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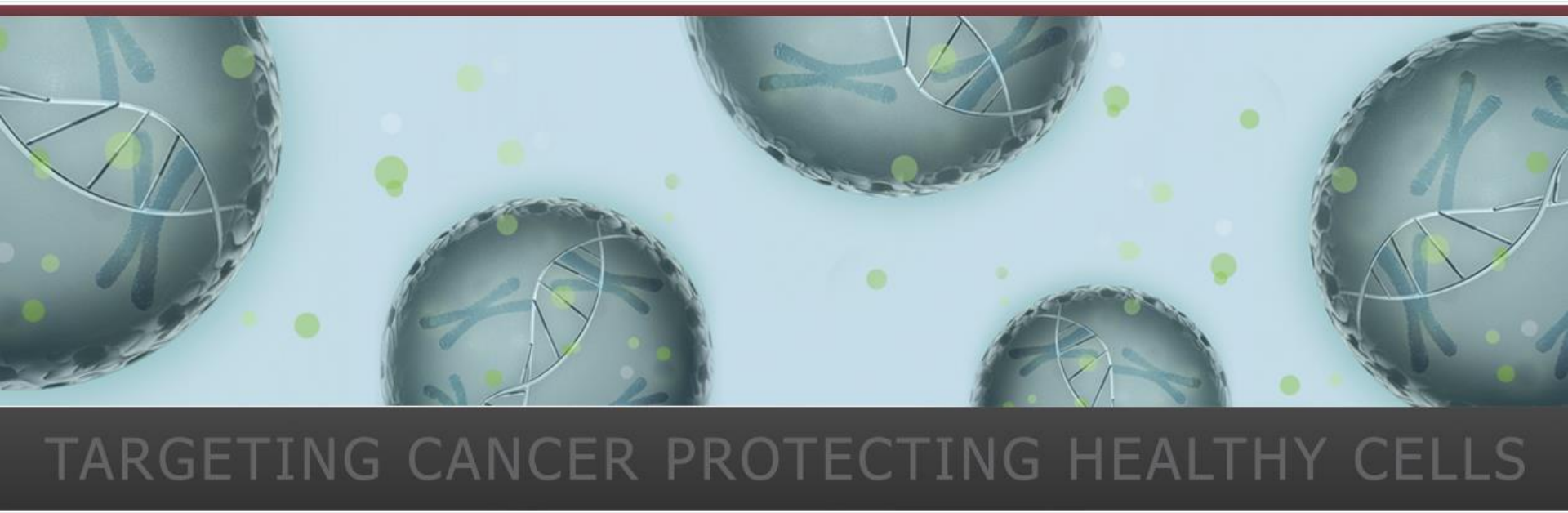

IMPLEMENTATION OF CLINICAL DATA REPOSITORY IN A SMALL BIOTECH – INVESTMENT THAT GUARANTEES THE RETURN

Onconova Therapeutics Inc (OTI) Case Study
Presenting at End to End Data Management Conference 2013
Patrick Zbyszewski, Senior Director, Data Management

Onconova Therapeutics Inc Background

- Small biotech organization with a leading drug in pivotal trial.
- Manages multiple parallel programs totaling over 21 studies in various phases and across several data providers.

Geographical Distribution	Development Phases	21 Studies' Status	4 Data Sources
15 Studies in USA	13 Phase I	8 Completed	4 Studies CRO 1
4 Studies in INDIA	4 Phase II	11 Ongoing	4 Studies CRO 2
1 Study in USA, INDIA and EU	2 Phase I/II		8 Studies CRO 3
1 Study in USA and EU	2 Phase III		5 Studies on EDC

OTI – *Presolutioning Scenario*

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- Convergence of opportunities in Clinical Development
  - Planning for a global launch and ramping up research pipeline required re-building foundation systems with the new processes
  - Innovative technology Maturity under the long range plan to move from Paper to Electronic and further to centralized control
  - Evolution of new development models and compliance requesting flexibility
- Global regulatory environment - strict and complex
- One Size Doesn't Fit All - Multiple CROs and EDCs, leading to:
  - Duplication of effort, redundant data points leading to inefficiencies, and decrease in productivity
  - Complex processes - multiple vendors' based systems are in place
  - Information Mining – Manual Process
  - Longer cycle time from data capture to review
  - Difficult to manage

