Efficient Patient Recruitment for Innovative Clinical Trials of Existing Drugs to other Indications

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PONTE Presentation

CETIC

Philippe Massonet

EU Open Day, Cambridge, 31/01/2012

This project is partially funded by the European Commission under the 7th Framework Programme

PONTE Description

- Efficient Patient Recruitment for Innovative Clinical Trials of Existing Drugs to other Indications
- Start Date: 01/03/2010
- Duration: 36 months
- Budget:
  - Commission contribution: 2 495 024 euros
  - Total budget: 3 276 699 euros
- Partners: 9

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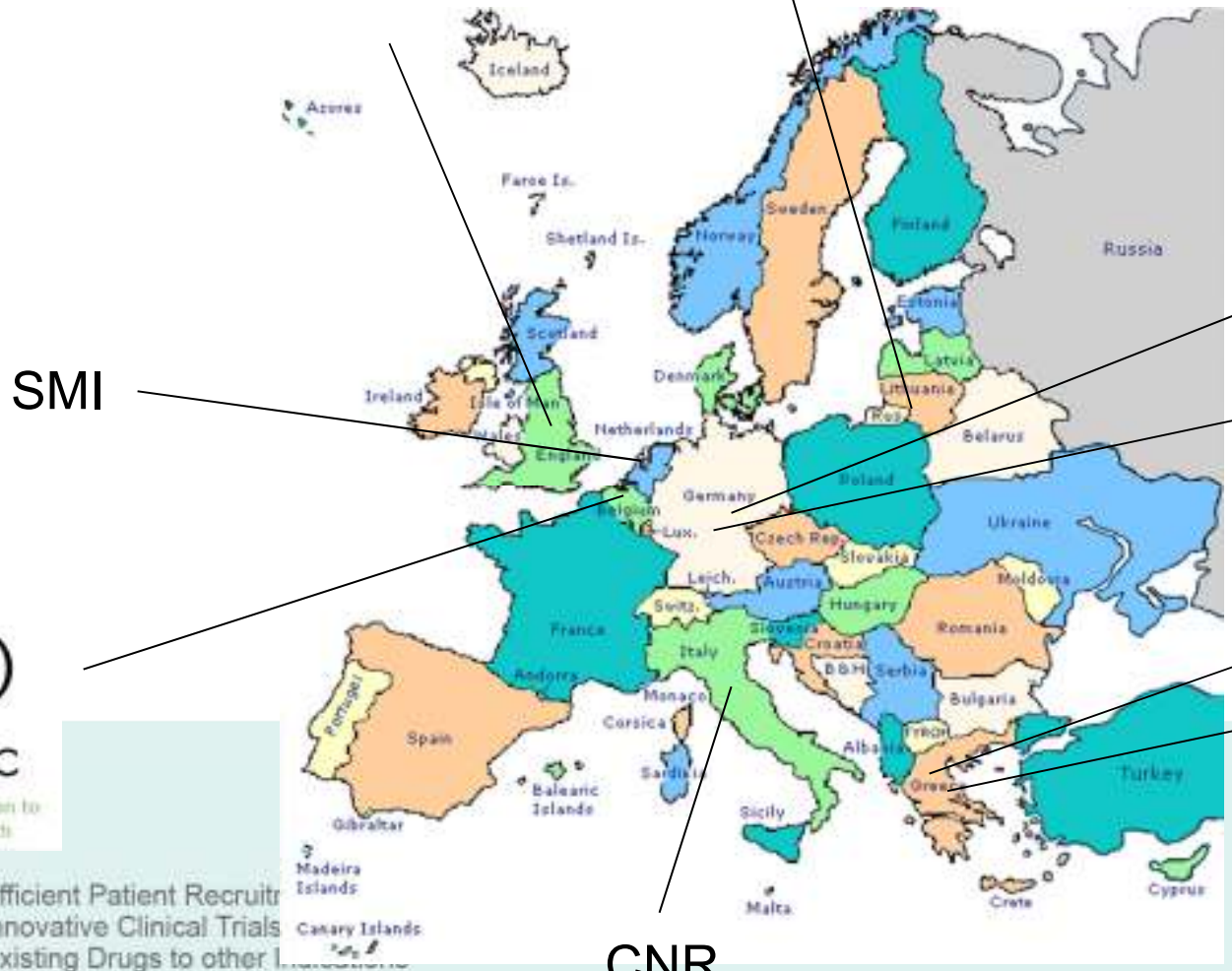
PONTE Consortium

7 countries
1 company
2 research institutes
6 universities



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Your connection to ICT research

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European Commission
Information Society and Media

Introduction

- Average Drug Development cost is € 500-700 million per drug candidate and timeline more than 10 years.
- Tremendous reduction in new active ingredients reaching the market yearly:
  - ~ 60/year (late 1980s), 52 (1991), 31 (2001), 20-25 (currently)
- Clinical trials :
  - ~ 1/3 of the costs of drug development half of which depends on duration
  - Low recruitment rates – Long recruitment periods
  - Subjects recruited represent only partially the target patient population
  - Mortality rates in clinical study findings vs real life
  - 1 out of 5000 new drug candidates reach the market
- Drug repositioning trend and Complex tests of hypothesis: testing new treatments of existing drugs on patients suffering from another disorder
- Adaptive trial trend
- Humans' high variability in response to a drug treatment requires large-scale clinical trial conduction for ensuring that the investigational treatment is safe and effective

The PONTE Solution

- A platform designed for the easy and efficient
  - definition, design and adaptation CT protocols
  - patients recruitment
- Inter linking of a huge amount of data from various, dispersed data sources
  - Intelligent queries
  - Advanced semantic data mining services
- Provision of decision-support services for CTP design and patient selection (CTP validation and parameter suggestion)

→ Bridging the gap between healthcare (especially EHRs) and clinical research will improve the design of CTs (more accurate, scientifically correct eligibility criteria) is a necessary condition to reduce patients' recruitment time, improve safety and efficacy, and reduce cost of CT.

