TransCelerate
BIOPHARMA INC.

ACCELERATING THE DEVELOPMENT OF NEW MEDICINES

Pre-Competitive Collaboration in Clinical Trials

March 17, 2014

David Jordan, PhD
Member of the Operations Committee and
Project Leader for Clinical Data Standards
TransCelerate Biopharma

Outline

- **TransCelerate Overview**
  - **Why**
  - **Who**
  - **What**
- CFAST Overview
- Opportunity for Collaboration

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Why do we need Pre-Competitive Collaboration in Clinical Trials?

Moore's Law: Transistor Count Doubling Every Two Years

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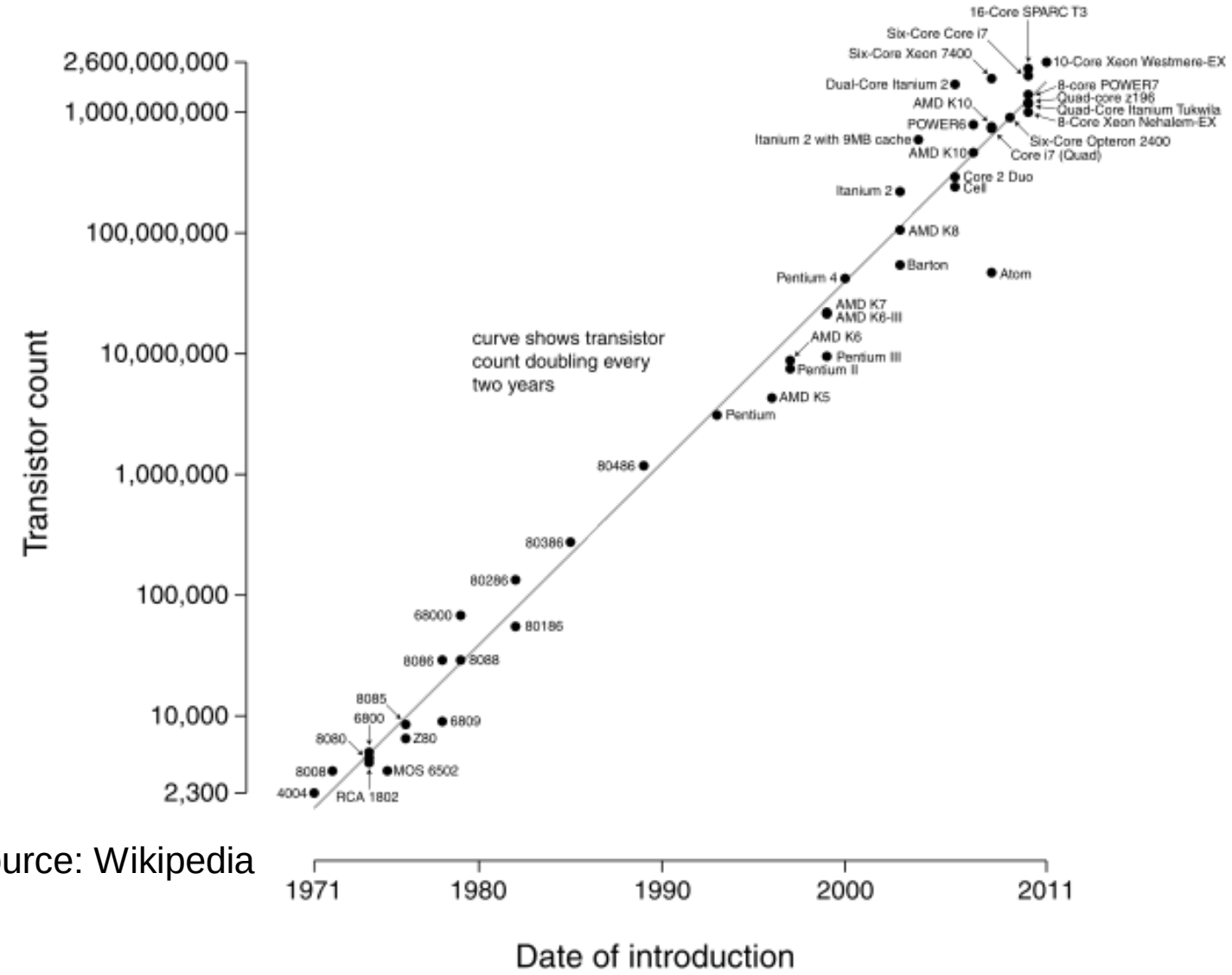

Source: Wikipedia

Eroom's Law: Number Of New Drug Approvals Per Billion US Dollars Halved Every Nine Years