- Business Scenario Before Solutioning –
  - Functional outsourcing has been the primary strategy in externalization of the non-core areas – not going to change
  - The total cost of managing the data directly equates to the number of distinct data management plans and data capture options.
  - Not enough control and visibility across the data management portfolio
  - Required matrix-based decisioning and reporting for internal and external stakeholders
  - Reliance on availability of various external resources to respond to critical/urgent business queries

Business Case for Change

- New Capabilities Needed to Manage Increasing Workload and Complexity, as well as faster response to key actionable information

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CHALLENGES	ANSWERS
Increasing Workload to capitalize on reach development pipeline	• New capabilities to manage clinical data flow more efficiently
Increasing volume and complexity of requests from regulatory authorities	• Seamless data access for rapid, comprehensive responses to internal as well external stakeholders and regulatory authorities
High effort for generation of regulatory compliant data	• All data in common metadata standards and FDA compliant format; • Automated submission with new standards
Increasing management costs for multiple vendors and data management plans	• Centralized data management and control solution that is provides end to end process in integrated and configurable fashion rendering layer of abstraction to common tasks
Lean management bandwidth, limited investments and time	• Out-of-the-box solution supporting business requirements with efficient implementation and reduced total-cost-of-ownership

Solution Definition, Approach and Objectives

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SOLUTION DEFINITION

An integrated data management platform that enables common data management functions as well as provides means to consume, aggregate, transform and enrich the data in such a way that its meaning remains verifiable, and that can be accessed via a variety of tools to enable full data exploration

APPROACH	OBJECTIVES
Migrate from Current isolated Data providers to New with standardized Metadata	• Study cycle time savings • Increase operational efficiency • User-friendly interface and centralized functions for common data management functions
A state of the art Clinical Data Repository with a submission and reporting platform	• Proactively detect safety signals • Implement and manage FDA compliant data standards • Increased automation based on new submission standards
Integrated data review and visualization environment	• Scalable computing platform • Web-based Reporting and visualization Tools • Role-based, collaborative dashboards for the key stakeholders • Matrix-based quality management, project management
Faster implementation, Low maintenance and support costs for the solution	• Out-of-the-box solution • Built-in support to industry data standards (SDTM, ODM, CDASH, ADaM)
Secured, Scalable and Regulatory Compliant Solution	• Centralized governance enabling role-based access to data and Functions • 21 CFR Part 11 Compliance • Web-based and advance technologies to support scale

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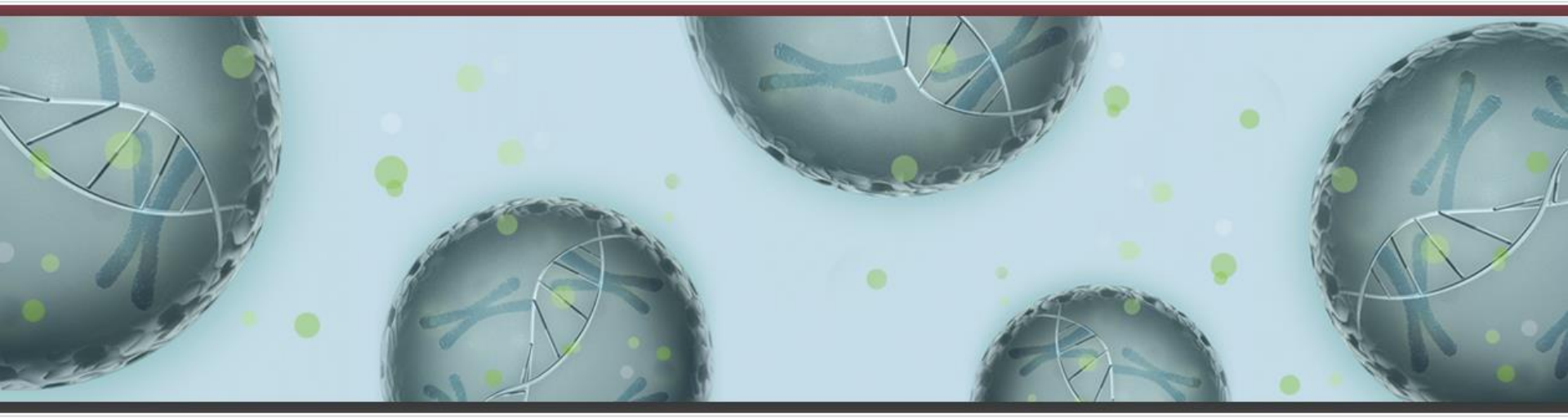

