임상시험글로벌사업단
KOREA CLINICAL TRIALS GLOBAL INITIATIVE

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- Strategic Approaches to Boost Early Phases Clinical Trials -

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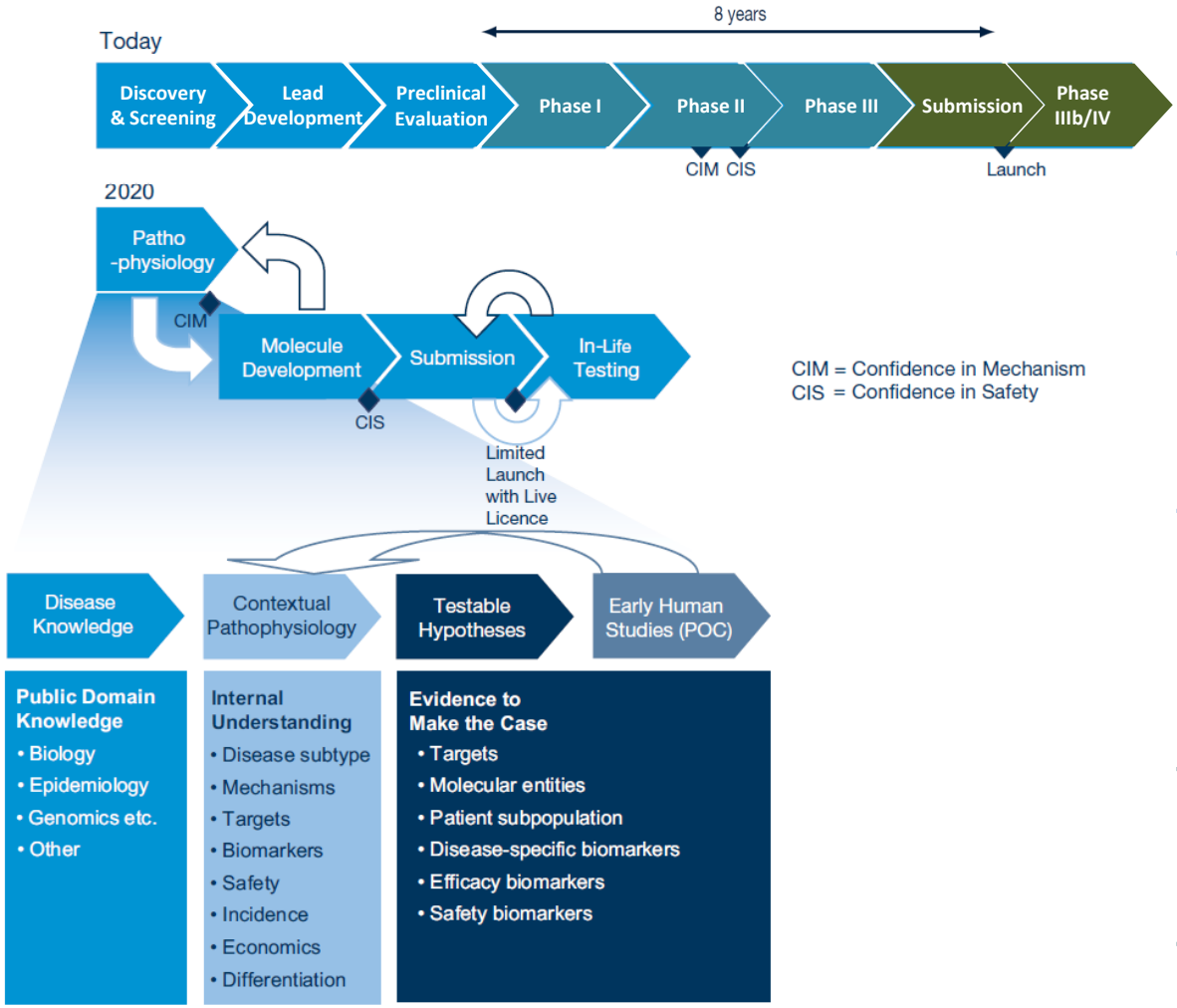
MINISTRY OF HEALTH & WELFARE
KHIDI Korea Health Industry Development Institute
KONECT 한국임상시험산업본부