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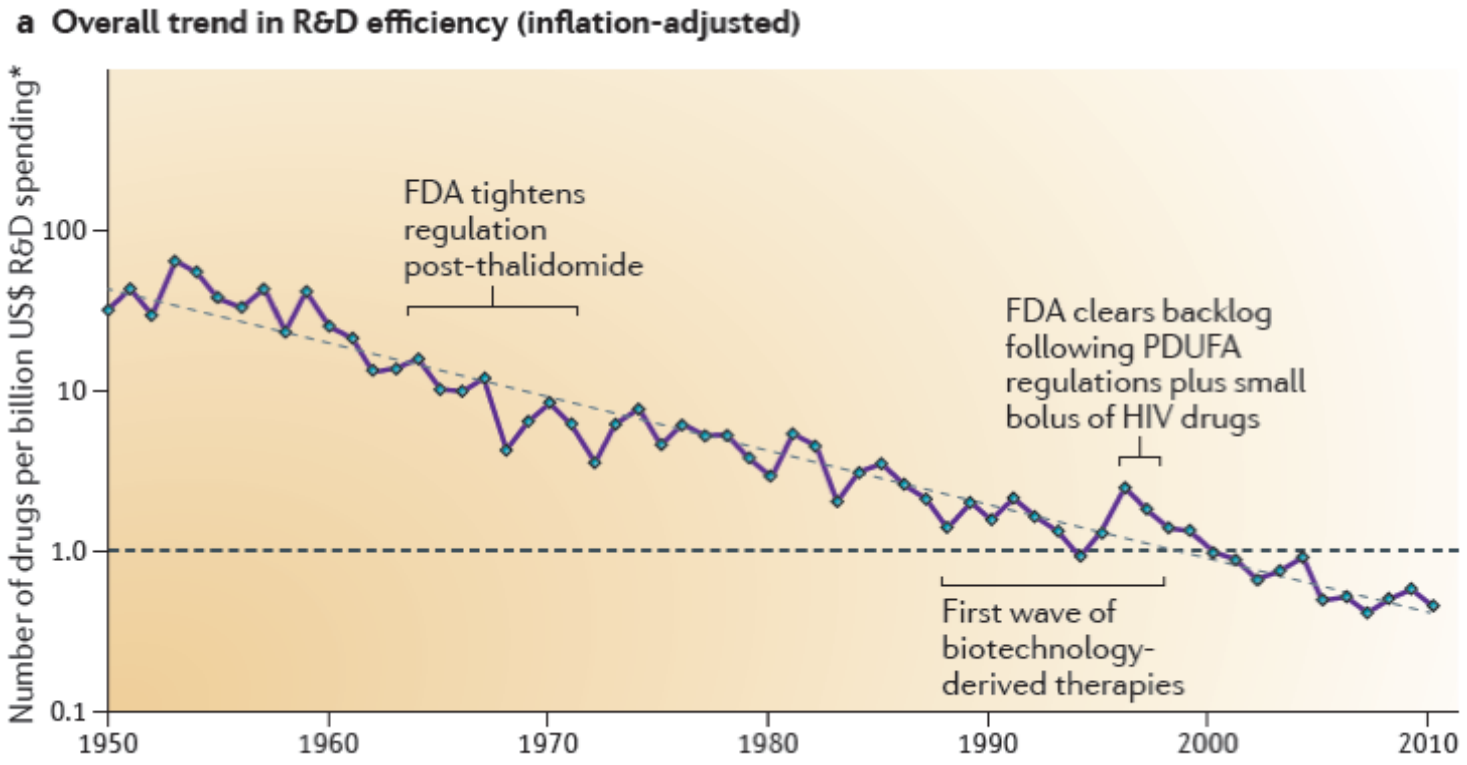

Source: Nature Reviews – Drug Discovery: Diagnosing the decline in pharmaceutical R&D efficiency Vol 11, March 2012, page 191 - 200

Some Causes of Declining Productivity in Drug R&D

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- Biomedical R&D increasingly complex*
- Higher regulatory hurdles *
- Challenges too large for individual companies to overcome

*Source: Nature Reviews – Drug Discovery: Diagnosing the decline in pharmaceutical R&D efficiency Vol 11, March 2012, page 191 - 200

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Who is TransCelerate
How does it operate?
What are its Initiatives?