PONTE Research and ICT Objectives

TO1. Specification language describing at a high level of abstraction domains' data, patients' profiles and their relationship with the CT

TO2.Core ontology-driven scheme incorporating existing clinical data standards

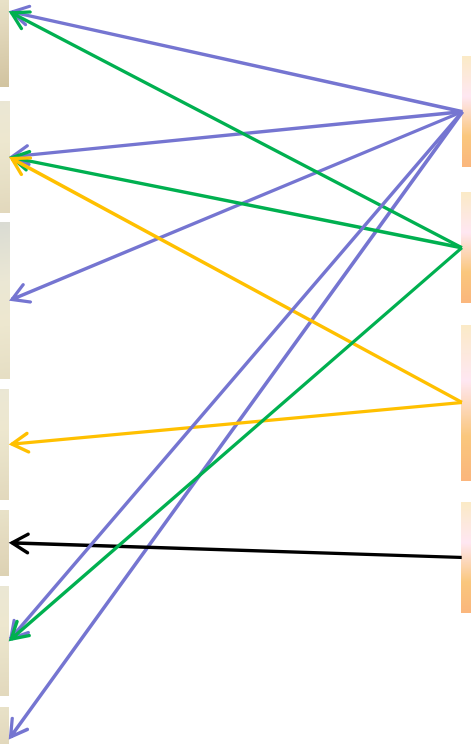
TO3. Semantic representations for describing the evolution of the patient symptoms in coherence with the evolution of the treatment

TO4. Advanced ontology-based data mining techniques on distributed data sources

TO5. Advanced security mechanisms

TO6. Intelligent advanced decision support mechanisms with focus on patient safety, study efficacy and cost

TO7. Semantic interlinking of heterogeneous databases



C1. EHR and clinical study data interlinking

C2. Clinical research data modeling

C3. Interlinking with data sources on clinical and non-clinical information

C4. Privacy-preserving secondary use of EHRs

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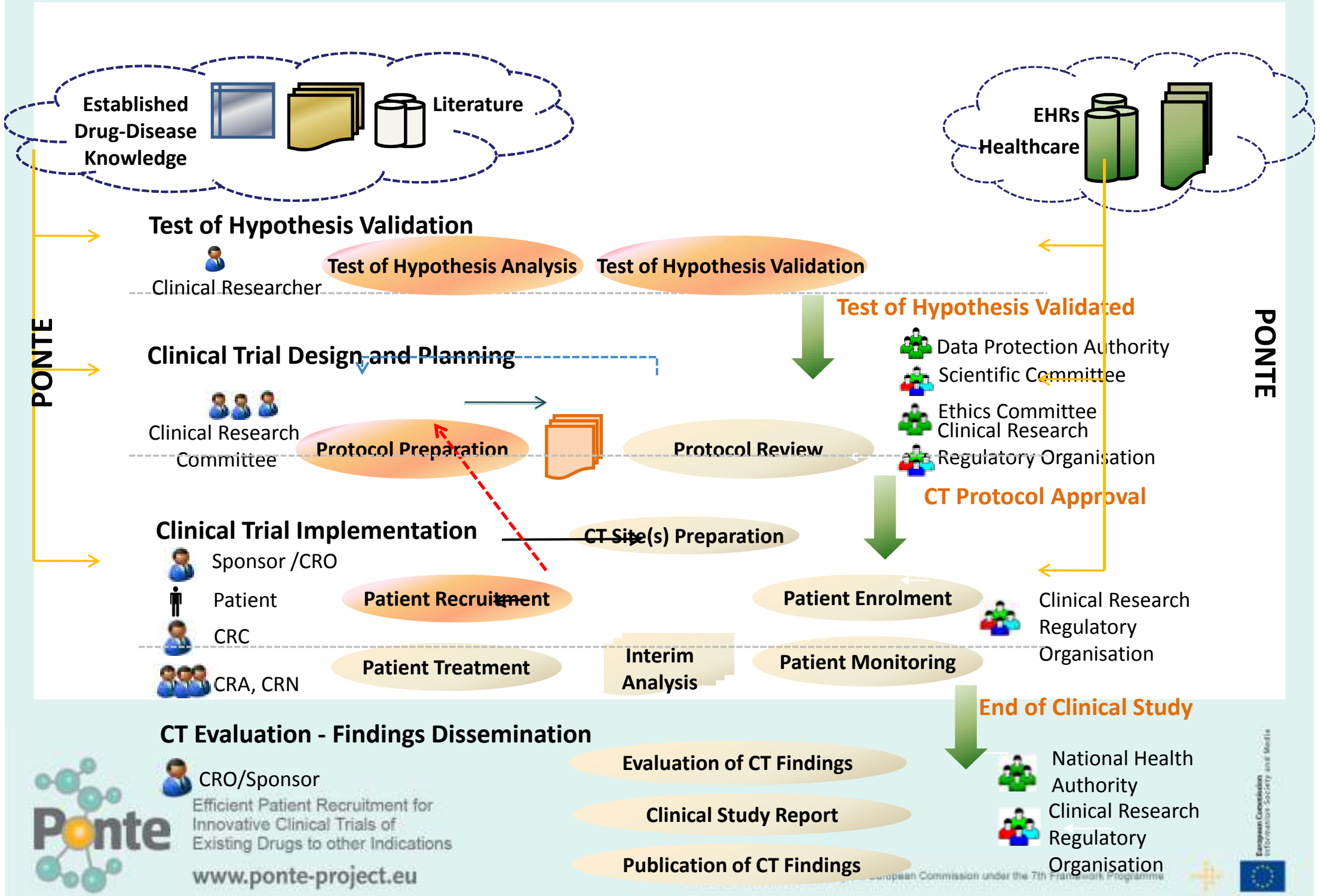
Established Drug-Disease Knowledge
Literature
EHRs Healthcare
PONTE
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Test of Hypothesis Validation
Clinical Researcher
Test of Hypothesis Analysis
Test of Hypothesis Validation
Test of Hypothesis Validated
Data Protection Authority
Scientific Committee
Ethics Committee
Clinical Research Regulatory Organisation
Clinical Trial Design and Planning
Clinical Research Committee
Protocol Preparation
Protocol Review
CT Protocol Approval
Clinical Trial Implementation
CT Site(s) Preparation
Sponsor /CRO
Patient
CRC
CRA, CRN
Patient Recruitment
Patient Enrolment
Clinical Research Regulatory Organisation
Patient Treatment
Interim Analysis
Patient Monitoring
End of Clinical Study
CT Evaluation - Findings Dissemination
CRO/Sponsor
Evaluation of CT Findings
Clinical Study Report
Publication of CT Findings
National Health Authority
Clinical Research Regulatory Organisation
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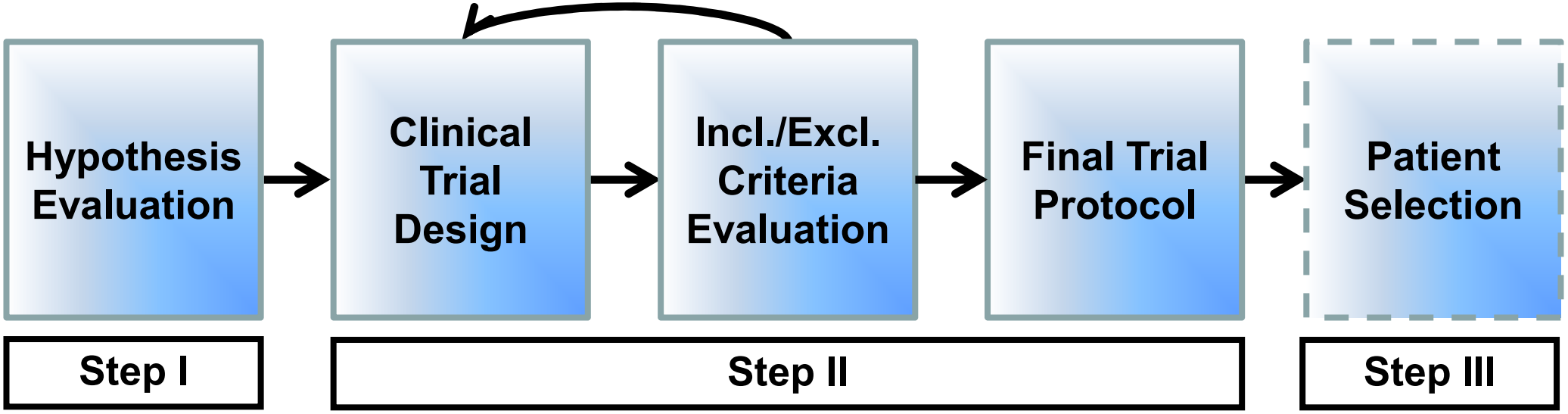
From Hypothesis to Patient Selection



