead who will interact with DARPA Program Security Representatives to develop and implement security plans for Phase 2.		X
General		
The reference list includes 1-2 sentences per citation regarding the relevance of the cited reference for the proposal.	X	
In the reference list, references are annotated by relative importance of cited research for the proposed work (***critical, **important, *informative)	X	
The proposal's executive summary is specific to the proposers' own technical approach and execution strategy and **does not** simply restate the program goals listed in this Program Solicitation.	X	X
Tasks are limited to those necessary for developing a NAC that is fully functional in a living cell.		X
Proposal includes specific milestones for the attendance of "pitch events" and the establishment of any necessary agreements with the ICCG.		X
A statement confirming the proposing team's intent to provide statements of interest/disinterest on research synopses submitted by workshop registrants who are not part of GO program performer teams is included.		X
A statement that no persons on the proposer's team work for DARPA as a Scientific Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS), or similar support services, is included.	X	X
Technical challenges with the proposed approach are identified and ranked; risk mitigation strategies are presented.	X	
A statement that identifies and substantiates which of the following condition(s) are met to permit use of OTs for Prototypes in accordance with 10 U.S.C. § 4022(d)(1) is included: (A) There is at least one nontraditional defense contractor or nonprofit research institution participating to a significant extent in the prototype project; (B) All significant participants in the transaction other than the Federal Government are small businesses (15 U.S.C. § 638) or nontraditional defense contractors; (C) At least one third of the total cost of the prototype project is to be paid out of funds provided by sources other than the Federal Government; or (D) The senior procurement executive for the agency determines in writing that exceptional		X

circumstances justify the use of a transaction that provides for innovative business arrangements or structures that would not be feasible or appropriate under a contract, or would provide an opportunity to expand the defense supply base in a manner that would not be practical or feasible under a contract.		
A notional commercialization strategy is described.		X
A complete draft of the OT agreement (Attachment C) with a task description document (TDD) is filled in for Phase 1.		X
Schedule of Milestones and Payments is included (tab in Attachment D)		X
Complete Representations and Certification (Attachment E is included)		X