IMPLEMENTATION OF CLINICAL DATA REPOSITORY

Clinical Data Repository Benefits

The CDR will enable OTI to focus on innovation and creation of added value by increasing operational efficiency and delivering actionable information on time

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- 1: Facilitates innovation and excellence in execution
  - Facilitates secondary analyses and reporting at study and program level
  - Facilitates Safety reporting, esp., signal detection and validation
  - Expedites access to broader range of data for pooled analysis, modeling and benchmarking
- 2: Integrated processes from data to information
  - Provide cross-study data review and clinical intelligence leveraging standardized review functions
  - Facilitates generation of knowledge to substantiate decisions
- 3: One stop shop for reliable clinical data and common functions
  - Facilitates loading and processing clinical data from several sources into one standard format (SDTM) in a central repository
  - Increased quality of submissions through adherence to CDISC compliant standards and dry-runs to detect deviations early
  - Additionally makes available data assets from legacy trials
  - Increase Operational Efficiency with Data Management Function
  - Improved re-usability of metadata and clinical reporting programs leading to automation of standard reports
  - Faster, more complete responses to regulatory questions, increasing the quality and decreasing the risk of submission

Solution Selection

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- MAXISIT Partnering
  - Global organization with 10 plus years experience in delivering integrated solutions for pharmaceutical and life sciences industry companies
  - Strong partnership with strong involvement for business specification
- CTRenaissance® eXchange
  - Industry leading Integrated Clinical Data Management Platform with required functionalities available out-of-the-box
  - Flexible delivery models and global strength to support scalable needs

What Did we get with eXchange

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- Out-of-the-box support for CDR Implementation Processes and CDISC Standards
- Minimum programming hence controlled costs
- Highly flexible and scalable platform
- Strong functionality for development and execution of repeatable, intelligent code
- Centralized access and tracking of data
- Key clinical functionality (e.g. blinding, security)
- Ability to expand to address new types of data, new usage, new data providers' interfaces/adapters (current focus on clinical data)

eXchange Integrated Data Management Platform

Clinical Data From Collection through Submission and Business Intelligence

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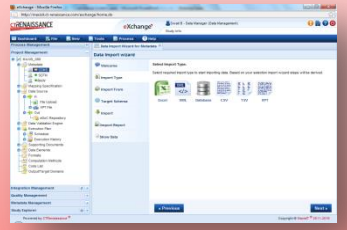
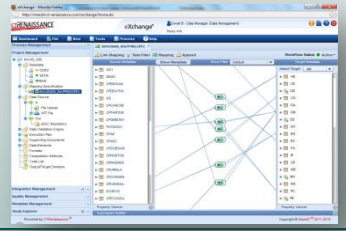
CRO | EDC | Safety Data | IVRS Data | Other… | FTP | Database | DMS | ODM XML | Other…

Integration Layer

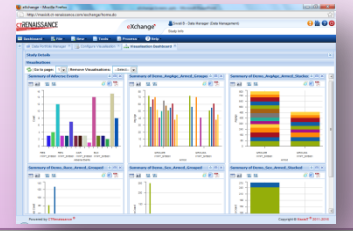
Data Acquire



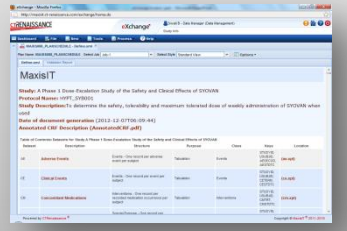
Data Transformation & Validation Rules



Data Explorer & Visualization



Publish



Clinical Data Repository

Metadata Management

Workflow Management

Governance – Role Based Security – Data Security – Data Blinding – Life Cycle Management

eXchange Based CDR Solution

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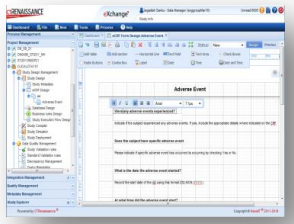
Data → Advanced technology enabled Integration, transformation and Standardization → Meaningful Information (Asset)