Drug
- Structure, homologues
- Metabolism
- Pharmacokinetics
- Route of administration

Disease
- Prognosis
- isease stratification
- Co-morbidities
- Diagnosis, symptoms

Target
- Sensitivity
-Selectivity
- Expression: genes
- Expression: proteins
- Mutations

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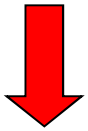
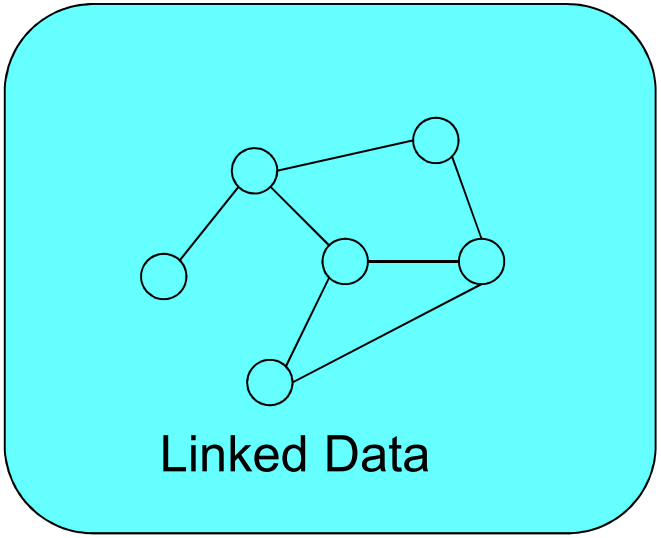
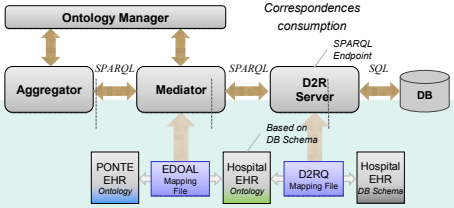
Semantic Interoperability