CHANGING PARADIGM IN DRUG DEVELOPMENT

FUTURE R&D PROCESS

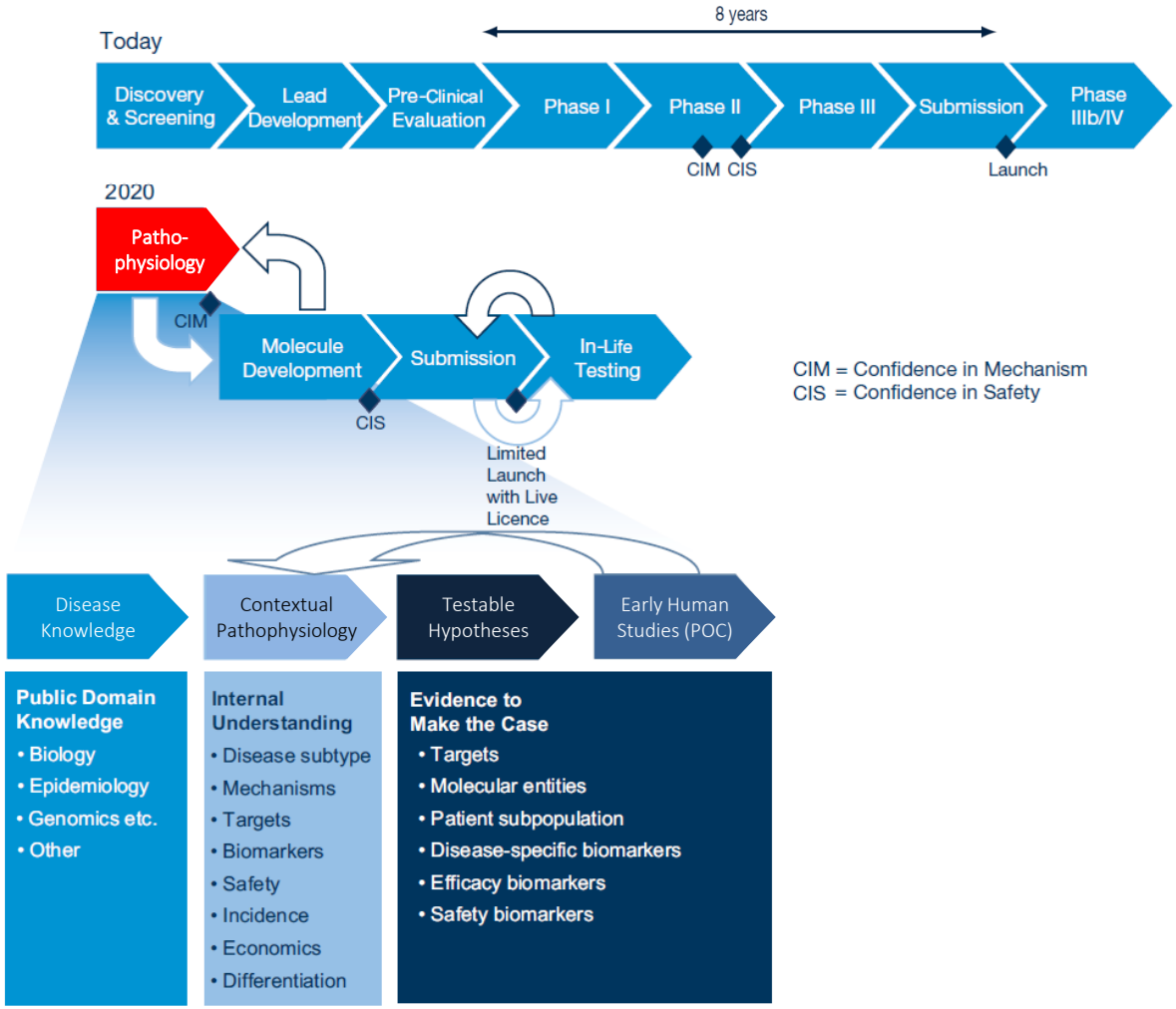


CIM = Confidence in Mechanism
CIS = Confidence in Safety

Stage	Site of Action
Discovery / Preclinical	Pharma / Research Institute
Clinical	**Hospital**
Approval / Marketing	Regulatory Agency / Pharma