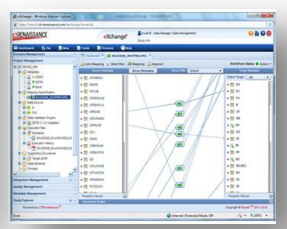
Maximizing asset Value, data Turned into information and used

before | during | after

Clinical trial Portfolio

Protocol design | Data Integration | Meta Analysis



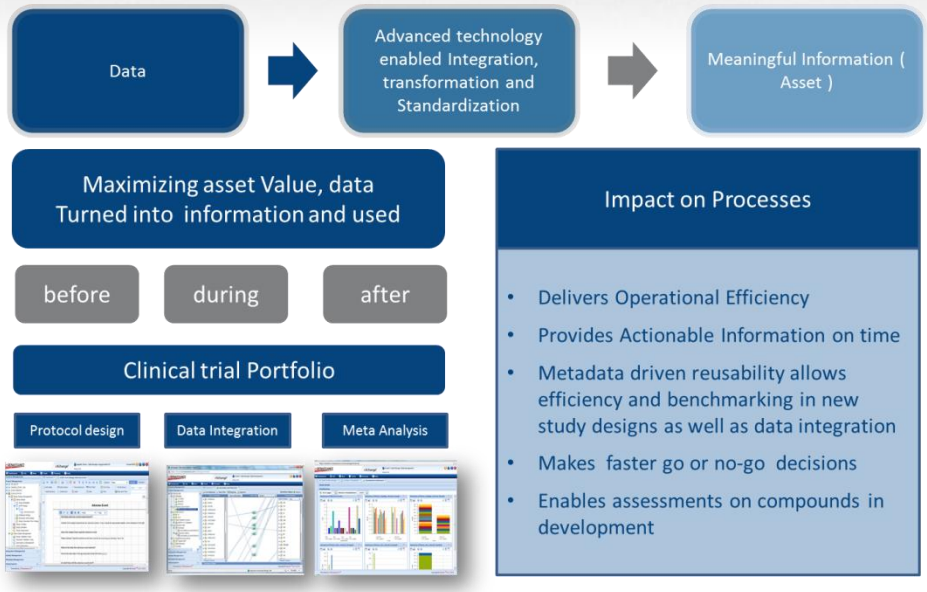


Impact on Processes

- Delivers Operational Efficiency
- Provides Actionable Information on time
- Metadata driven reusability allows efficiency and benchmarking in new study designs as well as data integration
- Makes faster go or no-go decisions
- Enables assessments on compounds in development

Integrated Data Management Technology

The CDR is based upon the eXchange Technology



eXchange Clinical Data Flow

- Acquisition of data from various sources
- Transformation of data into a common standard
- Delivering Metadata Management and Reusability
- Availability of data for
  - Meta-data based search
  - Reporting in visualization tools
  - Submission and publication

eXchange Unique Features

- Easier access to clinical data for a broader audience
- Revised data search through meta data (category) driven search
- Variations in data output due to consolidated reports and new standards
- CFR part 11 compliance enables validation within one environment
- Complete audit trail for statistical data and code
- Extendable and Integrated solution,