TransCelerate BioPharma - A Response to the Productivity Crisis in Drug Development

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- **TransCelerate launched September 2012 by ten of the largest global Pharmaceutical companies to**
  - **advance innovation in drug R&D**
  - **identify and solve common R&D challenges**
  - **further improve patient safety**

- **Clinical Trial execution identified as a key priority**

The Charter Members of TransCelerate Include Ten Major Pharmaceutical Companies

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TBA (Board Member)

David Jordan (Operations Committee)
Divisional VP, Stats & Data Mgmt

Briggs Morrison (Board Member)
EVP, Global Medicines Development
Sue McHale (Operations Committee)
Executive Director, Global Project Delivery

Klaus Dugi (Board Member)
Corporate SVP, Medicines
Thor Voigt (Operations Committee)
Head of Global Clinical Ops, Biometrics & Data Management

Brian Daniels (Board Member)
SVP Global Development & Medical Affairs
Jonathan Zung (Chairman, Operations Committee)
VP, Global Development Operations
Reb Tayyabkhan (Operations Committee)
Exec. Director, GDO Business Operations

Patrick Vallance (Board Member)
President, Pharmaceuticals R&D
Lynn Marks (Corporate Secretary)
SVP, Clinical Platforms & Sciences
Pete Milligan (Operations Committee)
VP, Clinical Platforms Transformation

Paul Stoffels (Board Member)
Worldwide Chairman of J&J Pharmaceuticals
Martin Fitchet (Treasurer to the Board, Operations Committee)
Chief Operating Officer

Jan Lundberg (Board Member)
EVP of Science & Technology
Jeff Kasher (Operations Committee)
VP and COO Global Medical R&D

John Hubbard (Board Member)
SVP Development Operations
Craig Lipset (Operations Committee)
Head of Clinical Innovation

Corsee Sanders (Board Member)
Global Head of Development Innov. & Clin Ops
Carol Harris (Operations Committee)
Global Head Project & Functional Excellence

Elias Zerhouni (Board Member)
President of Global R&D
Andy Lee (Operations Committee)
SVP, Head Global Clinical Operations

Nine new member companies joined TransCelerate in 2013

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Board Members

Peter Carberry (Board Member)
SVP & Head of Global Development Operations
Nancy Sacco (Operations Committee)
Executive Director, Development Sciences/Strategic

Alfred Sandrock (Board Member)
SVP, Head of Development Sciences & CMO
Murray Abramson (Operations Committee)
VP, Global Clinical Operations

Steve Gilman (Board Member)
EVP, R&D and CSO
Uschi Stoutenburgh (Operations Committee)
Senior Director, Clinical Operations

Annalisa Jenkins (Board Chair)
Global Head of R&D
Kathleen Ford (Operations Committee)
Senior VP, Head of Global Clinical Operations

Marco Taglietti (Board Member)
President, Forest Research Instituite & CMO
Ulo Palm (Operations Committee)
SVP, Clinical Operations & Biometrics