Source: PricewaterhouseCoopers

FUTURE R&D PROCESS



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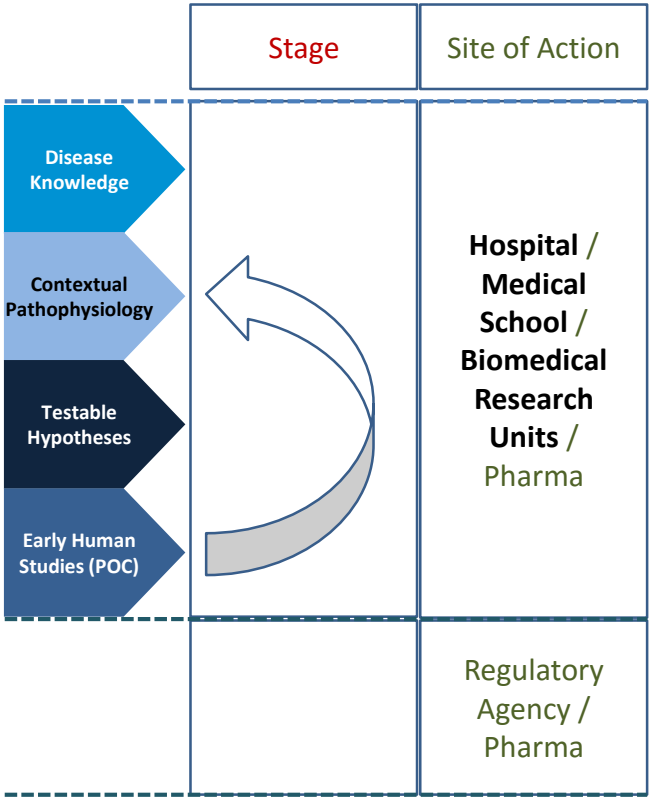
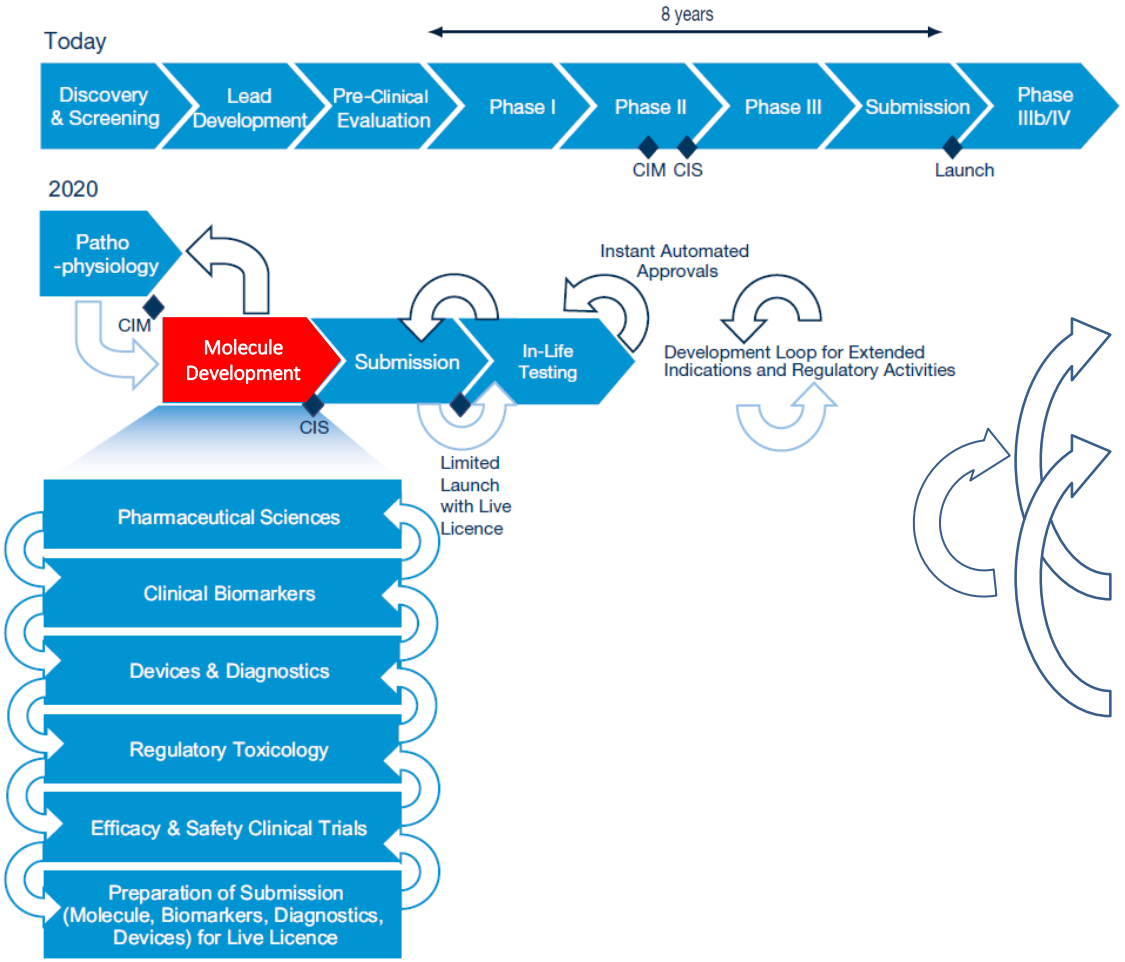
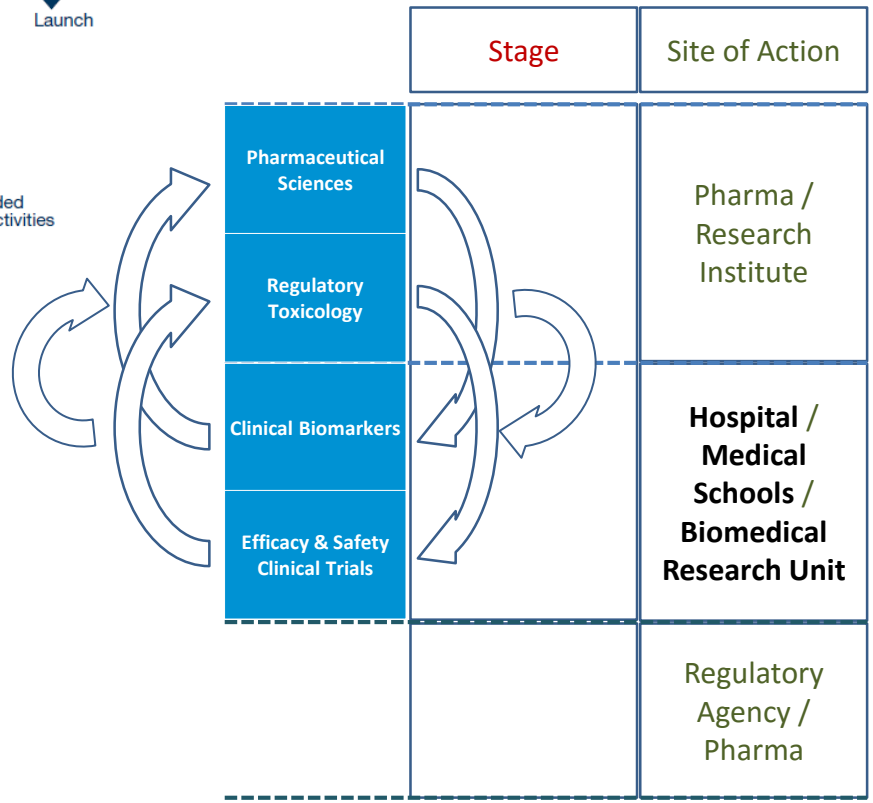