Ability to Leverage Emerging Trends in CDM

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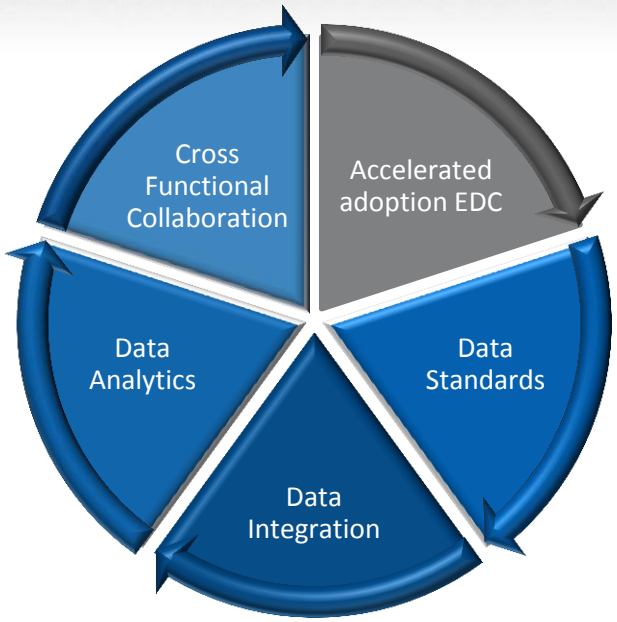
Clinical & DM

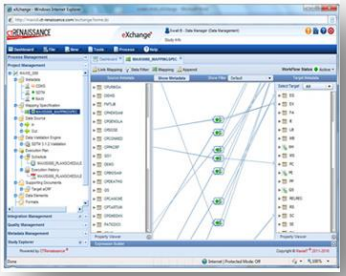
Key Functional Collaboration

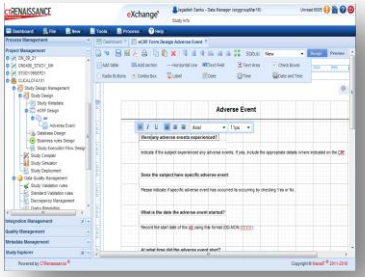
DM & BIOS



CDISC

CDASH





Lab,ECG ,IVRS, Safety etc

Cross Trial, Across Programs

CDR Implementation Approach

The CDR is implemented and gradually being populated with new and completed studies' clinical data during 2013

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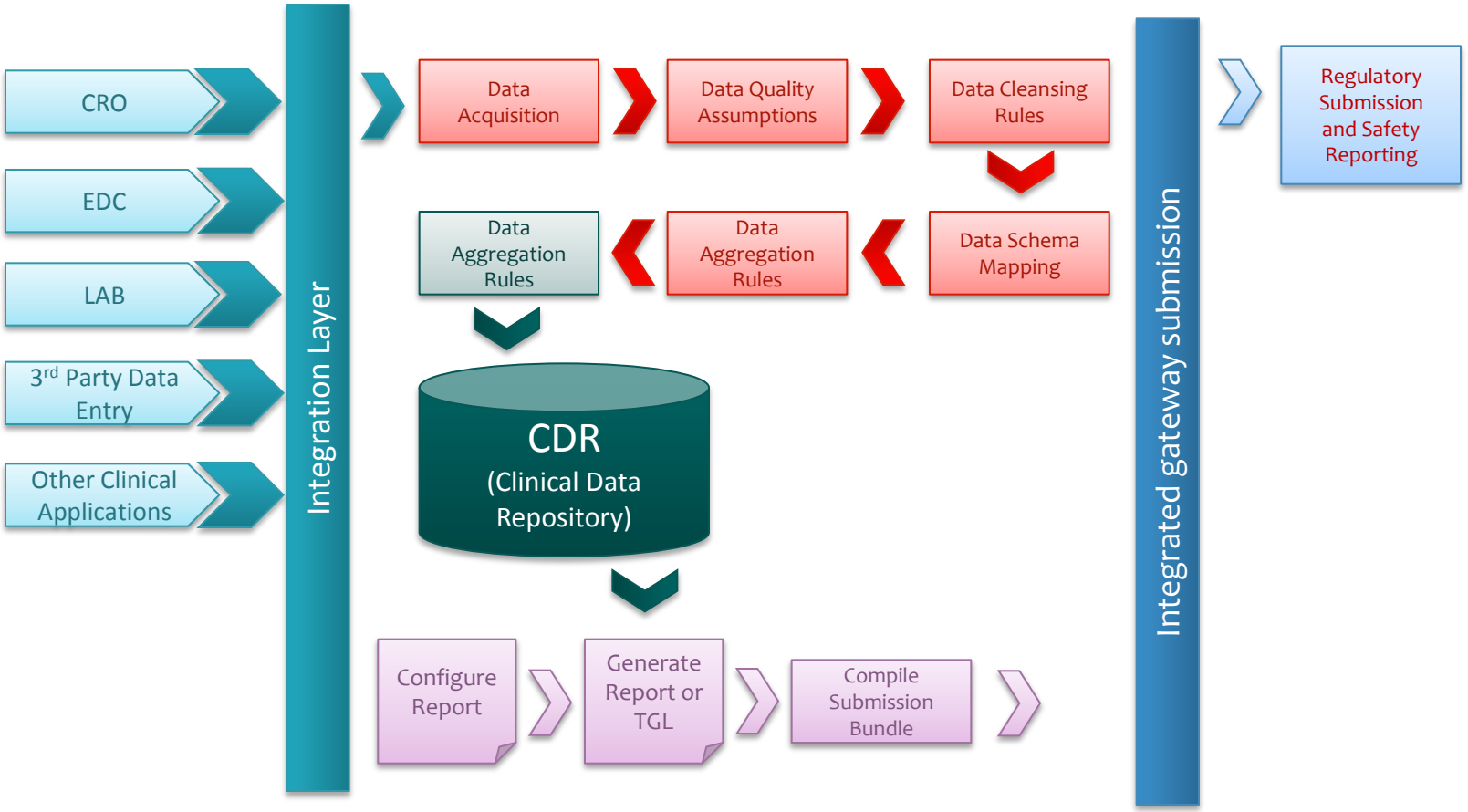

