Why N-of-One?

Who We Are

- History of working directly with oncologists and their patients to empower them with the most relevant molecular diagnostic and treatment options in the nascent precision medicine field
- Currently support large hospital systems and commercial laboratories to enrich interpretation of genetic tests for oncology patients
- Leading clinical interpretation business providing molecular marker-based, patient-specific, evidence-driven therapy options
- Diverse client base supports technology-enabled knowledgebase covering over 1,800 genes and 100,000 unique variants

Our Proprietary Knowledgebase

- Most comprehensive somatic database of curated genes and variants, with disease-specific evidence across hundreds of cancer subtypes
- Agnostic to gene panels and sequencing platforms across leading precision medicine clients
- Broadest coverage of panels and patients across hematological malignancies and solid tumors, including liquid and tumor biopsies.
- Established QMS process on both curation and database/technology development

Value Drivers

- Expert-powered variant curation and classification
- Co-occurring gene variant analyses
- Extensive data from liquid biopsy and tumor biopsy samples
- Real-world population database reflecting the location of patients and the cancer types being tested
- Collaborative model: Research questions reviewed, data analyzed, and results presented in a flexible format

Solutions Overview

Biomarker & Indication Evaluation
Gene Alteration Prevalence | Real-World Cancer Type Distribution

Trial Cohort & Companion Diagnostic Design
Variant Info | Co-occurring Analysis | Variant Extract | Assay Considerations

Molecular Interpretation
Clinical Trial Screening | Response Profile Analysis

Clinical Trial Accrual & Drug Market Plans
Real-World Patient Population Reporting | Clinical Trial Competitor Analysis

MarkerMine
- De-identified Patient Molecular Profile
- Genes, Variants, Cancer types
- Associated Drug Sensitivity
- Current Scientific Evidence

- 1,800+ Genes
- 900+ Cancer Types
- 100,000+ Unique Variants
- 100,000+ Patient Cases

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Biomarker & Indication Evaluation

Gene Alteration Prevalence

N-of-One can guide optimal biomarker and indication selection for targeted therapies. Our expert classification of variant activation type improves the value of our biomarker selection. Providing prevalence of gene alterations across cancer types and in cancer types of interest is important in identification of disease-focus for a therapy.

Receive a retrospective analysis of gene alteration prevalence in patient cases by:

- **Cancer Type**
  - Prevalence of gene alterations by cancer type (and/or subtype), with cancer types ranked by prevalence of alterations

- **Activation Type**
  - Prevalence of cases with gene alterations across all cancer types, with alterations categorized by activation type: analyses present actionable variants vs all variants (actionable variants plus variants of unknown significance)

- **Variant Type**
  - Prevalence of cases with gene alterations in all cancer types combined, delineated by variant type (e.g., short variant, copy number variant, rearrangement/fusion)

Gene Alteration Prevalence Example

"...This is a treasure trove of information for our program. A quick peek at just the indication data looks like the selection of the target mutations and the fusions in the panel are spot-on...."

— Recent Pharma Genomic Insights Customer

Real-World Cancer Type Distribution

N-of-One can provide additional support for indication selection by illuminating real-world cancer prevalence and testing effects. As part of disease selection for a therapy, it is important to understand who is being tested.

Cancer Type Distribution Analyses Includes:

- The distribution of cancer types, by frequency (%) and by total number of cases, within the actionable alteration-positive cases in the N-of-One database

The cancer type frequency in an alteration-positive population is independent of the gene alteration prevalence for that given cancer type. It is based on the prevalence of the cancer type itself and/or cancer type-specific testing practices.
Expert variant classification and variant frequency analyses support the selection of biomarkers and indications for the design of targeted therapy diagnostics, including companion diagnostics. Improve your clinical trial’s accrual and overall success with the most relevant biomarker criteria.

**Variant Catalog**
A snapshot list of the variants and associated data. The catalog includes gene name, variant name (HGVS compliant), variant type, activation type, sample type, cancer type, and molecular function (with supporting evidence).

**Variant-Cancer Type Frequency**
A retrospective analysis of the frequency (%) and number of gene variants by cancer type (and/or subtype), ranked by the variant frequency.

