SPECIFIC AIMS. For information technology to drive clinical and translational research, a shift in how we develop and share expertise, tools, and data is required. Individual CTSA hubs have advanced this goal within their institutions, but opportunities to better leverage activities and learn from our collective experience within and beyond the CTSA network are missed. Our vision is to develop **A National Center for Digital Health Informatics Innovation**. We have assembled a team of pioneers in complementary disciplines who are experts in key issues relevant to this RFA: large-scale coordination, collaborative communities of practice, the tools and data these communities employ, massive online training, and research impact.

Aim 1: Harmonize the data ecosystem. An improved data ecosystem will enhance and extend existing work being performed on the NCATS Data Translator system, which integrates clinical and translational data at scale for mechanistic discovery, as well as other emergent systems such as the NIH Commons. We will apply our strengths and existing activities to make data **FAIR-TLC**: **Findable, Accessible, Interoperable, and Reusable, as well as Traceable, Licensable, and Connected**. We will assist contributors and users to develop and apply data standards, Common Data Elements (CDEs), and other commonly utilized data models such as FHIR and OHDSI. We will extend and supplement infrastructure, training, and collaborative environments to enable data to be shared openly, so that groups can collaborate on its harmonization based on specific needs or standards. The data ecosystem will provision CTSA-wide quality assurance reports and data quality assessment, as well as gold-standard datasets and synthetic clinical data sets. Fundamentally, we aim to develop an open-science ethos and unite CTSA community data sharing with broader global efforts.

Aim 2: Realize a software tool ecosystem. Guided by FAIR-TLC principles, we will collaboratively develop, advance, and promote an ecosystem for open-source translational software development projects and the creation of aligned communities of practice. In this context, we define an ecosystem as the combination of people, technologies, and methods needed to predispose and enable successful collaborative projects. This ecosystem will support CTSA teams across the full lifecycle of software development and dissemination, including: 1) access to relevant expertise and knowledge resources to inform project design and execution; 2) collaborative innovation platforms for methodological development and benchmarking (Synapse); and 3) rapid dissemination and interaction mechanisms for the discovery and use/reuse of software and associated data assets across a full spectrum of maturity levels (CIELO). All of these activities will have as their foundation the use of community-accepted software engineering, quality assurance, and interoperability standards. In addition, we will refine metadata schemas for API standards, containerization, and cloud-based deployment to provide a common technology deployment model for these efforts. This overall approach enables transparent benchmarking, quality control, standards compliance, and efficient dissemination of software tools and supporting artifacts by promoting and enabling open source and collaborative development best practices and norms. We will evaluate, update, and optimize this ecosystem by conducting robust environmental scanning activities that will informing a continuous process improvement approach. This ecosystem will enable a systems approach to the collaborative, efficient, and high-quality conduct of software development and dissemination efforts across the entire CTSA network.

Aim 3: Synthesize a people ecosystem. We will adapt and expand our existing research profiling infrastructure to catalyze discovery, extending it where necessary using collaborative approaches built on science of team science open processes to empower the diverse teams needed for data-driven translational discovery. To achieve this, we will leverage effective strategies and inventive approaches to build connections within and beyond the CTSA Consortium. We will develop tools to identify, track, disseminate, and understand the contribution and impact of software, data, informatics, and other non-traditional scholarly products and activities to properly attribute credit. Finally, this extended knowledge about expertise across the CTSAs will be applied to assist in the creation and success of community-wide collaborative functions.

Aim 4: Catalyze technical and cultural evolution. Two translational areas will drive our **"Idea to Implementation (I2I)" pipeline**, that leverages the above Aims, develops community, and demonstrates impact: Rare Disease and Lifespan. Here we guide CTSAs to establish I2I data workflows and target software tools to meet clear needs of these areas (e.g. global patient-matchmaking, temporal data analysis, collaborative extension of algorithms, and CTSA-wide data sharing). Finally, we will provide mechanisms to utilize the proposed infrastructure and I2I process to improve communities of practice using the Sage DREAM challenges, which will promote friendly competitions and collaborations to benchmark methodologies in specific informatics areas.