CT Questions

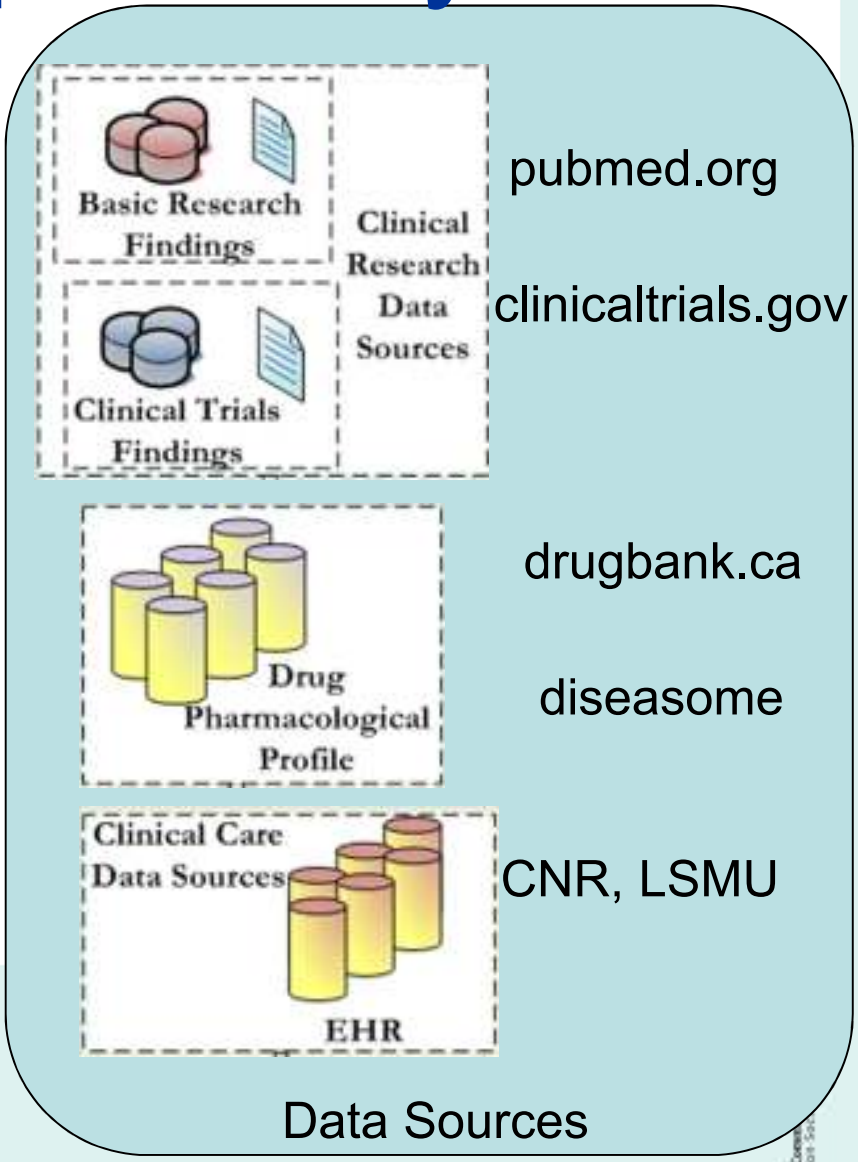


PONTE Ontology





Semantic Mapper



Data Sources

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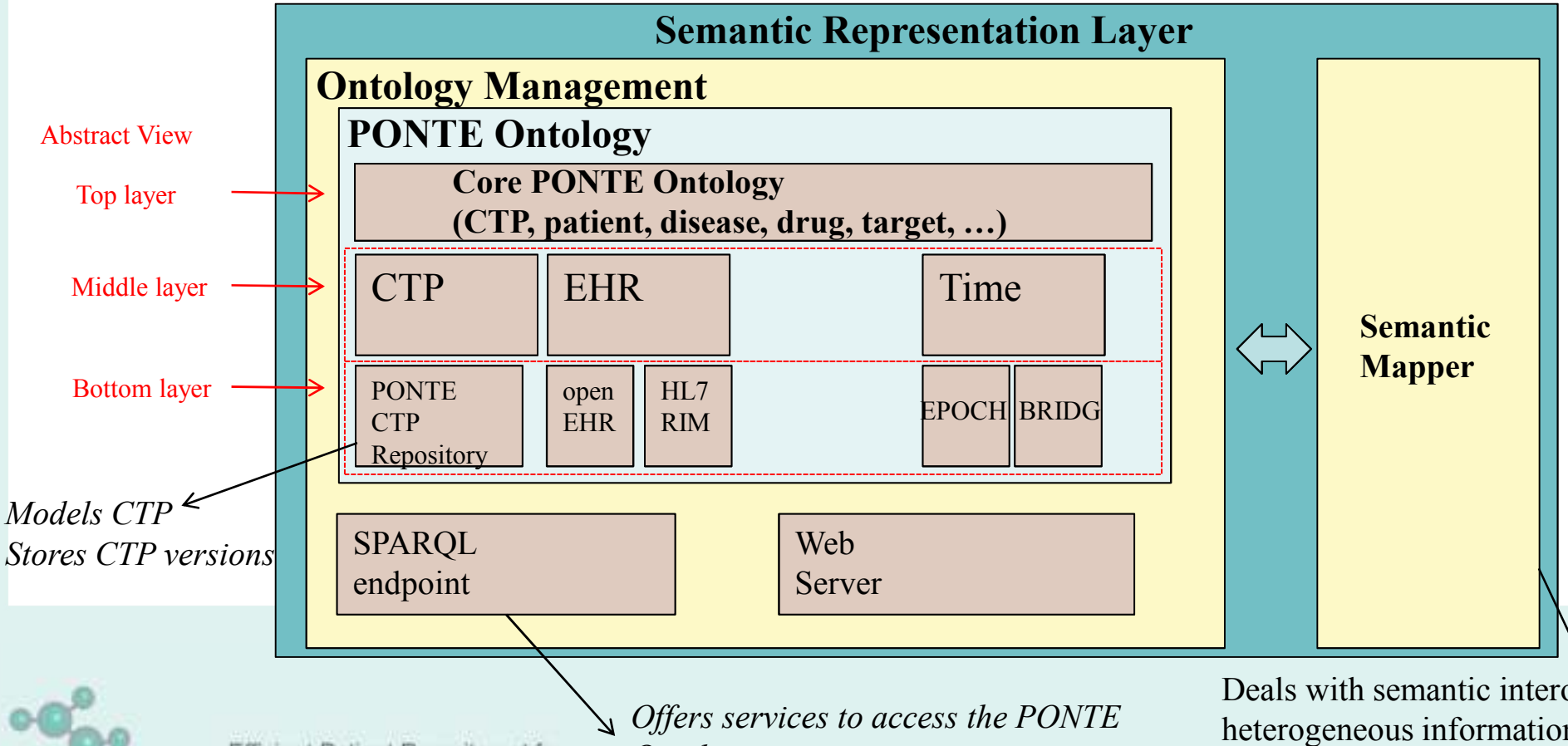
PONTE Ontology and Standards

- Development of the PONTE ontology based on existing standards in the domain of Health Care



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Main Use Cases

- UC1: Login
- UC2: User Management
- UC3: Role Management
- UC4: Set Test of Hypothesis
- UC5: Validation of “Test of Hypothesis”
- UC6: Select Cooperating Hospitals
- UC7: Set Clinical Trial Protocol Parameters
- UC8: Estimate Number of Eligible Patients
- UC9: Perform pre-defined queries
- UC10: Perform Free-Text Intelligent Search
- UC11: Save Search Results
- UC12: View Saved Search Results

UC13: View Clinical Trial Protocol
UC14: Save Intermediate Version of Clinical Trial Protocol
UC15: Validate CTP Parameters
UC16: Update Clinical Trial Protocol
UC17: Submit Clinical Trial Protocol
UC18: Update CTP Status after review
UC19: Request for Patient Selection
UC20: View List of Selected Patients
UC21: Define CTP Parameters for Adaptation

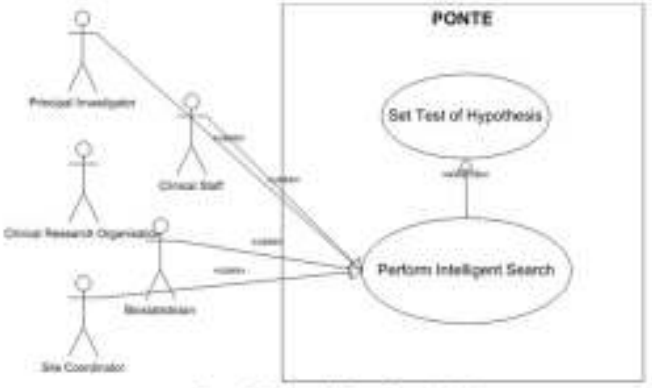

Figure 6 Perform Intelligent Search Use Case

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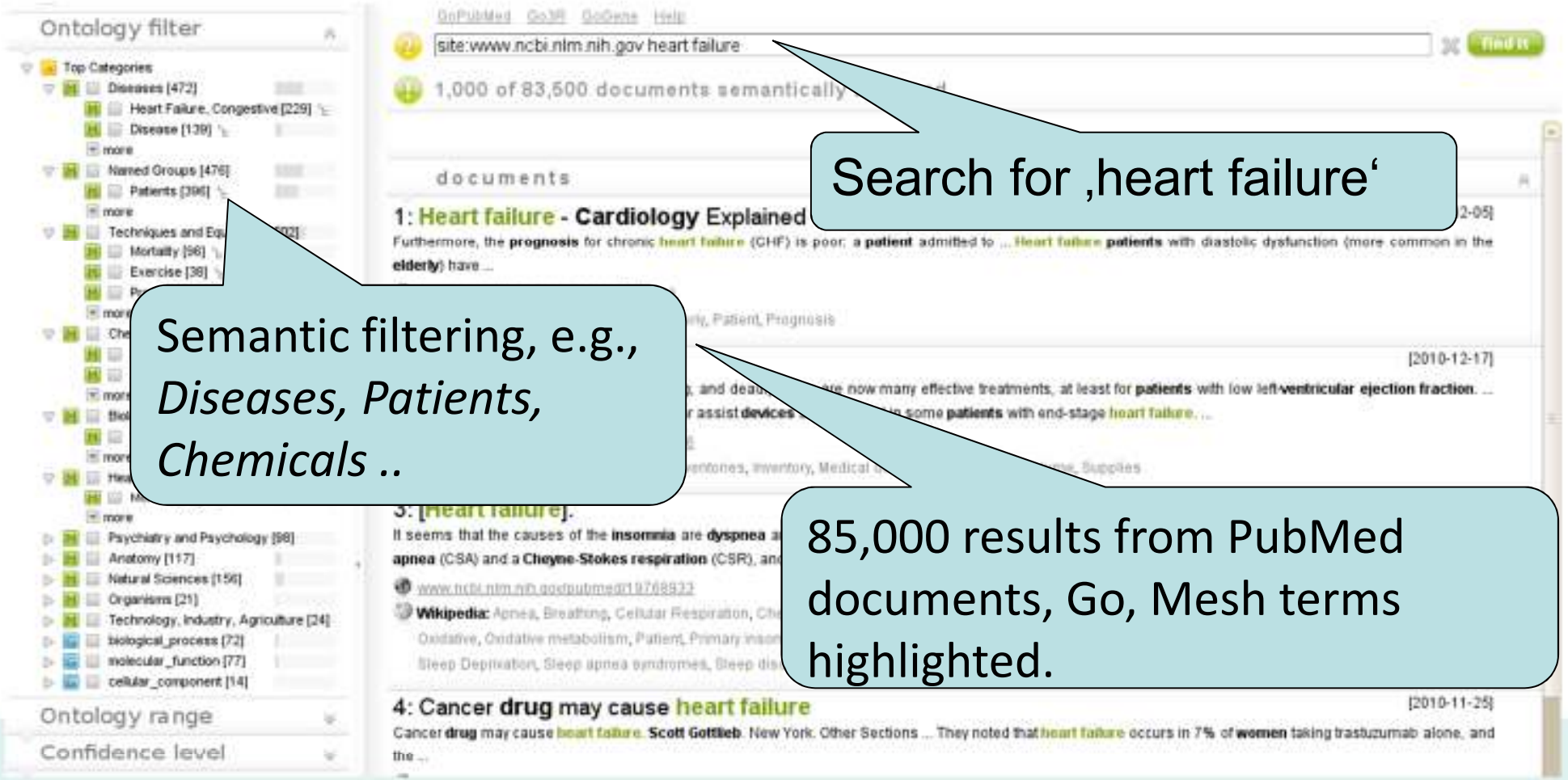
Ontology Based Search Engine



