NCI and FNIH Pediatric Preclinical Testing Public-Private Partnership (PPTP3)

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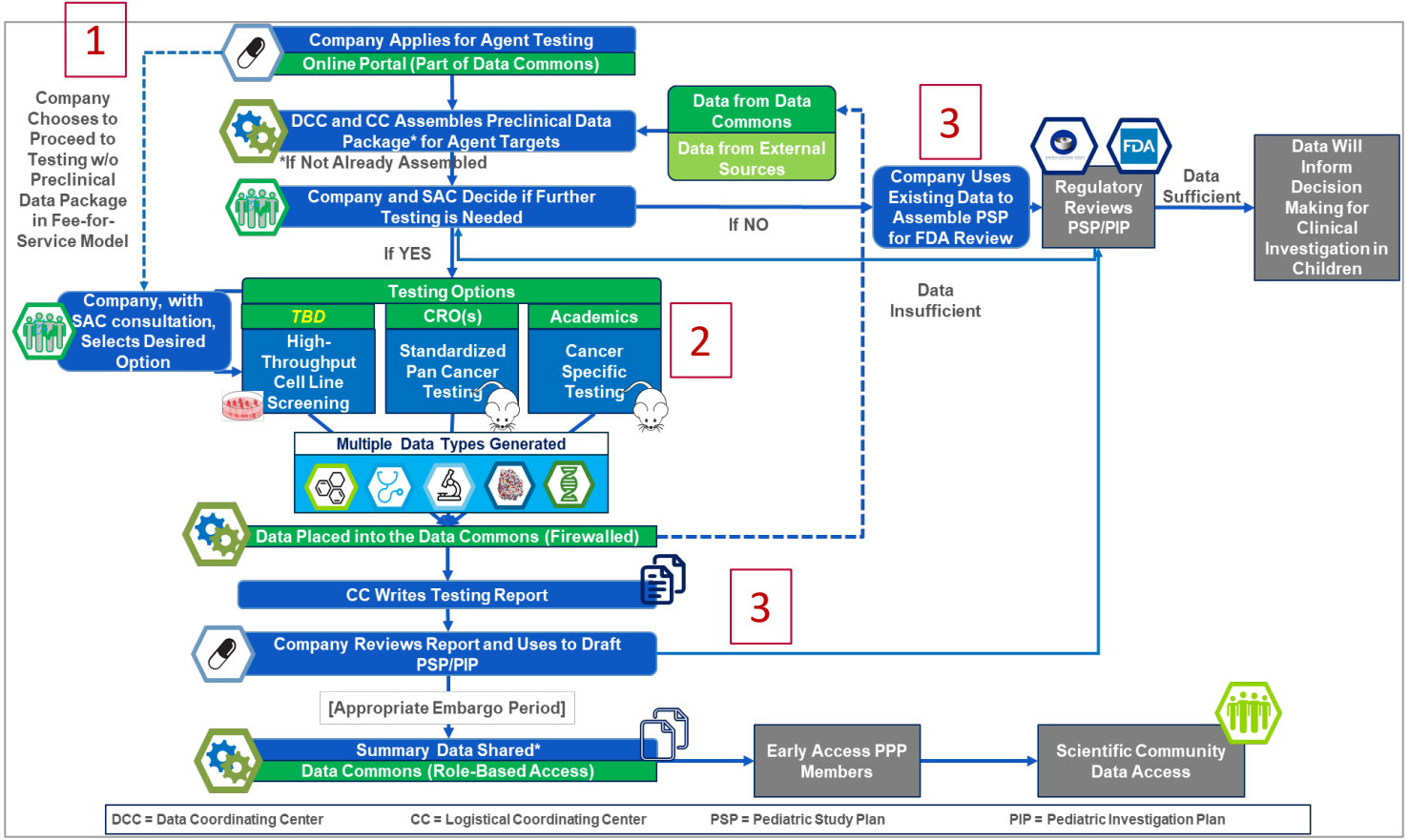
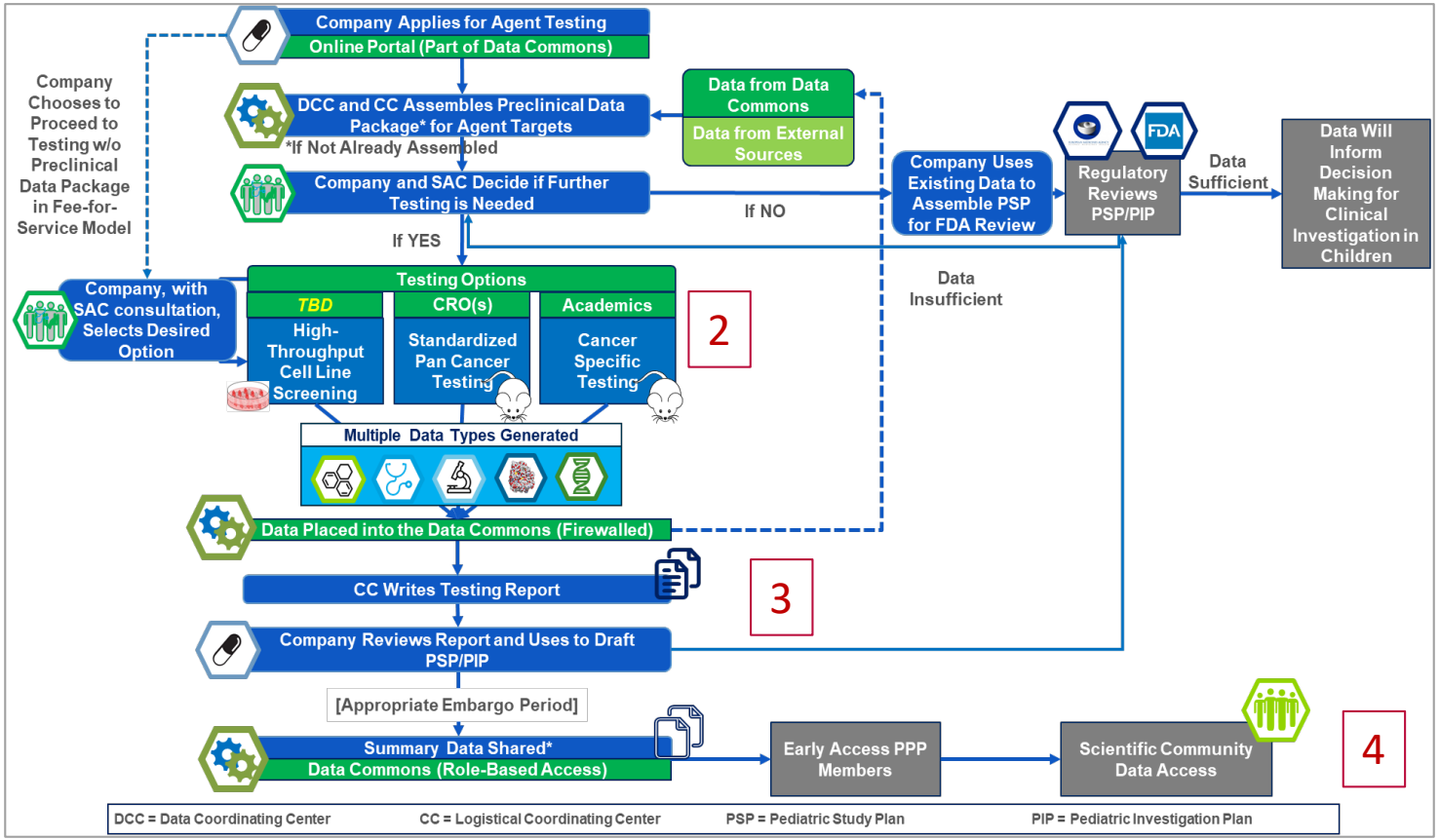
FNIH Preclinical Pediatric Oncology PPP

