INCYTES™:

REAL WORLD DATA LEADING TO REAL WORLD EVIDENCE

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The concepts of Real World Data ("RWD") and Real World Evidence ("RWE") are now recognized by regulatory agencies, providers, payers and patients as essential to determining the safety and efficacy of medical products, devices and procedures. [1] By definition, RWD and RWE are ***not*** derived from "traditional clinical trials", the limitations of which are increasingly recognized. These limitations include sole focus on regulatory approval [2], narrow inclusionary criteria, irrelevance of trial research structure to clinical practice, high cost and delay.

The FDA defines RWD as data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. RWE is defined as clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD. The increased focus on RWD and RWE stems from the availability of potentially relevant data from technical innovations in and outside of the clinic -- bio-sensors, registries, mobile devices, patient-reported outcomes -- as well as more powerful analytical capabilities which can be brought to bear on those data.

RWD and RWE have been identified as valuable in a number of contexts, including:

- regulatory decision-making;
- new indications;
- reporting and analysis of post-market safety and adverse events;
- design of large simple trials, pragmatic clinical trials, and observational studies;
- design, and improving the efficiency, of "traditional clinical trials";
- development of new treatment approaches;
- decisions by payers on coverage;
- generating hypotheses for testing in randomized controlled trials;
- identifying drug development tools, including biomarker identification;
- assessing trial feasibility by examining the impact of planned inclusion/exclusion criteria in the relevant population;

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[1] See here and here for introductory materials prepared by the European Medicines Agency and the U.S. Food and Drug Administration respectively.

[2] Industry expenditures on clinical trials exceed the entire U.S. National Institutes of Health budget.

- informing prior probability distributions in Bayesian statistical models;
- identifying prognostic indicators or patient baseline characteristics for enrichment or stratification;
- assembling research cohorts which are geographically distributed (e.g., in drug development for rare diseases or targeted therapeutics); and
- the development of guidelines and decision-support tools for use in clinical practice.

To date, RWD has been used principally to support product safety; however, the objective of regulators and other healthcare constituencies is to develop RWE which supports efficacy and helps develop evidence-based standards of care. Unfortunately, electronic health record ("EHR") systems rarely accommodate the aggregation of useful RWD – as opposed to "just data" – and even less so the derivation of real-world evidence from that data. This is due to many factors, including irrelevance of data, burdensomeness of data collection, poor design of observational datasets, failure to collect longer-term outcomes, inability to correlate data to specific outcomes, lack of interoperability among various systems, rigid templates leading to boilerplate inputs, failure to collect the patient story, clinically incomplete and/or unconnected data, and cost.

inCytes™ was developed by clinicians for clinicians for the express purpose of collecting RWD leading to RWE. Its core elements include:

- The ability of the clinician – or researcher, payer or study sponsor – easily to design the applicable observational protocol ("O.P.").
- The flexibility to design that O.P. to cover any indication, procedure, patient cohort, standardized outcomes report, or other variable.
- The ability easily to create teams [3], with assigned permission sets, to collect, review and analyze data resulting from each O.P.
- The ability to collect real-world data in a clinically-efficient, verifiable and non-burdensome manner.
- The generation of a variety of report formats correlating any one or more datapoints against outcomes or other datapoints.
- The automatic generation of post-TX patient-friendly surveys for the collection of outcomes

[3] Such teams are referred to in inCytes™ as "Circles". A Circle can be as simple as a physician and her physician's assistant, or as extensive as many dozens of collaborators across departmental and international boundaries sharing one or more O.P's in various languages.

data, as well as visually impactful reports to patients presenting such data in the context of their treatments. [4]

- Multi-lingual support for O.P's, reports and other functions, without losing the ability to aggregate and analyze data from clinically similar O.P's and resulting datasets.
- The low-cost, flexibility, automatic updating and convenience of modern cloud-based software.
- Compliance with HIPAA, GDPR and other patient-privacy considerations.

[4] The clinician of course determines the nature and timing of outcomes survey communications.