Source: PricewaterhouseCoopers

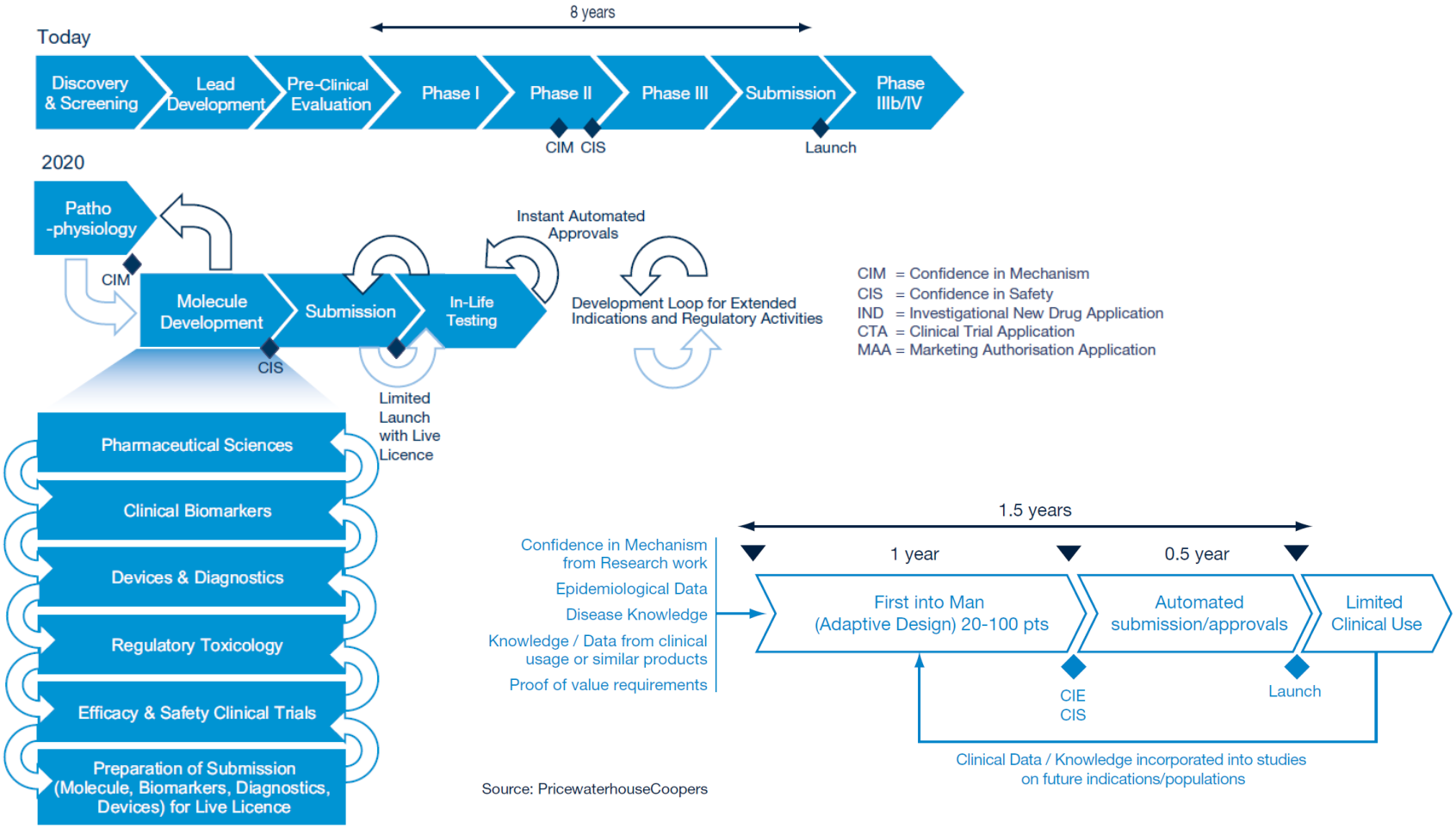
FUTURE R&D PROCESS





Source: PricewaterhouseCoopers

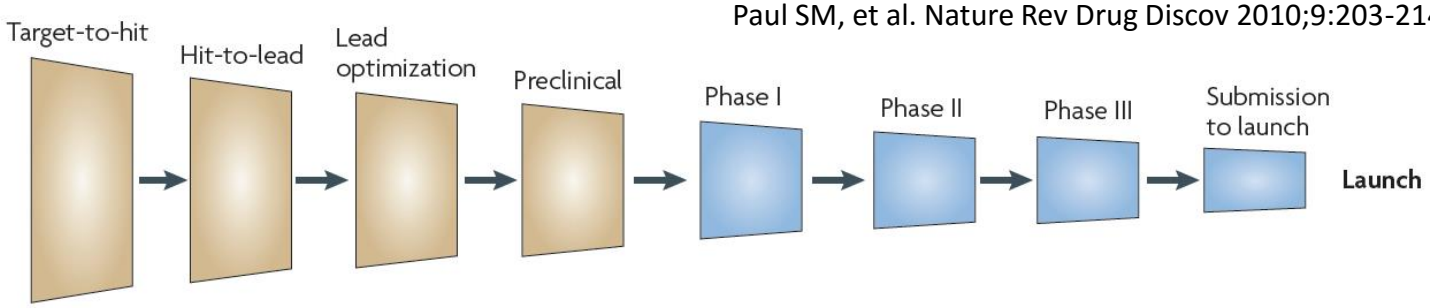
