Research Hub Framework: Optimizing T-Cell Redirecting Therapies Through Multi-Sector Collaborations and Data

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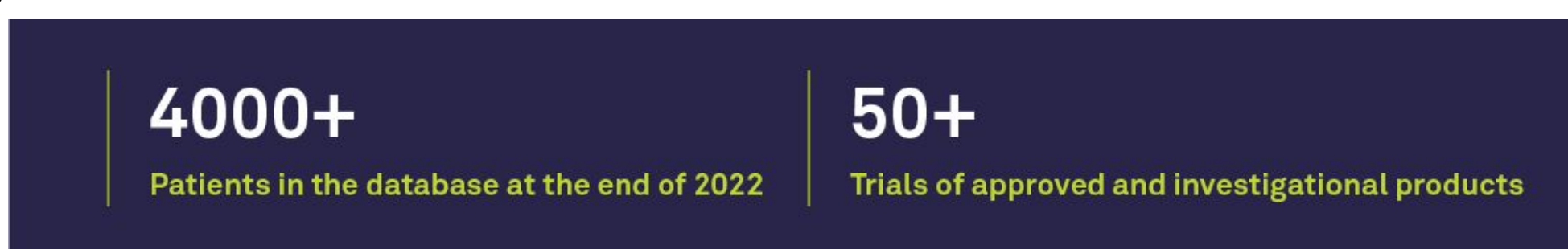
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BACKGROUND

- The field of immuno-oncology has witnessed remarkable advancements with the emergence of revolutionary therapies like T cell redirecting therapies.
- To further accelerate the progress and impact of these transformative therapies, Medidata AI has created a collaborative Research Hub: a unique forum that brings together academia, non-profits, and industry partners.
- The Research Hub leverages pooled clinical trial data from the Medidata Enterprise Data Store, comprising > 50 CAR-T/bispecific studies with > 4000 patients (Fig 1) to generate clinically impactful insights.
- This poster highlights the concept of the Research Hub and how it leverages data, analytics, and multi-sector collaborations to optimize safer, more accessible immunotherapy trials.
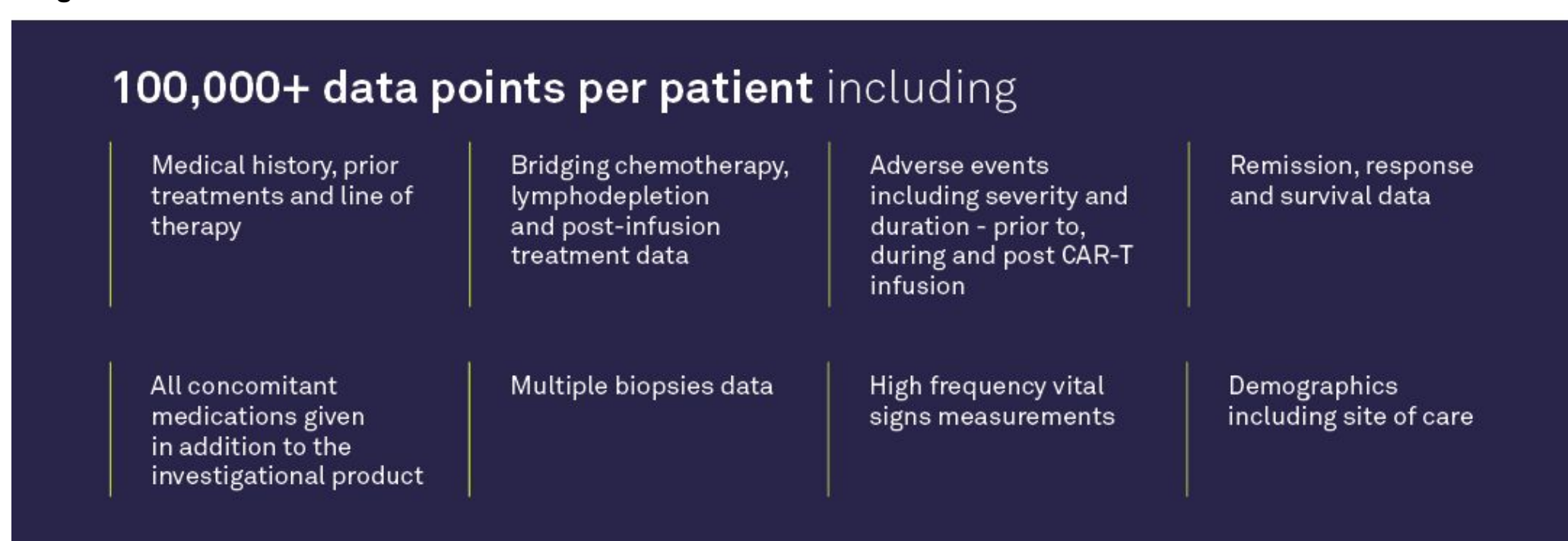
DATA + METHODS

Figure 1: Medidata AI CART-T Data Cube

4000+ Patients in the database at the end of 2022

50+ Trials of approved and investigational products

Indication	Studies	Patients	MoA
ALL	15+	1600+	Anti-CD19, Anti-CD52, BITEs
NHL	10+	1000+	Anti-CD19, chemo
AML/MDS	5+	400+	Bispecific antibodies (BITE/DART class)
MM	5+	450+	Anti-BCMA, BITEs
Solid Tumors	10+	500+	BITEs/DARTs/CARs
CLL	3+	100+	Anti-CD20 ,BITEs

- Curated from clinical trials of approved and investigational products, this CAR-T dataset consists of patient-level data from case report forms with >100,000 data points per patient (Fig 2). This Medidata AI CAR-T Data Cube continues to grow as more trials are being completed and added to the database.