Garry Neil (Board Member)
Global Head, R&D

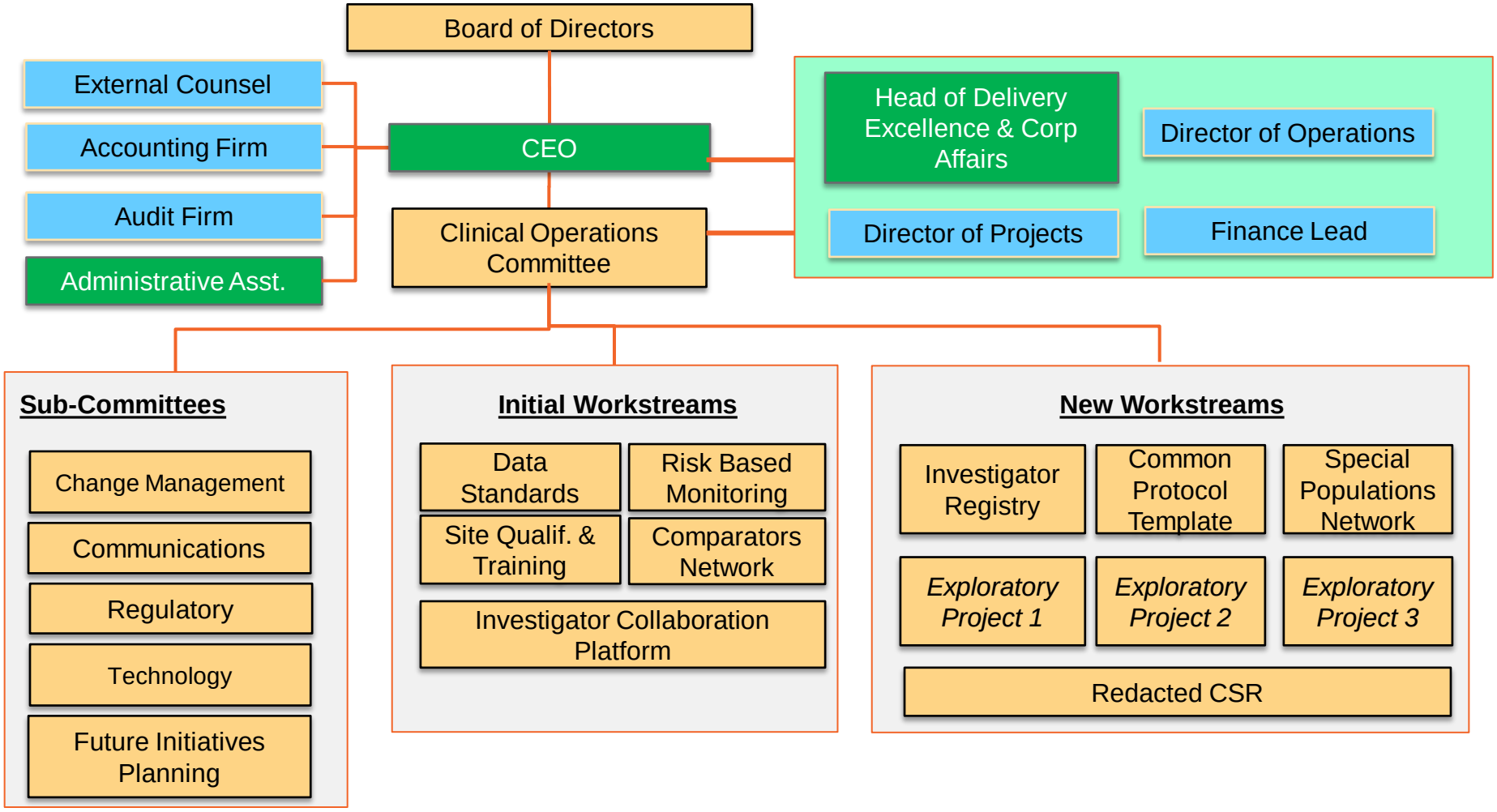
Non-Board Members

Steve Johnson (Operations Committee)
SVP, R&D Business Services

Gareth Morgan (Operations Committee)
SVP, Portfolio Management, Global Development Office

Brigitte Koch (Operations Committee)
VP, Head Global Clinical Project Management

A flat organization structure has been developed to manage projects and operational activities



Not for profit entity created to drive collaboration as means to developing solutions for overcoming inefficiencies

TransCelerate BIOPHARMA INC.
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Our vision

To improve the health of people around the world by accelerating and simplifying the research and development of innovative new therapies.

Our mission

To collaborate across the global research and development community to identify, prioritize, design and implement solutions that drive the efficient, effective and high quality delivery of innovative new therapies.

Our core values

- Quality
- Transparency & Openness
- Trust & Integrity
- Collaboration
- Courage

An Entity that Engages with the Wider Clinical Ecosystem Globally

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Strategically focusing engagement efforts with selected key stakeholder groups

The intent is not to recreate, but partner whenever feasible

Confidential - NOT FOR DISTRIBUTION

Ongoing Initiatives – progress (1 of 3)

Five Selected Areas of Focus Have the Shared Goals of Increased Quality, Patient Safety and Accelerated Development Timelines			
Initiative	Objective	Benefit	• Progress to date
Clinical Data Standards – Efficacy (in Partnership with CDISC and CFAST)	Accelerate current efforts underway through CDISC to establish efficacy data standards	Increased quality of clinical data and enablement of industry end-to-end data flow	• Partnered with CDISC, Critical Path Institute, FDA and NCI on CFAST Therapeutic Area Program Steering Committee • Asthma, Diabetes, Cardiovascular endpoints, QT studies, Multiple Sclerosis, Hepatitis C and Traumatic Brain Injury selected as first TAs of focus • Approved Breast Cancer, Influenza, Lipid-Lowering, COPD, CV Imaging, MDD, RA, Psoriasis & Schizophrenia project proposals • SHARE environment (metadata repository) press release issued with CDISC in June 2013; SHARE R1 Release went live Jan 31 2014 • Asthma Therapeutic Area User Guide V1.0 published Nov 27
Comparator Drugs for Clinical Trials	Establish a supply model to source comparator drugs between companies for use in clinical trials	• Reduce the cost and effort for comparator drug sourcing • Reduce the chance of counterfeit drug in study supply chain • Share critical data – like solid dose ambient temp excursions	• Determined in-scope products and required documentation for distribution model • Defined principles and process for drug distribution model • MSA's between members finalized • First set of transactions initiated in July 2013 • Press release issued in August 2013 • Multiple transactions continue to occur and direct benefits being realized • Expansion of network activities for 2014