CDR Implementation Timeline

In the mid 2013, the Integrated Clinical Data Repository Capability with New Processes, Technology and Organization will be handed over to OTI

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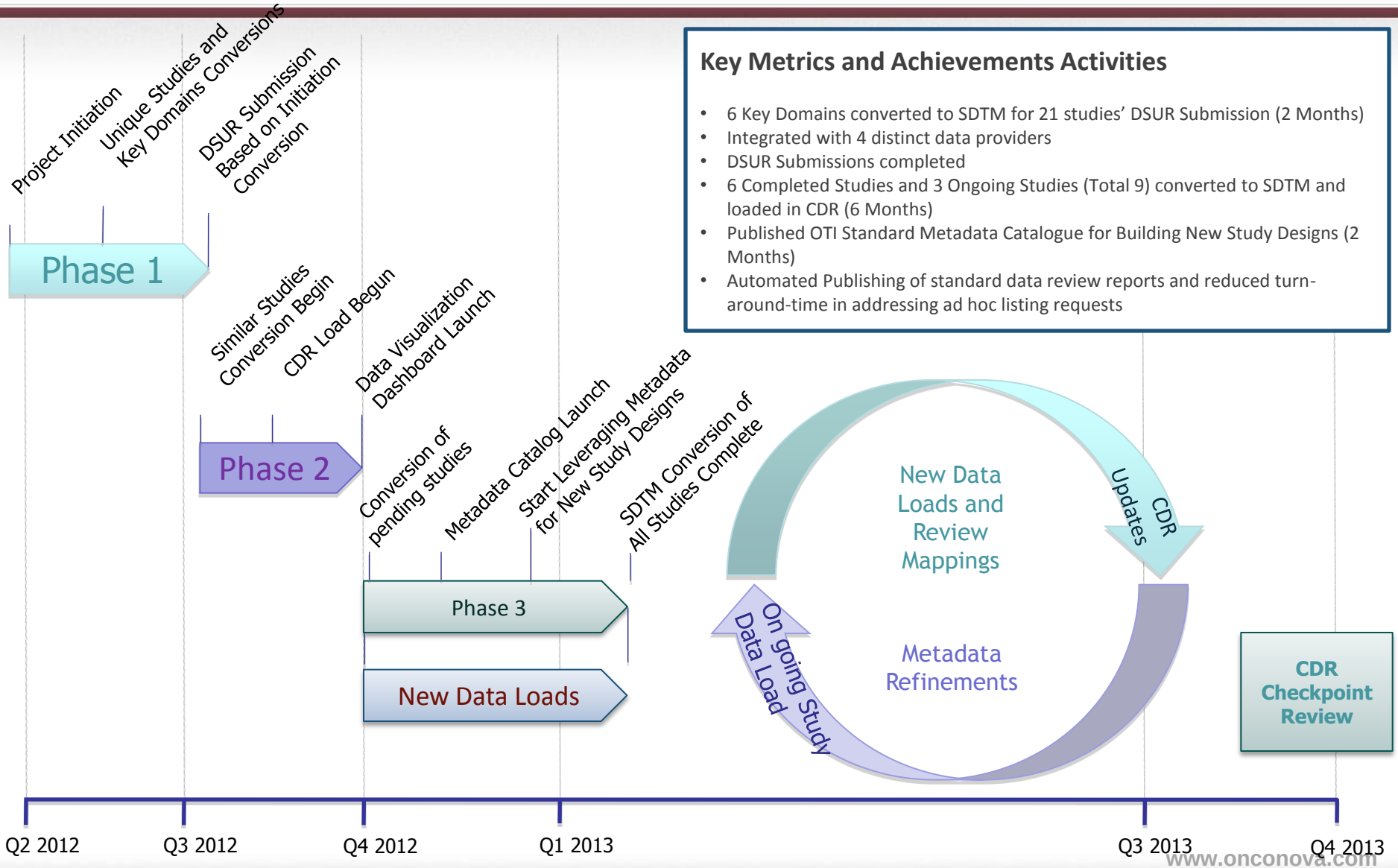