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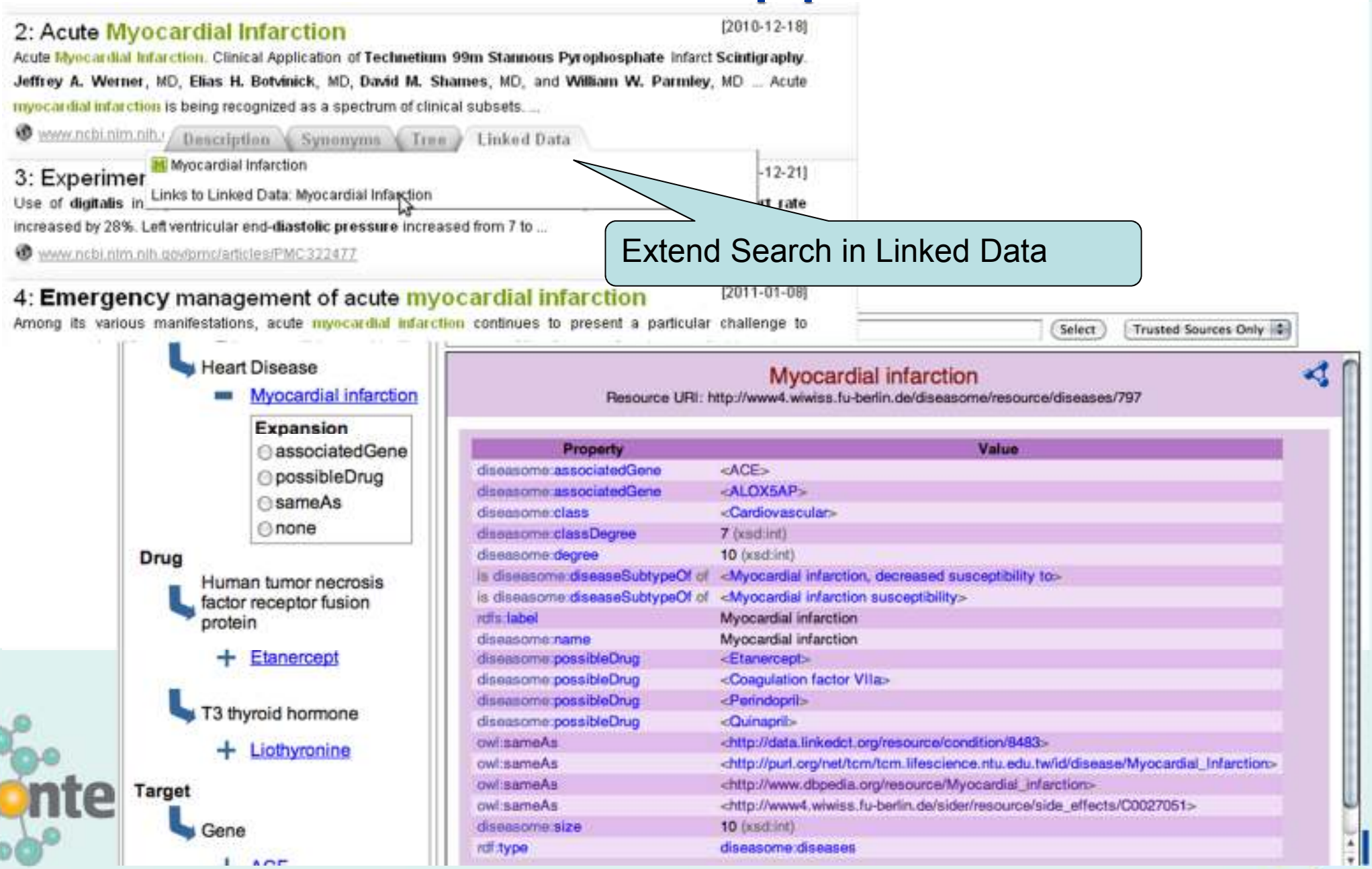
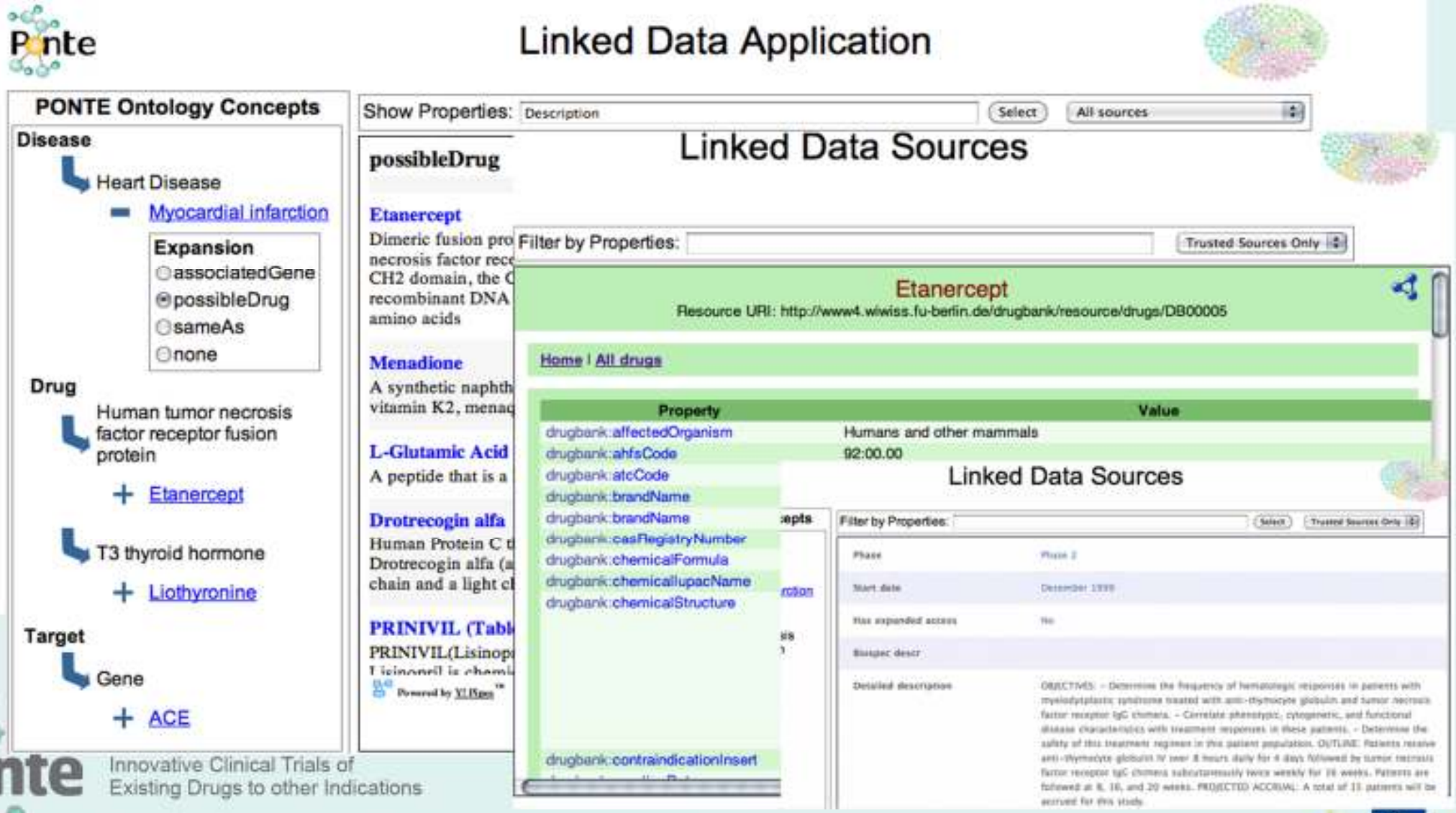
Linked Data Application