Figure 2: Medidata AI CART-T Data Cube

100,000+ data points per patient including

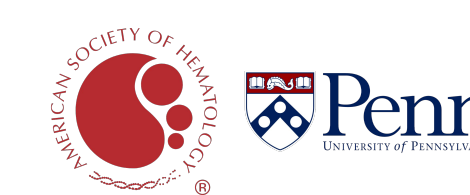|			
Medical history, prior treatments and line of therapy	Bridging chemotherapy, lymphodepletion and post-infusion treatment data	Adverse events including severity and duration - prior to, during and post CAR-T infusion	Remission, response and survival data
All concomitant medications given in addition to the investigational product	Multiple biopsies data	High frequency vital signs measurements	Demographics including site of care

METHODS: Academic-Industry Collaborations

- The Research Hub's goal is to democratize this robust dataset to ensure that these data can be used to transform patient care and propel the field forward with our physician-scientist collaborators.
- The Research's Hub's mission is to bring together academic-industry partners to make trials more efficient and more inclusive for wider spread adoption of promising therapeutic advancements, like CAR-T/bispecific therapies.
- The working model of the Research Hub is for our partners to learn from one another and to work collectively towards bridging insights from data to clinical practice. Each collaboration is unique, and generally includes project scoping based on a variety of factors (hypotheses of-interest, data feasibility, clinical utility, target output, etc):
  - Medidata AI provides the clinical data and analytics lens with industry expertise in clinical trial management.
  - Research Hub academic collaborators contribute a deep understanding of immunology, cancer biology, and clinical practice, enriching the design and interpretation of immunotherapy trials based on their research topics of-interest.
- Research Hub collaborators also have opportunities to network and meet one another to further discuss latest findings in the field and additional ways to partner.

RESULTS

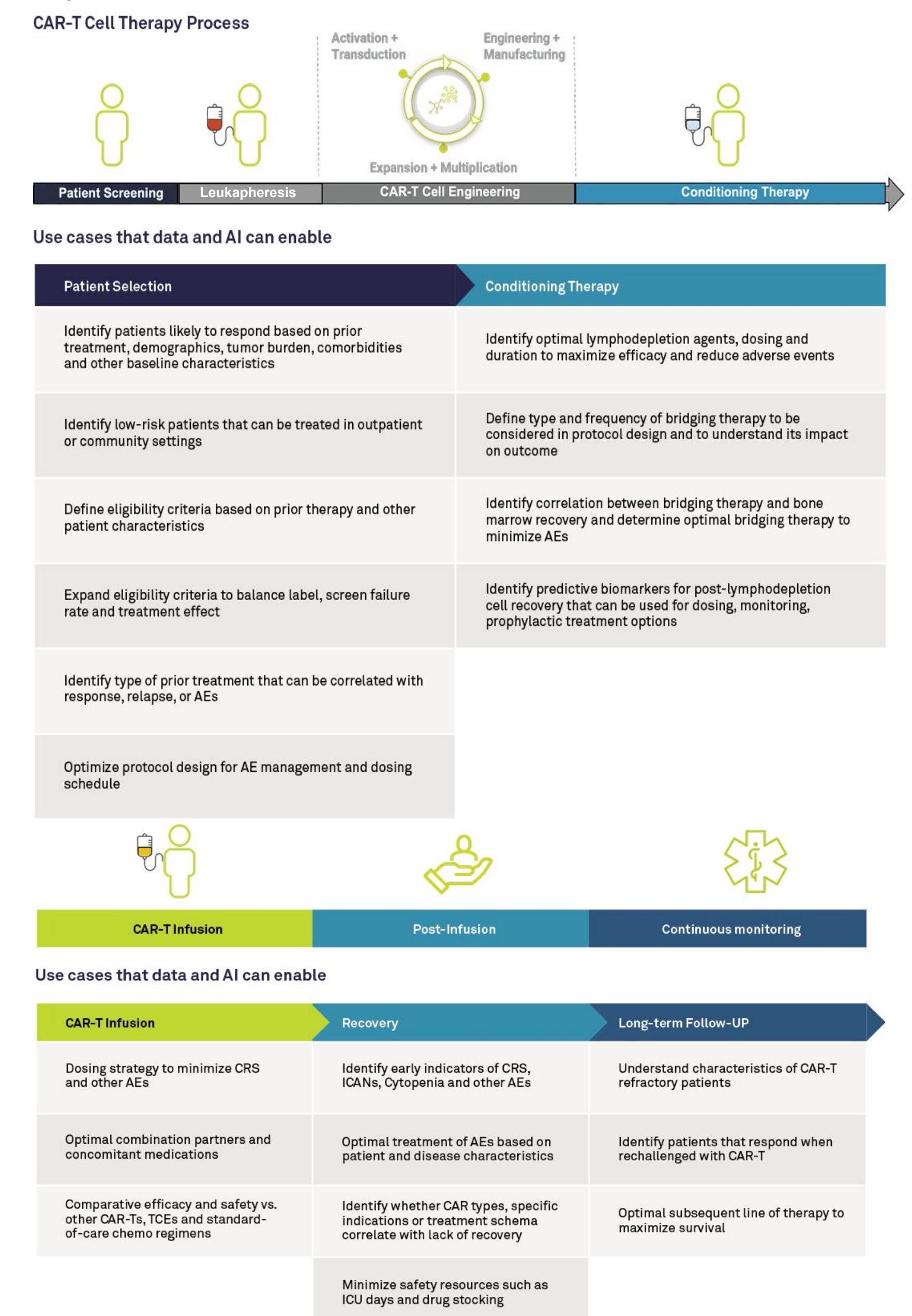- **Our network of collaborators continues to grow and includes academic physician-scientists, industry leaders, and leading AI data scientists. Below are select examples of key findings:**