Key Metrics and Achievements Activities

- 6 Key Domains converted to SDTM for 21 studies' DSUR Submission (2 Months)
- Integrated with 4 distinct data providers
- DSUR Submissions completed
- 6 Completed Studies and 3 Ongoing Studies (Total 9) converted to SDTM and loaded in CDR (6 Months)
- Published OTI Standard Metadata Catalogue for Building New Study Designs (2 Months)
- Automated Publishing of standard data review reports and reduced turn-around-time in addressing ad hoc listing requests

Key Questions and Answers

1. Identify what is your data model for your repository?
   - SDTM 3.1.2 IG amendment 1
2. How much do you standardize and when?
   - Progressive / Incremental – Collection, Derivations/Imputations, Cleaning, Transformation, Submission data, Reference tables, Reports/TLGs, Code lists
   - Submission Data in Compliance with SDTM 3.1.2
3. How do you manage metadata?
   - Centralized Metadata Management Support within eXchange
4. What processes or activities benefit from being metadata driven (e.g. programming, transformation)?
   - SDTM Conversion and New Data Integration
   - Data Review Visualizations
   - Clinical Programming and Reporting
   - New Study Designs – eCRFs, Edit Checks, DB Schema
5. What is the appropriate governance and versioning approach?
   - Centralized Role-based Governance and Configurable Versioning (element, domain, study, standard, programs, processes, data load level) within eXchange

Summary

- Project is strategic to the company
  - Classified as a High Risk / High Impact project with Measured Investment
  - In addition to the value of integration and a centralized data repository for all data, enabling automation through metadata driven functionality is a key value of eXchange.
- Investment = Value
  - Metadata driven reusability saving cost on new study designs and setup
  - Faster time to actionable information
  - Reduced effort on new study integration and load
  - Reduced management overhead across multiple vendors
  - Full control on metadata accuracy across the vendors for new studies
- Global Project Team with Scalable Implementation
- Excellent relationship with MAXISIT Services team and CRO partners
  - Close collaboration with MAXISIT Product Development Team
  - Productive face-to-face meetings and teleconferences
  - MAXISIT Team - thorough understanding of business complexity and needs
  - Efficient response from the MAXISIT team
- Strong internal management support at the Exec level

Next Steps

- Next Conversion of Pending Studies to SDTM standards and loading them to CDR with Data Consolidation at the company level for all portfolio studies:
  - Turn data into actionable information then into knowledge
- Efficiently building and deploying new study designs leveraging OTI standard metadata catalogue – reducing dependency over EDC designers and setup
- Thin integration into the collaboration era
  - Standardized Metadata for Clinical Reports and Integration with Biostat
  - eCTD Submission integration as a framework
  - Integration from various sources int/ext