Query Expansion across heterogeneous but linked Datasources



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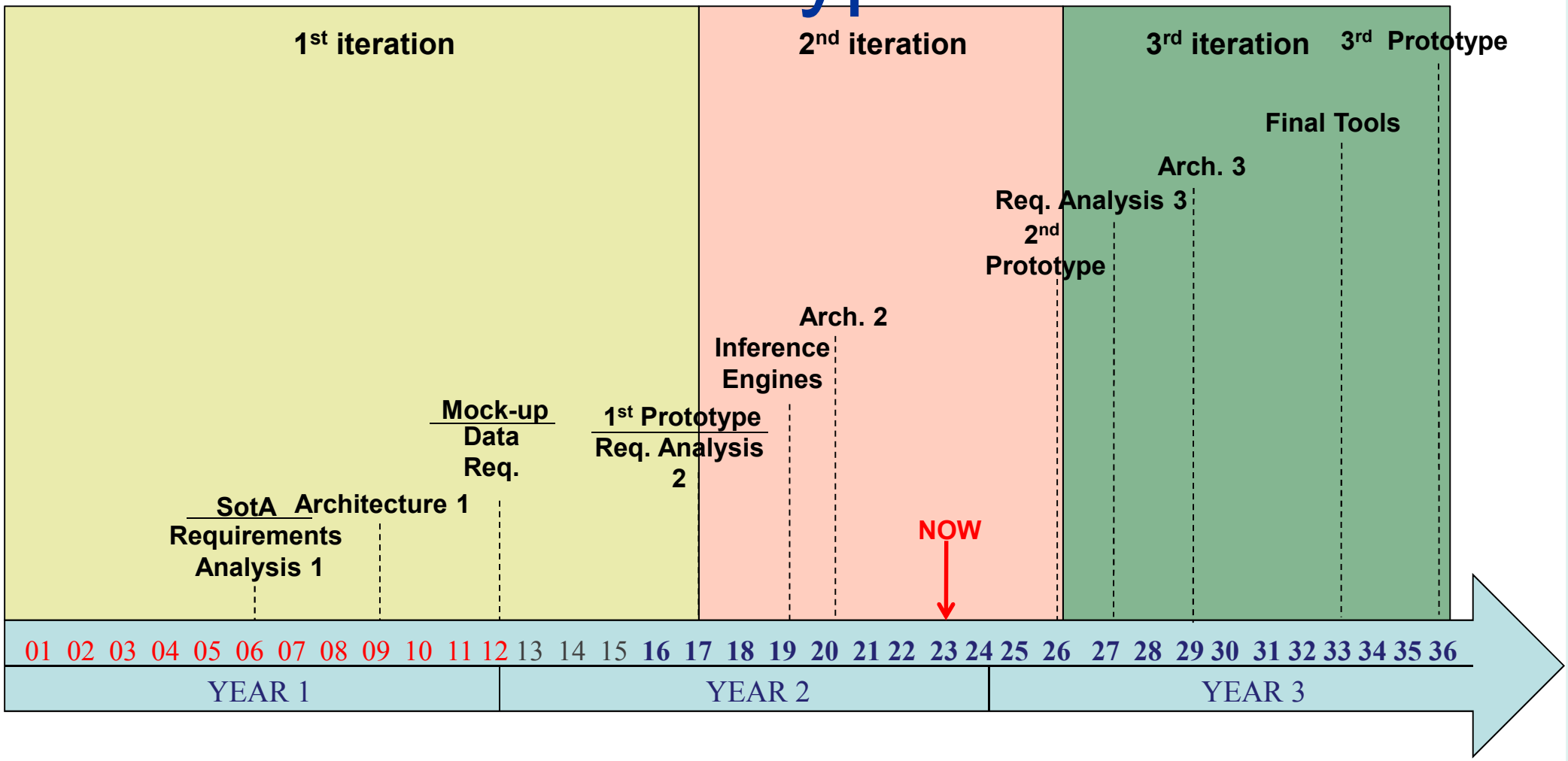
PONTE Prototype Iterations



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Conclusions and outlook

- Designing Drug Repositioning Clinical Trials
  - Improving safety
  - Improving efficacy
  - Reducing cost
- Approach
  - Integrating clinical research and healthcare (EHR) data sources
- Results
  - Advanced clinical trial design prototype

