Introducing a Highly Integrated Approach to Translational Research: Biomarker Data Management, Data Integration, and Collaboration
Translational Informatics Overview

Precision’s suite of services is dedicated to the development of targeted therapies. This includes Biomarker Data Management, Translational Informatics and Biomarker Statistics, Immuno-informatics, and the PATH Platform, our data management delivery and collaboration tool to accelerate translational research.

Our team has been brought together to deliver subject matter expertise as well as operational scale to biomarker-guided drug discovery and development efforts. The Precision team is proficient in a wide range of translational research efforts and biomarker-guided drug development programs including:

- Identification of pharmacodynamic biomarkers to assess target engagement
- Validation of mechanism of action
- Selection of optimal dose
- Drug target identification
- Development of multimarker patient stratification strategies
- Integration of data across assays

PATH: A Robust Platform Propelled by Proprietary Technology

Along with our subject matter experts (SMEs), Precision’s PATH Platform provides a robust solution to the challenges of managing, synthesizing, and reporting information generated from complex biomarker assays—from DNA/RNA-seq (high-throughput genomic data) to flow cytometry (high-content data). All our collaborations use our scalable cloud-based solution, which employs an intuitive user interface for collaboration, customized reporting, and data integration.

Leveraging our platform, we address key translational research objectives across our three primary service lines:

1. **Harmonize**
   - Biomarker Data Management

2. **Synthesize**
   - Translational Informatics, Biomarker Statistics, and Immuno-informatics

3. **Collaborate**
   - Integrated Access to Data and Insights

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**Figure 1: Selected subset of biomarker assays used for data integration and signature development**

- Gene Expression
- Next-Gen Sequencing
- Immunoassays
- IHC
- Novel or Custom Technologies
- Flow Cytometry
Harmonize:
Biomarker Data Management

Streamlining the Management of Massive Amounts of Biomarker Data

Collecting, managing, and processing specialty lab data from multiple assays (eg, immunoSEQ, NanoString nCounter, IHC) in an efficient, high-quality manner appropriate to inform evaluations in a clinical trial is a major challenge. Precision experts help streamline this effort, ultimately resulting in the reduction in time and cost by orders of magnitude for the Sponsor and mitigating a major risk that has the potential to seriously impact the study.

Precision provides expert biomarker data management services, including:

- Design and setup of the PATH database and application for specific studies and/or programs
- Creation of global biomarker project plan and data workflows
- Creation of data transfer protocols with each specialty lab vendor (including other vendors such as the external lab supporting PK data generation)
- Generation of custom biomarker data sets for use in analysis (eg, dose evaluation)
- Generation of CDISC-compliant data sets for biomarker data submitted to FDA
- Execution of assay-specific quality control and processing workflows
- Support data reconciliation (between EDC and labs) with programming and issue tracking
- Serving as the primary point of contact for Sponsor, CRO, and labs on biomarker data

Leveraging the PATH Platform to Improve Biomarker Data Management

Precision provides all stakeholders (Sponsor, CRO, and specialty labs) with a technology specifically engineered to address the challenges of biomarker data in clinical studies.
This access to the PATH Platform offers the following functionality for biomarker data management:

- Secure, centralized database for specialty lab data (including TCRB sequencing, NanoString, IHC)
- Secure, web-based data transfer via PATH interface (point-and-click upload or download)
- Complements LIMS and EDC systems
- Complements technologies from lab vendors (eg, Adaptive’s immunoSEQ Analyzer)
- Interactive, integrated data visualization—heat maps, 3-D plots, PCA, descriptive summaries
- Customizable and downloadable biomarker patient profiles
- Collaboration facilitated across team members for data review
- Real-time reporting on status and assay metrics (eg, assay failures, missing data)

**Synthesize:**

Translational Informatics, Biomarker Statistics, and Immuno-informatics

**Generating Novel Insights in Clinical Development**

Precision’s Translational Informatics, Biomarker Statistics, and Immuno-informatics offerings specialize in the prospective, integrated analysis of diverse types of biomarker data. We regularly support Sponsors in their efforts to generate novel insights and inform critical decisions such as dose evaluation, characterization of MoA, and patient selection, and support FDA submissions through the use of biomarker data-driven evidence packages.

Precision’s senior team includes thought leaders in the space of biomarker-guided drug and diagnostic development. Our experts have published peer-reviewed articles on novel methodologies for translational research.