- Compliance with the Research to Accelerate Cures for Children (RACE) Act is the compelling ‘impending event’
  - RACE Act adds a new molecularly targeted pediatric investigation requirement for certain oncology medicine applications
  - Expansion of bandwidth for preclinical testing needed to inform evidence-driven prioritization decisions
- FNIH has established a partnership framework research agenda with all interested parties with White Paper released March, 2020
- Partnership includes Pharma, NCI, FDA, and Academia
- Partnership will involve both NIH funding as well as private sector funding

FNIH and NCI PPTP3 Operating Model (Company Perspective)

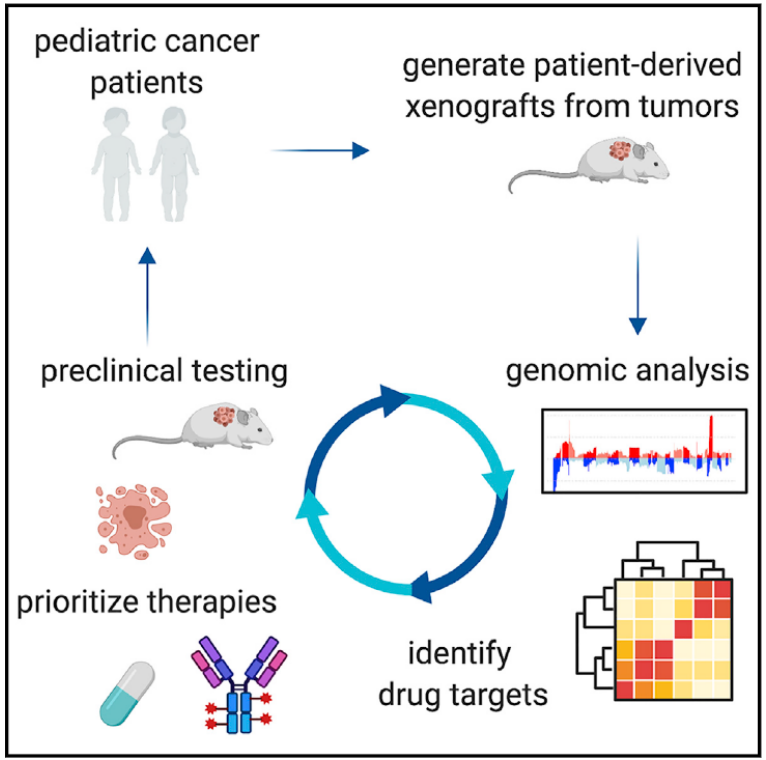


FNIH and NCI PPTP3 Operating Model (Academia Perspective)



PPTC Accomplishments – Genomic Characterization

- PPTC created an annotated genomic dataset of somatic oncogenic regulation across 37 distinct pediatric malignancies encompassing 261 patient-derived xenograft models
- Data available through PedcBioPortal https://pedcbioportal.org/study?id=pptc#summary
- Plans for additional genomic characterization of PDX and cell line models in FY2020



Rokita JL, et. al; Cell Reports 2019

PPTC Accomplishments (examples)

- Validation of **DLL3** and **DLK1** as therapeutic targets for neuroblastoma
- Validation of **CD276** (B7-H3) as therapeutic target for multiple pediatric solid tumors
- Identification of **OBI-3424** (**AKR1C3-activated** alkylating agent) as highly active for T-ALL → S1905 (NCT04315324)
- Identification of limited activity for **HDAC inhibitor** with SOC agents for RMS
- Identification of activity of **Aza-TdCyd** for pediatric ALL, but limited activity for TdCyd
- Identification of a **menin inhibitor** as highly active for ALL with MLL-rearrangement → NCT04065399 (SNDX-5613) (AACR 2020, Jerry McGeehan)
- Validation of **STEAP1** as an IO target for Ewing sarcoma using the extended half-life bispecific antibody AMG 509 (AACR 2020, Olivier Nolan-Stevaux)

Concept for NCI components of PPTP3

- PPTP3 In Vivo Testing Program
- PPTP3 Coordinating Center for the in Vivo Testing Program
- Future components:
  - High Throughput in Vitro Testing Program
  - Data Commons

NCI PPTP3 in Vivo Testing Program (inVivoTP)

- Plan for 8 awards for research programs for in vivo testing
- Open competition for in vivo testing sites with plan to encourage applications from new research teams
- Agnostic in terms of models (e.g., PDX in immunodeficient mice, murine genetic models engineered to reflect the characteristics of specific pediatric cancers, and murine syngeneic models)
- Potential disease areas of focus include: ALL, AML, neuroblastoma, osteosarcoma, rhabdomyosarcoma, Ewing sarcoma, renal and hepatic tumors, & CNS tumors

NCI PPTP3 in Vivo Testing Program (inVivoTP) - Continued

- Each team anticipated to test 8-10 agents per year
- Plan for broader utilization for single-mouse trial (SMT) design for agents for which tumor-regressing activity is sought
- Selection criteria to include:
  - Number and breadth of models proposed and the extent to which the proposed tumor panels faithfully recapitulate key biological characteristics of molecularly defined subtypes of specific pediatric cancers
  - Scientific leadership that the research team is anticipated to bring to the PPTP3 and its Scientific Advisory Committee
  - Ability to conduct testing with required throughput