**Co-Occurring Gene Variant Analysis**
An assessment of gene variants that co-occur with a gene of interest in a statistically significant manner. Co-occurring analysis can identify and rank the most common co-occurring gene variants or interrogate specific co-occurring gene variants with a gene of interest.

<table>
<thead>
<tr>
<th>Gene co-occurring with GenX</th>
<th>Cancer type</th>
<th>Total (n)</th>
<th>Co-occurrence frequency in GenX-positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC</td>
<td>Head and neck</td>
<td>802</td>
<td>24% (834)</td>
</tr>
<tr>
<td>BRCA2</td>
<td>Ovarian</td>
<td>412</td>
<td>11% (871)</td>
</tr>
<tr>
<td>BRCAl1</td>
<td>Breast</td>
<td>8384</td>
<td>7% (29265)</td>
</tr>
<tr>
<td>CTNNB1</td>
<td>Hepatocellular</td>
<td>646</td>
<td>37% (22599)</td>
</tr>
<tr>
<td>KRAS</td>
<td>Endometrial</td>
<td>660</td>
<td>30% (33110)</td>
</tr>
<tr>
<td>NF1</td>
<td>Endometrial</td>
<td>664</td>
<td>20% (27110)</td>
</tr>
<tr>
<td>NF1</td>
<td>Gastrointestinal</td>
<td>1005</td>
<td>12% (14122)</td>
</tr>
<tr>
<td>NF1</td>
<td>Ovarian</td>
<td>1776</td>
<td>47% (28659)</td>
</tr>
<tr>
<td>NF1</td>
<td>Endometrial</td>
<td>664</td>
<td>47% (32110)</td>
</tr>
<tr>
<td>NF1</td>
<td>Breast</td>
<td>315</td>
<td>45% (156385)</td>
</tr>
<tr>
<td>PHA3CA</td>
<td>Gastrointestinal</td>
<td>1063</td>
<td>23% (28122)</td>
</tr>
<tr>
<td>PHA3CA</td>
<td>Colorectal</td>
<td>6067</td>
<td>31% (69222)</td>
</tr>
<tr>
<td>PHA3CA</td>
<td>Uterine</td>
<td>412</td>
<td>30% (22171)</td>
</tr>
<tr>
<td>PHA3CA</td>
<td>Gastrointestinal</td>
<td>1063</td>
<td>23% (28122)</td>
</tr>
<tr>
<td>PTEN</td>
<td>Pancreatic</td>
<td>2482</td>
<td>14% (13892)</td>
</tr>
<tr>
<td>PTEN</td>
<td>Endometrial</td>
<td>664</td>
<td>56% (80110)</td>
</tr>
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</table>

**Variant Extract**
Designed to provide ongoing insights, Variant Extract for specified genes offers a recurring export of variants with variant data and variant classification. This can help pharmaceutical companies with ongoing questions about gene variants.

This is a one-time extract of variant data and may be followed by monthly/quarterly variant data extracts, which include:
- Gene name
- Variant name (HGVS compliant)
- Variant type (short variant, copy number variant, or rearrangement/fusion)
- Transcript ID
- Activation type (actionable or VUS)
- Therapy and trial applicability (disease neutral)
- Variant classification (including supporting evidence and references)

**Sample Type Analysis**
Comparison by sample type (ctDNA vs non-ctDNA) of cases with gene alterations in all cancer types combined, for consideration of liquid biopsy as an assay methodology.

**Platform/Panel Type Analysis**
Comparison of platform/panel type of cases with gene alterations in all cancer types combined.
Molecular Interpretation

Patient Screening for Clinical Trials

Enabling pharmaceutical companies and treating physicians to guide patients toward enrollment in the most appropriate clinical trial & treatment options with patient-specific molecular interpretation of sequencing.

This approach encourages patients to test for a trial, even if the result shows they are not eligible for that trial by providing additional trial and therapy options.

Gene/Variant Interpretation in Context of Cancer Type

- Molecular interpretation to provide molecular qualification information to oncologists and their patients for the appropriate clinical trial within a pharmaceutical company
- Clinical reports that provide additional treatment and clinical trial options, if the patient does not qualify for a clinical trial within the pharmaceutical company

Response Profile Analysis

Interrogation of gene variants altered in patients or preclinical models showing evidence of response to biomarker-driven therapies.

