Definitions: A "Biomarker" is a “defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers. A biomarker is not an assessment of how an individual feels, functions, or survives.” (Biomarkers, Endpoints and other Tools (BEST) glossary). For the purpose of this table, biomarker “Discovery” includes identification and initial measurement and demonstration that the candidate biomarker is associated with the concept/outcome(s) of interest; “Validation” refers to studies that seek to demonstrate that an identified biomarker can be reliability and predictably used to indicate the concept/outcomes of interest. “Validation” may refer to analytical or clinical validation (validation of the detection method or validation of the biomarker’s clinical utility, respectively).

<table>
<thead>
<tr>
<th>Funding opportunities for clinical biomarker discovery and/or validation studies</th>
<th>Research Project Grants (Parent R01s)</th>
<th>Development of Biomarkers and Biomarker Signatures for Neurological and Neuromuscular Disorders</th>
<th>Analytical Validation of Candidate Biomarkers for Neurological or Neuromuscular Disorders (U01, U44)</th>
<th>Clinical Validation of Candidate Biomarkers for Neurological or Neuromuscular Disorders (U01, U44)</th>
<th>EPPIC-Net</th>
<th>Rare Disease Clinical Trial Readiness</th>
<th>NeuroNEXT</th>
<th>StrokeNET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allows Biomarker Discovery?</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Disease/Conditions allowed?</td>
<td>Within NINDS Mission</td>
<td>Within NINDS Mission</td>
<td>Within NINDS Mission</td>
<td>Within NINDS Mission</td>
<td>Pain Conditions (all NIH ICs)</td>
<td>Rare Neurological &amp; Neuromuscular Diseases within NINDS Mission</td>
<td>Within NINDS Mission</td>
<td>Stroke</td>
</tr>
<tr>
<td>Prior-approval required?</td>
<td>No (unless &gt;$500K DC/yr)</td>
<td>No (unless &gt;$500K DC/yr)</td>
<td>No (unless &gt;$500K DC/yr)*</td>
<td>No (unless &gt;$500K DC/yr)*</td>
<td>Yes</td>
<td>*</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Multisite design required?</td>
<td>Not required</td>
<td>Not required</td>
<td>Yes (some exemptions allowed)</td>
<td>Yes (some exemptions allowed)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Uses existing clinical site infrastructure?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Allows early feasibility studies (EFS), safety, or efficacy outcomes as primary objective?</td>
<td>not specified</td>
<td>Ready for Definitive Analytical or Clinical Validation</td>
<td>Ready for Definitive Clinical Validation</td>
<td>Ready for use in Phase 2 CTs or for FDA Biomarker Qualification Program package</td>
<td>Validated target engagement or therapeutic “proof-of-principle”</td>
<td>Ready for use in specified CT</td>
<td>Ready for use Phase 2 CTs</td>
<td>Ready for use Phase 2 CTs</td>
</tr>
<tr>
<td>Expected end goals?</td>
<td>not specified</td>
<td>Ready for Definitive Analytical or Clinical Validation</td>
<td>Ready for Definitive Clinical Validation</td>
<td>Ready for use in Phase 2 CTs or for FDA Biomarker Qualification Program package</td>
<td>Validated target engagement or therapeutic “proof-of-principle”</td>
<td>Ready for use in specified CT</td>
<td>Ready for use Phase 2 CTs</td>
<td>Ready for use Phase 2 CTs</td>
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<tr>
<td>Milestone driven?</td>
<td>No</td>
<td>Milestones for transition between R61 and R33 Phase</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>SBIR option?</td>
<td><a href="https://sbir.nih.gov/funding">https://sbir.nih.gov/funding</a></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>FOA/Program Contact</td>
<td>Find Your Program Director</td>
<td>Carol Taylor-Burds, PhD</td>
<td>Carol Taylor-Burds, PhD</td>
<td>Carol Taylor-Burds, PhD</td>
<td>Barbara Karp, MD</td>
<td>Glenn Nuckolls, PhD</td>
<td>Codrin Lungu, MD</td>
<td>Scott Janis, PhD</td>
</tr>
<tr>
<td>Notes:</td>
<td></td>
<td></td>
<td></td>
<td>*Not applicable to SBIRs (U44). Budget information: Phase 1: up to $700K (TC); Phase 2: up to $3 mil (TC) across 3 years can be requested</td>
<td>*Not applicable to SBIRs (U44). Budget information: Phase 1: up to $700K (TC); Phase 2: up to $3 mil (TC) across 3 years can be requested</td>
<td>Budgets must be under $650K DC</td>
<td></td>
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</tbody>
</table>