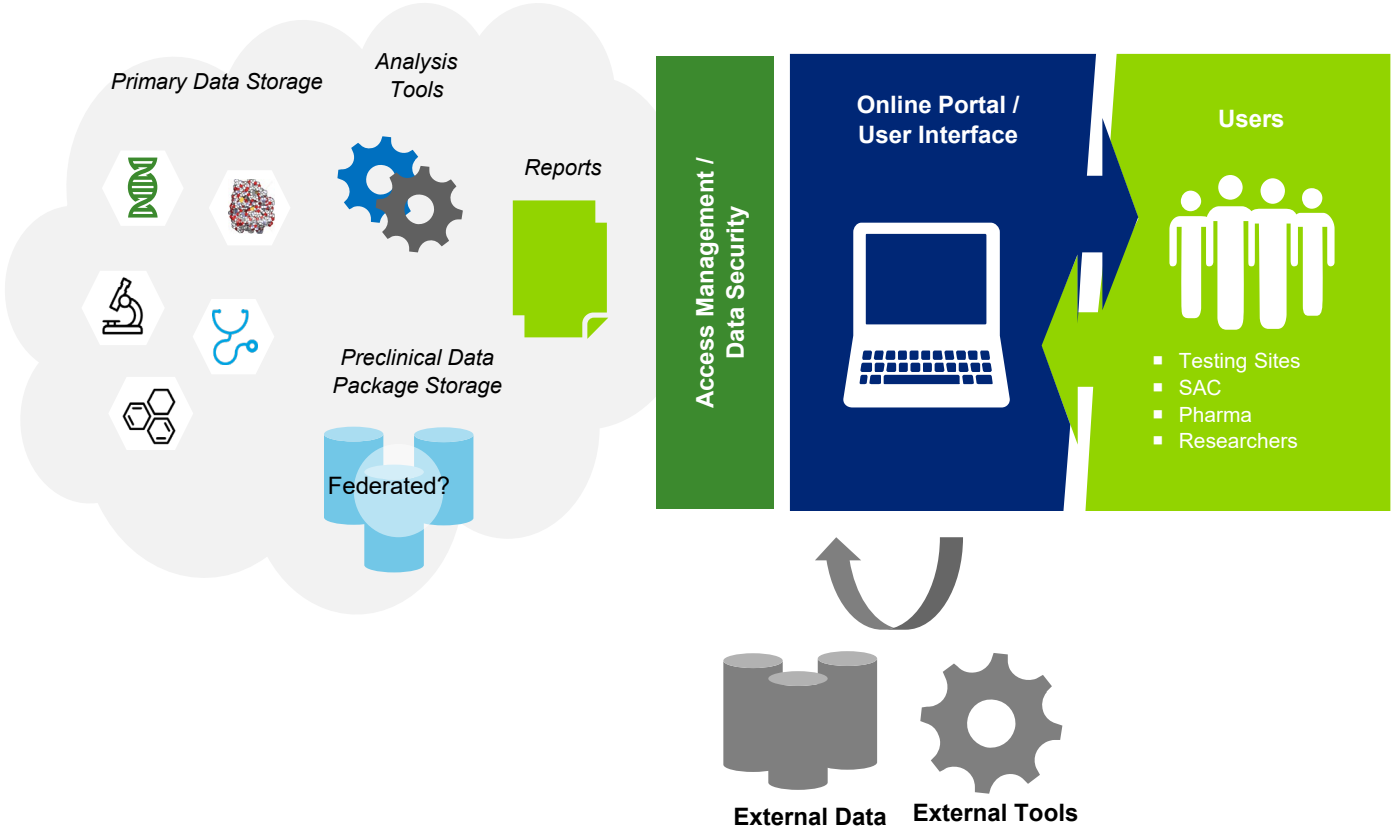
PPTP3 Coordinating Center

- Administrative management, logistics, & coordination of in vivo testing sites
- Establishment of a confidential and private project information site
- Development of quality assurance/quality control procedures
- Management of laboratory specimens and a biospecimen tracking system
- Coordination of shipments of compounds supplied by companies to testing sites
- Collection, analysis and storage of testing data from the testing sites
- Preparation of technical study reports for agents tested through the PPTP3
- Collaboration with research programs in developing, presenting, and publishing manuscripts

PPTP3 Data Commons (competed through future RFA)

- To aggregate/federate and analyze genomic, proteomic, and epigenomic characterization data for cell lines and PDX models from both PPTP3 research teams and from external research teams
- To aggregate/federate and analyze genomic, proteomic, and epigenomic characterization data for clinical specimens to establish as comprehensive a dataset as possible to facilitate robust comparisons to preclinical data
- To aggregate, store, and compare existing and new testing data both from PPTP3 research teams and from external research teams
- Provide analyses of genomic, proteomic and epigenomic data to support decision-making for preclinical evaluations and for clinical development plans
- Make data available in ways that are easily accessible by the research community

PPTP3 Data Commons



Timeline for Moving NCI Component of PPTP3 Forward

- June 2020 – Publication of RFA in NIH Guide
- Aug 2020 – Application receipt data
- Nov 2020 – Peer review
- April 2021 – Award

Budget

Component	Direct Costs Year 1	Total Costs Year 1
PPTP3 in vivo testing program (inVivoTP) (n=8)	$3.2 million	$5.1 million
PPTP3 Coordination Center	$0.5 million	$0.80 million
PPTP3 in vitro testing program (inVitroTP)	TBD	TBD
PPTP3 Data Commons	TBD	TBD
Total Combined	$3.7 million	$5.9 million

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