This analysis helps to determine which treatment response profiles identified in clinical studies or preclinical studies should be pursued for pharmaceutical targeting based on their prevalence in the general cancer population.

Response Profile Analysis Includes:

- Interpretation of sequencing profiles for trial participants or preclinical models
- Identification of gene variants and co-occurring gene variants associated with sensitivity or resistance
- Determine prevalence of treatment response profiles within a real-world database

Response Profile Analysis Example

Analysis of genes and variants in context of patient’s cancer type

Relevant clinical and scientific evidence

Multi-variant analysis of each patient’s molecular profile to evaluate drug sensitivity, resistance and combination therapies

May include additional therapies or clinical trial matching based on “Molecular Eligibility”

Clinical Trial Subjects/Preclinical Models

<table>
<thead>
<tr>
<th>Sequencing Profile</th>
<th>% “Real World” NSCLC Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR, MET, RET</td>
<td>0.05%</td>
</tr>
<tr>
<td>EGFR, MET</td>
<td>1%</td>
</tr>
<tr>
<td>EGFR, MET, TP53</td>
<td>3%</td>
</tr>
</tbody>
</table>

Exceptional Responders

Non-Responders

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Clinical Trial Accrual & Drug Market Plans

Real-World Patient Population Reporting

Augmenting clinical trial accrual efforts with ongoing platform testing trends and geographic targeting options, allowing pharmaceutical companies to make more informed plans for trial accrual.

Reporting of individual patient cases from N-of-One database based on either:
- The presence of a specific molecular-cancer type profile and cancer type that would allow eligibility for a specific clinical trial.
- The matching of a patient to a specific clinical trial using the N-of-One clinical trial matching rules.

Retrospective or prospective reporting options:
- Monthly, ongoing prospective reporting
- One-time retrospective report for cases across 24 months

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date</th>
<th>Disease</th>
<th>Gene</th>
<th>Variant</th>
<th>Actionable status</th>
<th>Patient Location if available</th>
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<tbody>
<tr>
<td>1</td>
<td>1/17/18</td>
<td>NSCLC</td>
<td>RET</td>
<td>KIF5B-RET fusion</td>
<td>Activating</td>
<td>New York</td>
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<tr>
<td>2</td>
<td>1/20/18</td>
<td>NSCLC</td>
<td>RET</td>
<td>NCOA4-RET fusion</td>
<td>Activating</td>
<td>Massachusetts</td>
</tr>
<tr>
<td>3</td>
<td>1/21/18</td>
<td>NSCLC</td>
<td>RET</td>
<td>KIF5B-RET fusion</td>
<td>Activating</td>
<td>California</td>
</tr>
<tr>
<td>4</td>
<td>1/22/18</td>
<td>Thyroid carcinoma</td>
<td>RET</td>
<td>M918T</td>
<td>Activating</td>
<td>Maryland</td>
</tr>
<tr>
<td>5</td>
<td>1/24/18</td>
<td>NSCLC</td>
<td>RET</td>
<td>NCOA4-RET fusion</td>
<td>Activating</td>
<td>Utah</td>
</tr>
<tr>
<td>6</td>
<td>1/26/18</td>
<td>Thyroid carcinoma</td>
<td>RET</td>
<td>M918T</td>
<td>Activating</td>
<td>Georgia</td>
</tr>
<tr>
<td>7</td>
<td>1/27/18</td>
<td>NSCLC</td>
<td>RET</td>
<td>Amplification</td>
<td>Activating</td>
<td>Massachusetts</td>
</tr>
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Population Insights Reporting

Month of January 2018

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Clinical Trial Competitor Analysis

Informing clinical trial design with identification of US states with high patient populations and low numbers of open competitor clinical trial sites.

N-of-One can support pharmaceutical companies’ efforts to make more informed decisions on location of clinical trial sites, and later, on-going sales/marketing efforts.

Retrospective clinical trial competitor analysis for clinical trial site planning:
- Reporting on US locations for patients with molecular profile of interest:
  - Includes patients tested and patients positive for alterations in gene of interest, competitor clinical trials, competitor drugs, US locations for open competitor clinical trial sites
  - Analysis provided as listing and maps of resulting trial sites
- Includes target states with high patient population and low number of open clinical trial sites

Clinical Trial Competitor Analysis Example

= open competitor clinical trial site