Ongoing Initiatives – progress (2 of 3)

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Five Selected Areas of Focus Have the Shared Goals of Increased Quality, Patient Safety and Accelerated Development Timelines			
Initiative	Objective	Benefit	Progress to date
Model Approach for High-Quality, Risk-Based Monitoring	Develop an industry framework for targeted, risk based clinical trial monitoring	• Improvement in data quality and patient safety for clinical trials • Reduction in effort expended on low-value activities	• FDA and EMA feedback incorporated • Position paper and methodology published in May 2013 for access to entire clinical trial community; ➢ Update to the paper and associated training materials published in January 2014 • More than 30 pilots identified and launched with 8 of these reviewed by FDA prior to initiation • Over 2000 unique downloads of position paper • Conducted FDA orientation for the TransCelerate RBM methodology
Shared Site Qualification and Training	Mutual recognition of GCP training between pharmaceutical companies and streamlining site qualification process	• Improved quality of clinical sites and accelerated study start-up times • Reduce site burden	• Team formed to streamline site documentation • Establishment of framework for mutual recognition of GCP training completed ➢ Minimum content elements ➢ Process for awarding certificates ➢ Process for training providers to self attest to minimum criteria/courses • Mutual recognition framework established • Created and published to TransCelerate website: ➢ CV and Site Profile Documents and Guidance ➢ Guidance for completion of FDA document 1571/72 ➢ Guidance and Delegation of Responsibility form • Planning for PI Oversight Training and Training for Sites Less Experienced with Clinical Trials

Ongoing Initiatives – progress (3 of 3)

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Five Selected Areas of Focus Have the Shared Goals of Increased Quality, Patient Safety and Accelerated Development Timelines			
Initiative	Objective	Benefit	Progress to date
Shared Site Collaboration Platform (formerly Common Investigator Site Portal)	Establish a single, intuitive interface for investigators, regulators and member companies	• Ease of use and harmonized retrieval of content and services for investigators • Reduce site burden • Reduce member company costs	• Defined components to leverage from existing industry portals • Board approval for analysis phase in June • Systems integrator, product partner and hosting partner selected • Early adopters of system confirmed

The future - a roadmap was created with the future state in mind

Current State

- Disconnected interfaces
- Manual processes and interventions
- Limited standardized processes
- Lot of customization
- Rework
- Variable quality
- Wait time
- Missing information
- High costs
- Long cycle times
- Duplication of efforts

Approved TransCelerate projects

Ongoing projects

- Data Standards
- Risk Based Monitoring
- Comparator Network (ES)
- Site Qualification and Training (ES)
- Collaborative Technology Platform

New projects for 2014

- *Data Transparency/CSR Redaction**
- Common Protocol Template
- Investigator Registry
- Clinical Trial Networks
  - Pediatric patients
  - Minority patients

Exploratory projects for 2014

- Exploratory project I
- Exploratory project II
- Exploratory project III

Future State

- Patient-centric clinical trial design
- End-to-end electronic data flow
- Seamless interfaces
- Automated
- Transparent
- Increased standardized processes
- Less rework
- Quality by design
- Shorter cycle times
- Cost efficient
- Integration of Regulatory, Safety and Medical Sciences
- Elimination of redundancies
- Conducting clinical trials together
- "Colossal Data Analytics"

(ES) – Expanded Scope for 2014

** Workstream initiated to meet compliance deadline*

New Initiatives (1 of 2)

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Three New Initiatives Will Further Support the Goals of Increased Quality, Patient Safety and Accelerated Development Timelines			
Initiative	Unmet Need	Description	Benefit
Common Protocol Template	• Format of study protocols vary from company to company making interpretation difficult for study sites, IRBs, and regulators. • Study protocols have become increasingly complex as no agreed upon standards exists driving up cost and time. • Manual set-up of clinical systems based on non-standard “manual” protocols are time consuming, costly, and prone to error	Standardize the format of clinical protocols to ease interpretation & enable down-stream automation of many clinical processes. Develop industry-wide & regulator accepted standards for required protocol endpoints	• Higher productivity of sponsors, sites, IRBs, and regulators • Less costly and time consuming clinical trials • Enabler for downstream automated setup of clinical and operational systems & disclosure activities

New Initiatives (2 of 2)