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PONTE Rationale

- Clinical trials are most often based on inadequate inclusion of critical study populations due to:
  - *focus on single interventions*
  - *lack of access to and linking with important data (patient pool, other clinical research findings)*

  resulting in results of low external validity:
  - great deviation between real world and clinical trials results
  - inability to predict off-target effects and potential at-risk populations

  which seriously affect patients' safety.
- Almost half of the delays in clinical trials are due to patient recruitment problems
- Drug repositioning trend
- Reduction in the allocation of funds for new research in pharmaceutical sector due to the world economy shrinking

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PONTE Platform Objectives

- A platform designed for the easy and efficient
  - definition, design and adaptation CT protocols
  - Patients recruitment
- **Inter linking** of a huge amount of data from various, dispersed data sources
  - Intelligent queries
  - Advanced semantic data mining services
- Provision of interactive **decision-support** services for CTP design and patient selection (CTP validation and parameter suggestion)
- Automatic selection of eligible patients from **cooperating hospitals (pre consented patient pool)**
- Privacy compliant solution

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The PONTE Solution

- Objectives and innovation
  - Development of a research question into a Clinical Trial
  - Clinical Trial design management
  - Effective decision support (*patient selection*)
  - Efficient navigation capabilities

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The PONTE Platform

- Hypothesis Evaluation
- Clinical Trial Protocol Authoring Tool
- Intelligent search of data sources through the platform (PubMed, ClinicalTrials.org, drug/disease data, etc.)
- Guidance in every section of the Clinical Trial Protocol through available pre-defined queries

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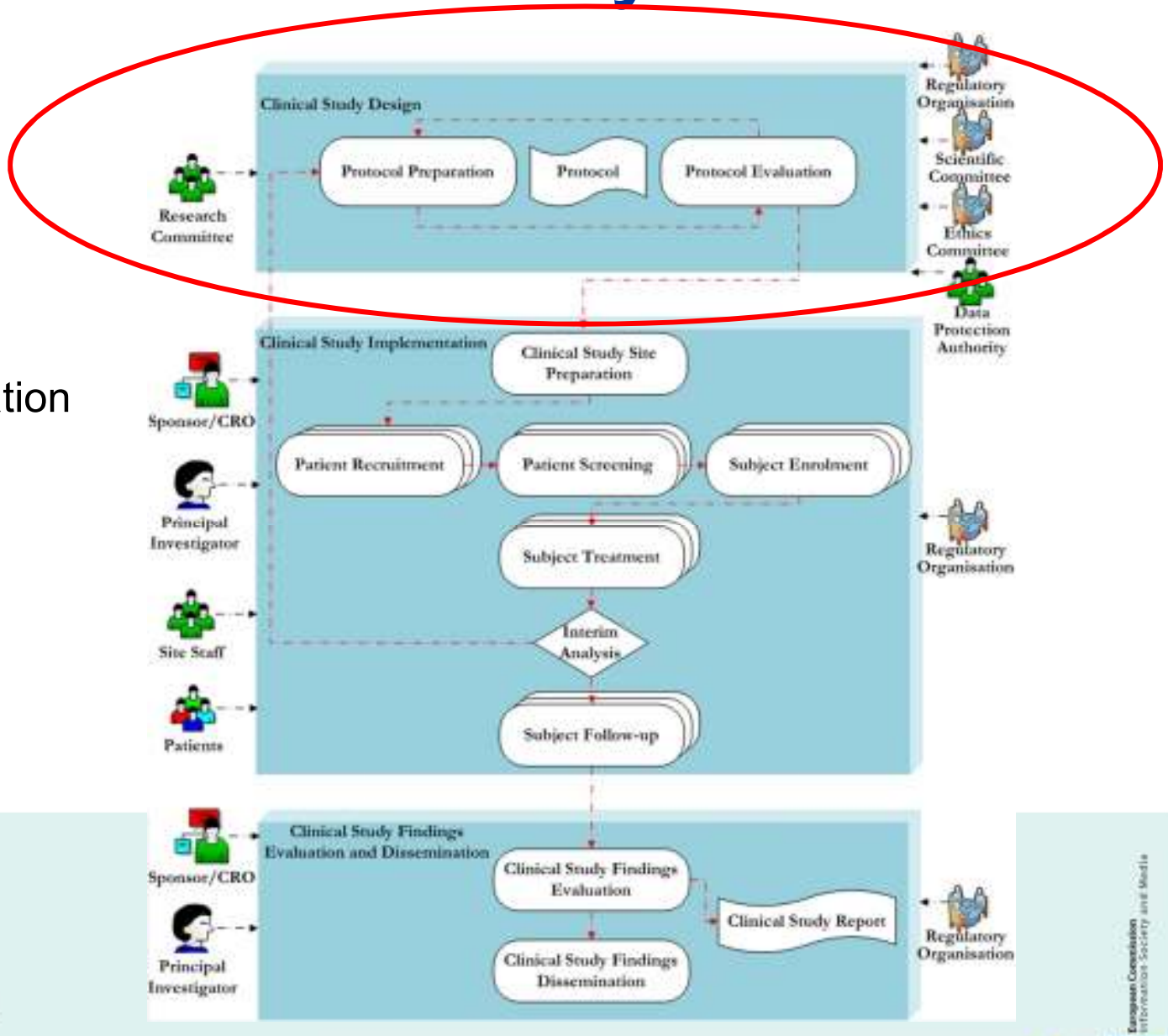
Project Context, Objectives

- *Drug repositioning trend* and *Complex tests of hypothesis*: testing new treatments of existing drugs on patients suffering from another disorder
- Humans' high variability in response to a drug treatment requires *large-scale clinical trial conduction* for ensuring that the investigational treatment is safe and effective
- Repositioning and Adaptive CT gain ground

→ Bridging the gap between healthcare (especially EHRs) and clinical research will improve the design of CTs (more accurate, scientifically correct eligibility criteria) and will reduce patients' recruitment time

Clinical Trial Lifecycle

Clinical Study Design
Clinical Study Implementation
Clinical Study Findings Evaluation and Dissemination