- In collaboration with Esther Nie, MD, PhD (Stanford U) we studied the association of ICANS with CRS. Results show that pre-emptive treatment of CAR-T recipients with tocilizumab and dexamethasone reduces severe CRS rates, but does not decrease rates of ICANS. *Presented at the 2023 EBMT-EHA 5th CAR-T Meeting.*

- In collaboration with David Fajgenbaum, MD, MSc (UPenn) we performed an analysis on pre-infusion clinical data to capture longitudinal patterns in common lab markers and vitals. Results highlight that dynamic tracking of patient status will be key to effective mitigation of severe CRS. *Presented at the 2022 64th ASH Annual Meeting.*

- In collaboration with Michael Kattan, PhD (Cleveland Clinic) we analyzed lab tests with repeated measurements to identify differences in trends that persist across a variety of CAR-T trials. Results highlight that the temporal dynamics of routine clinical lab values can predict the likelihood of CRS for patients prior to CAR-T infusion. *Presented at the ASCO 2022 Annual Meeting.*

- In collaboration with David Fajgenbaum, MD (UPenn) we explored early risk of moderate-to-severe CRS in the first 7 days following CAR-T therapy. This analysis demonstrates how pooled trial data enables robust assessment of factors independently associated with development of CRS (grade 2+) after CAR-T therapy. *Presented at the 2022 NCCN Annual Congress.*

DISCUSSION

- Within this pooled clinical trial database are millions of data points, providing a holistic, longitudinal view of the patient's treatment journey. There are a variety of growing research use cases that our data can enable, including but not limited to the following (Fig 3):

Figure 3: Example Use Cases

CAR-T Cell Therapy Process

Use cases that data and AI can enable

Patient Selection	Conditioning Therapy
Identify patients likely to respond based on prior treatment, demographics, tumor burden, comorbidities and other baseline characteristics	Identify optimal lymphodepletion agents, dosing and duration to maximize efficacy and reduce adverse events
Identify low-risk patients that can be treated in outpatient or community settings	Define type and frequency of bridging therapy to be considered in protocol design and to understand its impact on outcome
Define eligibility criteria based on prior therapy and other patient characteristics	Identify correlation between bridging therapy and bone marrow recovery and determine optimal bridging therapy to minimize AEs
Expand eligibility criteria to balance label, screen failure rate and treatment effect	Identify predictive biomarkers for post-lymphodepletion cell recovery that can be used for dosing, monitoring, prophylactic treatment options
Identify type of prior treatment that can be correlated with response, relapse, or AEs	
Optimize protocol design for AE management and dosing schedule	

Use cases that data and AI can enable

CAR-T Infusion	Recovery	Long-term Follow-UP
Dosing strategy to minimize CRS and other AEs	Identify early indicators of CRS, ICANs, Cytopenia and other AEs	Understand characteristics of CAR-T refractory patients
Optimal combination partners and concomitant medications	Optimal treatment of AEs based on patient and disease characteristics	Identify patients that respond when rechallenged with CAR-T
Comparative efficacy and safety vs. other CAR-T types, TCEs and standard-of-care chemo regimens	Identify whether CAR types, specific indications or treatment schema correlate with lack of recovery	Optimal subsequent line of therapy to maximize survival
	Minimize safety resources such as ICU days and drug stocking	

- The combination of using data and AI applications, and partnering with the field's wide range of experts/stakeholders allows us to (1) extract deep insights throughout the patient treatment journey and (2) derive valuable information for optimizing development.
- **To learn how to get involved, contact Sheila Diamond, MS, CGC (Research.Hub@3ds.com)**

Acknowledgements