**Precision Biomarker Analysis Services**

To support key scientific and translational research objectives, Precision provides:

- Development of a biomarker SAP (focused on dose-evaluation phase)
- Statistical programming in SAS or R (as appropriate)
- Validation of programming in accordance with source code management SOPs
- Creation of custom visuals with interactive functionality to display biomarker data, including PK data, for purposes of informing clinical decision-making in dose evaluation
- Generation of CDISC-compliant data sets and documentation for FDA submission

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**Seamlessly Integrating With Existing Data Management Systems**

Precision’s biomarker data management offering is complementary to clinical data management and existing systems (eg, LIMS, EDC), reducing burden on the Sponsor in managing lab vendors, expediting activities for specialty lab data reconciliation, and processing data with assay-specific workflows to deliver CDISC-compliant, analysis-ready data sets.

To meet requirements of changing FDA guidance for electronic data submissions, Precision generates CDISC-compliant data sets and documentation for specialty lab data. For studies starting after December 17, 2016, Sponsors must submit data in the data formats supported by FDA and listed in the FDA Data Standards Catalog.
**Precision Methodologies**

To address key scientific objectives, Precision employs a suite of methodologies:

- Machine learning, artificial intelligence, and systems biology to identify key biomarkers
- Bayesian analytics with latent variable estimation for construction of complex multimarker signatures to identify biomarker-defined patient subpopulations with desired profile
- Structural equation modeling to construct networks and integrate external data sources
- Autogating pipeline for flow cytometry data

**A Platform Specifically Engineered to Address the Challenges of Biomarker Analysis in Clinical Development**

Precision will leverage its proprietary PATH Platform to provide the Sponsor with the following:

- Secure, web-based user interface with interactive data visualization and reporting
- Data integration within and across assays, including NanoString, TCRB sequencing, and IHC, as well as PK data and serum cytokine data
- Link data-driven findings to vast knowledge base of pathways, chemistry, and networks
- Access to proprietary immunomics/immuno-informatics functionality, including an interactive autogating pipeline for efficient and reproducible research on flow cytometry experiments

**Collaborate:**

Integrated Access to Data and Insights

**An Informatics Tool That Lets You Take a Deeper Dive: PATH**

Precision will provide expert consulting services and proprietary technologies to support collaboration and delivery of analysis of high-throughput and high-content biomarker data by leveraging our scalable cloud-based platform, PATH.

- Data delivery and knowledge generation via interactive visualization (eg, 2D and 3D visualizations) and network maps, biological annotation, and integration with relevant genetic databases/knowledge bases
- Secure, web-based data transfer for large files common in sequencing, allowing for ease of data movement and centralized access to molecular testing results and QC summaries
- Customized reporting
- Data integration and dimensionality reduction techniques
Put Our Extensive Experience to Work for You
Our Translational Informatics and Biomarker Statistics Team has extensive experience supporting translational research efforts.

200+ successful engagements in the space of translational research/biomarker studies

40+ translational informatics and biomarker statistics engagements in CNS and autoimmune

Across phases: Phase 1, 2, and 3 clinical drug trials as well as diagnostic studies

Across assays: Next-generation sequencing (NGS), microarrays, flow cytometry, quantitative PCR, IHC, immunoassays, and custom technologies

Across indications: Alzheimer’s disease, schizophrenia, bipolar, MDD, rheumatoid arthritis, multiple sclerosis, Crohn’s disease, and many others

Pioneering analytics advancements in: Multimarker molecular signatures, machine learning and artificial intelligence, subgroup identification, data integration, and data visualization/knowledge generation for biomarker studies
Select Publications
The Precision team has published extensively in the space of methods development and strategy development as it relates to analysis of genomics data in pharmaceutical research.

1. Developed a variance components framework for testing of genomic regions (eg, gene-based testing, targeted GxG and GxE interactions; Qu et al, 2013)
2. Evaluated the applicability of estimating heritability in the context of pharmaceutical research (Marshall et al, 2013)
3. Developed a framework for simultaneous estimation of a genomic signature and testing for the existence of a subgroup (Li et al, 2014)
4. Developed and evaluated a strategy to demonstrate the power of region-based testing vs single-variant association testing (Kohler et al, 2014)
5. Developed a strategy to demonstrate the power of leveraging biomarker data across a series of studies (in submission)
6. Presented on machine learning and artificial intelligence for interrogation of complex genomic data at various conferences (Molecular Medicine Tri-Con 2016, San Francisco, CA; Bio-IT World Conference 2016, Boston, MA)
7. Collaborated with world-class scientists to generate knowledge from cutting-edge research projects (Chen et al, 2011, Kang et al, 2011)

References:

To learn more about Translational Informatics, please contact us at info@precisionformedicine.com, call 855.222.5010, or visit precisionformedicine.com.