Three New Initiatives Will Further Support the Goals of Increased Quality, Patient Safety and Accelerated Development Timelines			
Initiative	Unmet Need	Description	Benefit
Investigator Registry	Sponsors invest significant time and money in identifying qualified investigators and setting up study sites	To create a shared repository of investigators to support targeted patient selection	Reduced cost and time of setting-up and running clinical trials
Special Populations Clinical Trial Networks (minority & pediatrics)	• Qualified investigators with adequate study patients are difficult to find for special populations – e.g. pediatric and minority • Studies in minorities and pediatrics are costly and lengthy • Efforts are put into repeatedly establishing a network for a single study only to disperse the network after study completion	Lead the development of global investigator networks for pediatric and minority populations including governance, investigator and patient registries, and technical infrastructure	• Faster development of new drugs in both pediatric and minority populations • Reduced costs of pediatric and minority trials

Summary

- **Drug Development is facing a productivity crisis**
- **TransCelerate BioPharma Inc. has been founded to address aspects of this issue**
- **A number of critical initiatives are ongoing or will start to improve the clinical trial process in key areas**

Outline

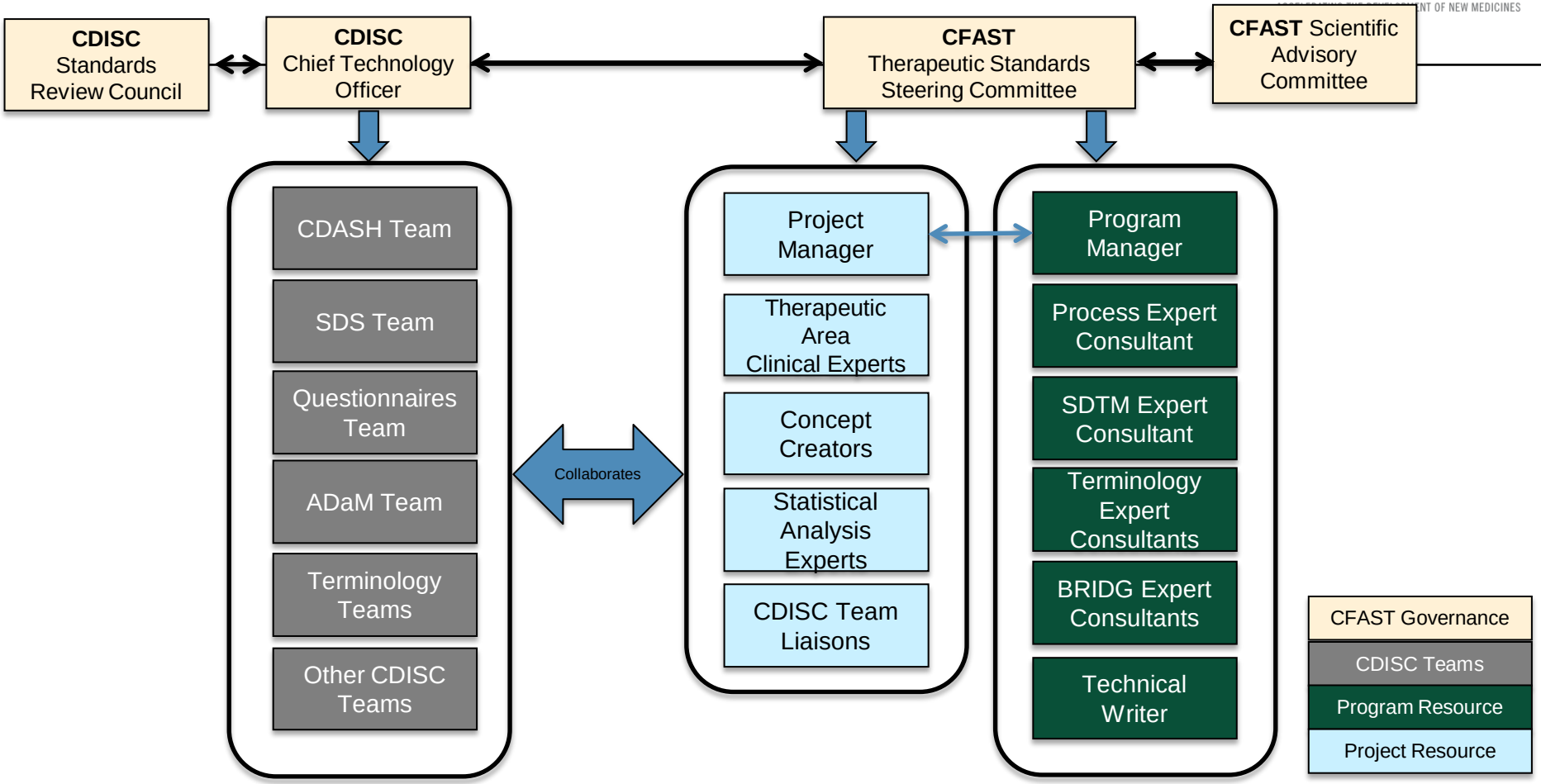
- TransCelerate Overview
- **CFAST Overview**
  - **Therapeutic Area Data Standards Organization**
  - **TA Data Standards Projects**
- Opportunity for Collaboration

