## Establishing a Framework for Evaluation of Real-World Response

### Goal

Develop and establish methodology for using real-world data (RWD) to measure rw-response to guide regulatory decision-making

### Pilot Cohort

Adult patients diagnosed with metastatic NSCLC, treated with a first-line platinum doublet chemotherapy regimen in the metastatic setting

7 Participating EHR-Data Vendors Contributing 200 Patients Each

### Pilot Objectives

<table>
<thead>
<tr>
<th>Assess Availability of Core Data Components for Measuring rw-Response</th>
<th>Evaluate the Consistency of a Composite Measure of rw-Response</th>
</tr>
</thead>
</table>
| Assess availability and frequency of key data components for measuring rw-response, including:  
  - Raw images  
  - Image reports  
  - Clinician assessment | Evaluate the consistency of a measure of rw-response across data sources in the aligned patient population |
Real-World Response Pilot
RWE Pilot 3.0: Establishing a Framework for Evaluation of Real-World Response

**Broad Goal:** Develop and establish methodology for using RWD to demonstrate benefit to patients to guide regulatory decision-making

**Pilot 1.0**
Established aligned definitions and protocols for capturing rw-endpoints in a feasibility study

**Pilot 2.0**
Assessed performance of rw-endpoints to identify the direction and magnitude of treatment effect
Evaluated the internal consistency of real-world datasets by applying RCT I/E criteria

**rw-Response**
Establishing a framework for evaluating rw-response and assessing the consistency of the measure to generate RWE
Measuring Real-World Response

<table>
<thead>
<tr>
<th>The Definition</th>
<th>The Problem</th>
<th>The Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real-world response (rw-response) is a clinical outcome derived from real-world data (RWD) that provides valuable details about therapeutic efficacy.</td>
<td>Currently, there is no consensus definition or approach for measuring rw-response.</td>
<td>A unique research partnership to develop an aligned framework for measuring rw-response across datasets and a pilot to assess the feasibility and consistency of the measure.</td>
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<tr>
<td>Data vendors largely derive rw-response from the clinician’s assessment of change in tumor burden. This endpoint has promise in the post-market setting to attribute a real-world outcome to a drug intervention in a single arm cohort.</td>
<td>In the real-world setting, data are not consistently captured in a structured or systematic way. Further, there is not a uniform criterion (e.g., RECIST 1.1) in the observational setting for determining tumor response. Therefore, an effort to evaluate, establish, and validate a uniform definition for rw-response is needed.</td>
<td>Friends has assembled data partners with EHR-based datasets to develop an aligned framework for measuring rw-response and conduct a pilot to evaluate the availability of data for the measure and the consistency of rw-response through an assessment across groups based upon an aligned patient population.</td>
</tr>
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</table>
rw-Response Approach

**Pilot Cohort**

Adult patients diagnosed with metastatic NSCLC, treated with a first-line platinum doublet chemotherapy regimen in the metastatic setting.

**Pilot Objectives**

**Assess the Availability of Core Data Components for Measuring rw-Response**

Assess the availability and frequency of key data components for measuring rw-response, including:

- Raw images
- Image reports
- Clinician assessment

**Evaluate the Consistency of a Composite Measure of rw-Response**

Evaluate the consistency of a measure of rw-response across data sources in the aligned patient population

7 Participating Data Vendors Contributing 200 Patients Each
# rw-Response Analysis Strategy Overview

## Objective 1

### Assess Availability and Frequency of Data Components

<table>
<thead>
<tr>
<th>Availability of Core Data Components</th>
<th>Frequency and Timing of Data Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Percent of patients with each data component</td>
<td>• Time between index date and first occurrence of data component</td>
</tr>
<tr>
<td>• Median (IQR) data components per patient</td>
<td>• Time between the 1st and 2nd data components</td>
</tr>
<tr>
<td>• Percent of clinician assessments with a specific source of assessment</td>
<td>• Time between each sequential pair of components</td>
</tr>
<tr>
<td>• Percent of imaging with a specific indication and modality</td>
<td>• Time between all sequential pairs</td>
</tr>
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</table>

## Objective 2

### Measure rw-Response

#### Estimation of rw-Response Rate and 6-Month rwR Duration Rate

- Within and across datasets, with subgroup analyses planned

#### Calculation of rw-Duration of Response

- Kaplan-Meier analysis, also accounting for interval censoring

#### Association between rw-Response and Time to Event rw-Endpoints

- Association with rwOS, rwTTD, rwTTNT
## rw-Response Timeline

<table>
<thead>
<tr>
<th>Create Framework</th>
<th>Plan Pilot</th>
<th>Evaluate Objective 1</th>
<th>Assess Objective 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2–Q3 2021</td>
<td>Q4 2021–Q1 2022</td>
<td>Q2–Q3 2022</td>
<td>Q3–Q4 2022</td>
</tr>
<tr>
<td>Establish working group to develop discussion draft describing key components of a rw-Response framework.</td>
<td>Plan the pilot, including identifying the patient population and aligning on key data components.</td>
<td>Evaluate the availability of core data components for measuring rw-response across datasets.</td>
<td>Assess the consistency of the rw-response measure across data sources.</td>
</tr>
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</table>