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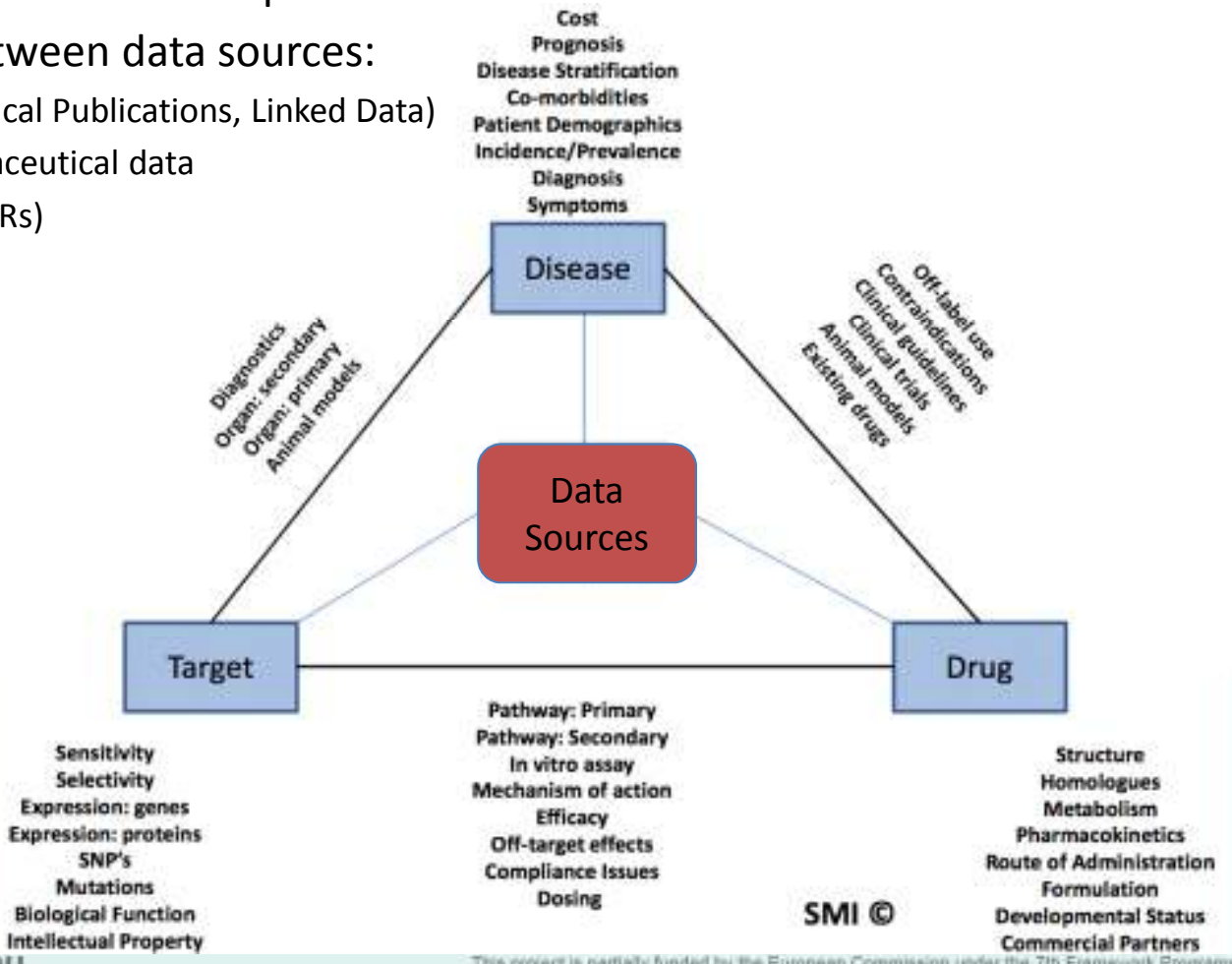
Clinical Hypothesis Investigation Ontology

- User enters the problem from one of the main perspectives
  - Ontology bridges across these primary concepts/perspectives
  - Assists formulation of research question
  - Semantic Links between data sources:
    - Public data (Medical Publications, Linked Data)
    - Validated Pharmaceutical data
    - Hospital data (EHRs)



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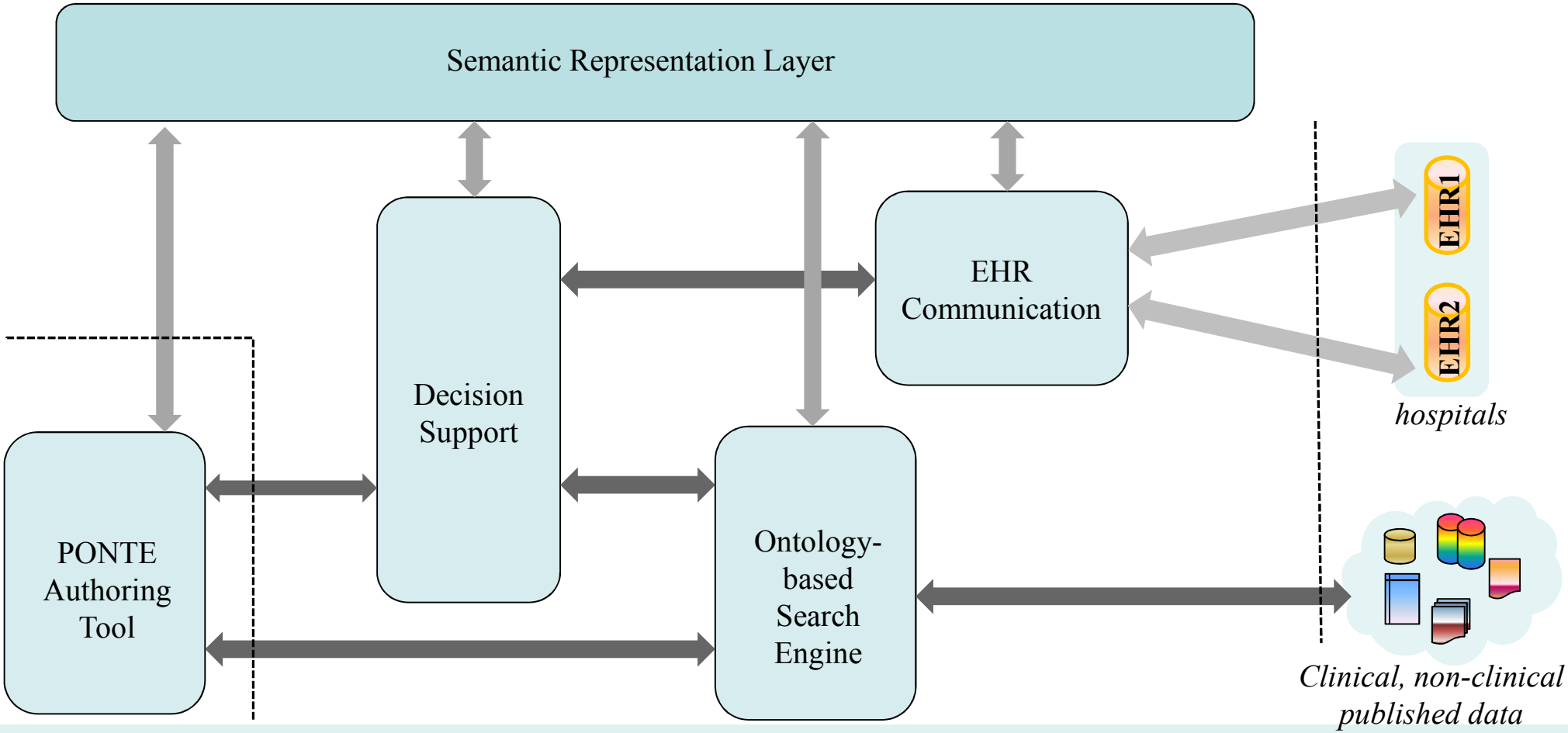
PONTE Overall Architecture



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