  - **BRIDG**: The **B**iomedical **R**esearch **I**ntegrated **D**omain **G**roup (**BRIDG**) Model
  - **SHARE:** The CDISC **S**hared **H**ealth **A**nd Clinical **R**esearch **E**lectronic Library (**CDISC SHARE**)

Coalition For Accelerating Standards & Therapies -- CFAST

- CFAST - an initiative to accelerate clinical research and medical product development by creating and maintaining data standards, tools and methods for conducting research in therapeutic areas that are important to public health
- An Objective - Identify common standards for representing clinical data for studies of drug products in specific, prioritized therapeutic areas [TA]
  - To be implemented using CDISC structures (CDASH, SDTM)
  - Support integration of clinical data from disparate sources as a foundation for end-to-end data flow

Project Organization



Review Community: CDISC, C-Path, FDA, TransCelerate BioPharma, Key Opinion Leaders, Medical Associations, U.S. National Institutes of Health, Innovative Medicines Initiative

CFAST TA Data Standards Development 2013 List of Projects

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1. Asthma v1.0 - completed Nov 2013
2. Alzheimer's Disease v2.0 – completed Dec 2013
3. Multiple Sclerosis
4. Diabetes in adults
5. Cardiovascular Endpoints
6. QT Studies
7. Traumatic Brain Injury
8. Virology – Hepatitis C

CFAST TA Data Standards Development 2014 Partial List of Projects

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1. Oncology – Breast Cancer
2. Schizophrenia
3. Influenza
4. Lipid-Lowering
5. Rheumatoid Arthritis
6. Major Depressive Disorder (MDD)
7. Cardiovascular Imaging (echo)
8. COPD
9. tbd
10. tbd
11. tbd
12. tbd

See http://www.cdisc.org/therapeutic for more information

TA Standards: Baseline Content

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- Mindmap/model of disease area clinical concepts
- Essential core data elements with definitions, data types (simple & ISO 21090), BRIDG and SDTM mappings
- SDTM domains and examples
- Minimum value sets (code lists) with definitions and c-codes
- User/Implementation Guide with permissions statement
- Standard CDASH CRFs with SDTM annotations, as appropriate
- ADaM Analysis model examples as available
- Possibly study design models

Outline

- TransCelerate Overview
- CFAST Overview
- **Opportunity for Collaboration**

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What are opportunities for collaboration ?

Contact Points within TransCelerate

- **Clinical Data Standards**
  - **David Jordan** david.jordan@abbvie.com
  - **Rhonda Facile (CDISC)** rfacile@cdisc.org
- **Comparator Drugs for Clinical Trials - Terry Walsh** terry.walsh@transceleratebiopharmainc.com
- **Risk Based Monitoring - Reb Tayyabkhan** rehbar.tayyabkhan@bms.com
- **Shared Site Qualification and Training**
  - **Sue McHale** susan.mchale@astrazeneca.com
  - **Katarina Hugeneck** hugeneck_katarina@lilly.com
- **Shared Site Collaboration Platform - Jackie Kent** kent_jacalyn_m@lilly.com
- **Common Protocol Template - Rob DiCicco** robert.a.DiCicco@gsk.com
- **Investigator Registry - Bill Jordan** william.jordan@sanofi.com
- **Special Populations Clinical Trial Networks - Susannah Hammond** susannah.3.hammond@gsk.com

Safety Standards Domains

i/p = In progress
n/a = Not applicable
dft = Drafted
✓ = completed
? = not sure who / status
CDISC, PhUSE

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Topics	Collected (CDASH)	Observed (SDTM)	Analysis (ADaM)	Reporting (TFL)
Adverse Events	✓	✓	✓	i/p
Comments	✓	✓	n/a	n/a
Concomitant Medications	✓	✓	?	i/p
Deaths (AE)	✓	✓	?	i/p
Demographics	✓	✓	?	i/p
Disposition	✓	✓	?	i/p
ECG Test Results	✓	✓	?	dft
Exposure	✓	✓	n/a	n/a
Hepatotoxicity (central lab)	n/a	✓	?	i/p
Laboratory Data	✓	✓	?	dft
Medical History	✓	✓	?	i/p
Pharmacokinetics (lab, exposure?)	✓	✓	?	i/p
Subject Visits	✓	✓	n/a	n/a
Vital Signs	✓	✓	?	dft

Adapted from Scott Getzin

Therapeutic Area Standards (Defined)

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Topics	Observed (SDTM)	Analysis (ADaM)	Reporting (TFL)
Alzheimer's Disease v1	✓	?	?
Pain v1	✓	?	?
Parkinson's Disease v1	✓	?	?
Polycystic Kidney Disease v1	✓	?	?
Tuberculosis v1	✓	?	?
Virology v1	✓	?	?
Asthma v1	✓	-	?
Alzheimer's Disease v2.0	✓	?	?
Multiple Sclerosis	i/p	?	?
Diabetes in adults	i/p	i/p	i/p
Cardiovascular Endpoints	i/p	?	?
QT studies	i/p	i/p	?
Hepatitis C	i/p	i/p	?
Etc., Etc.	i/p	?	?

i/p = In progress
n/a = Not applicable
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Adapted from Scott Getzin

Alignment of Clinical Data Flow

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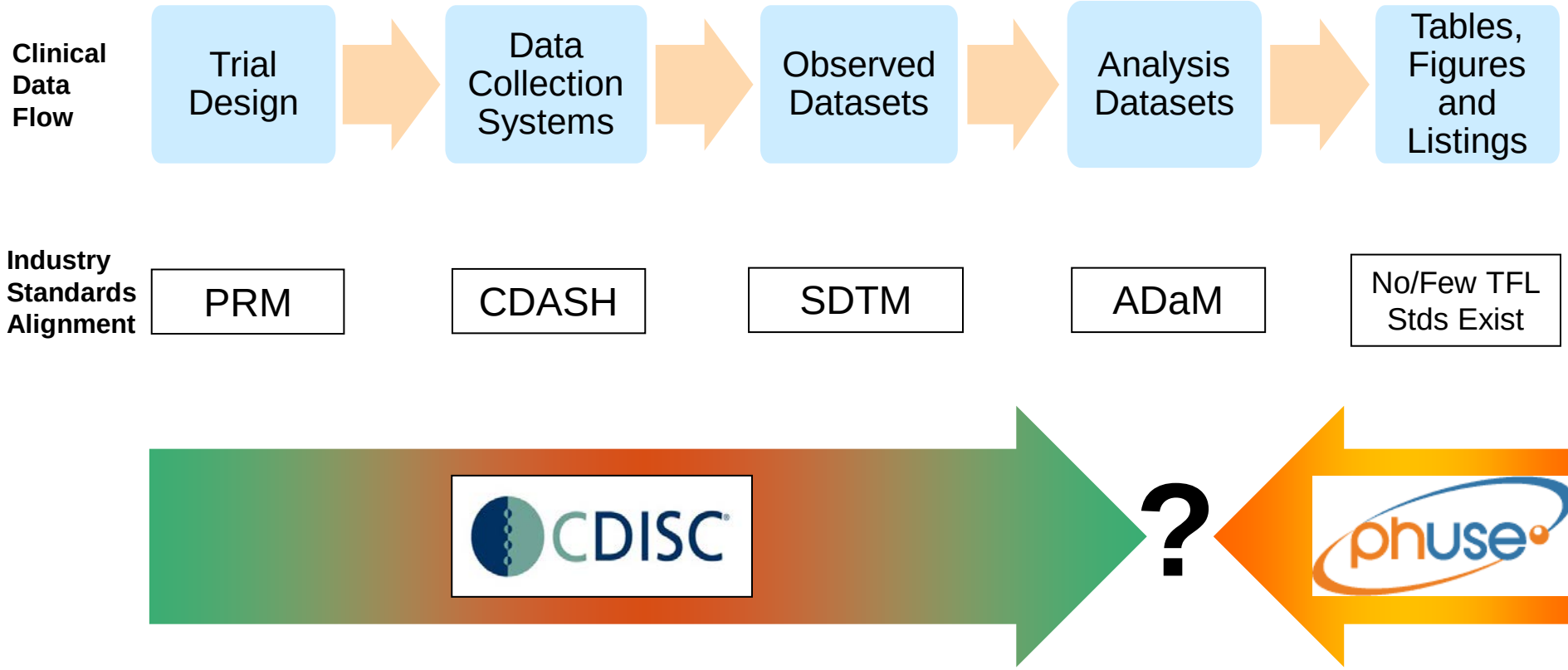

Courtesy of Scott Getzin

Questions?