FUTURE R&D PROCESS



Source: PricewaterhouseCoopers

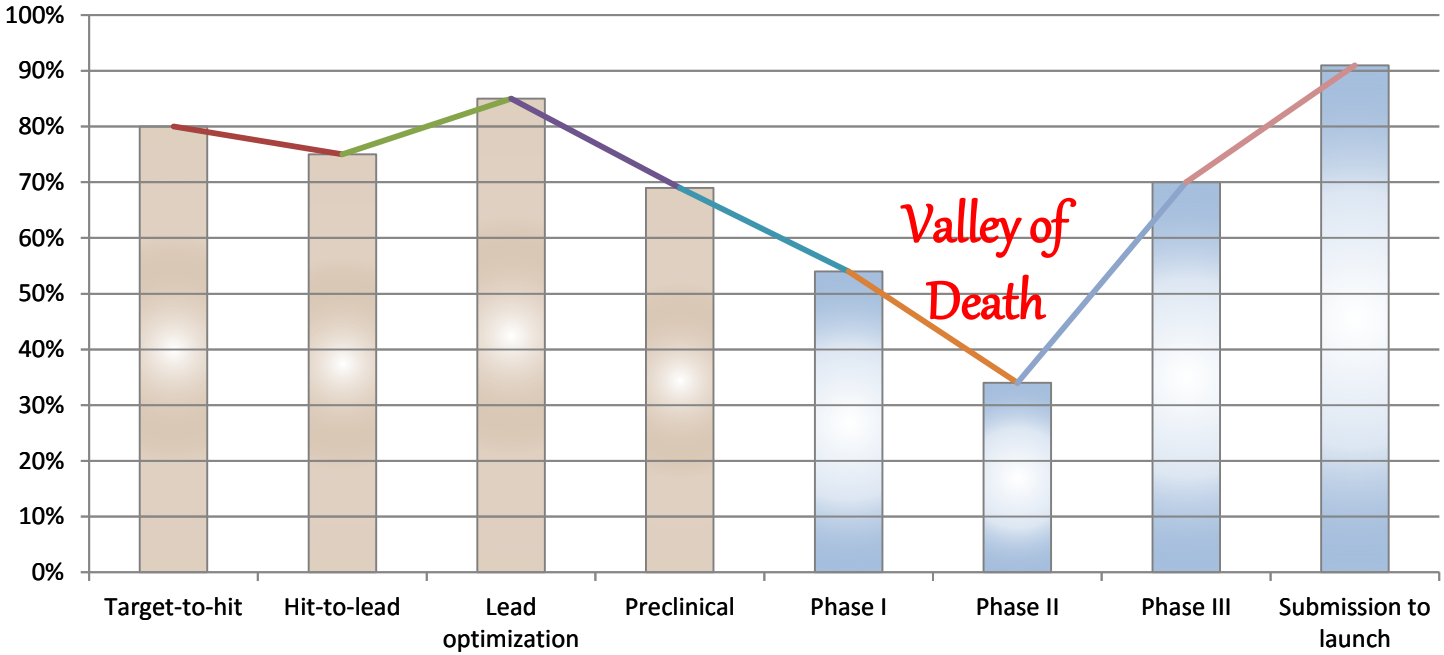
LONG PATH TO SUCCESSFUL DRUG DEVELOPMENT

Paul SM, et al. Nature Rev Drug Discov 2010;9:203-214

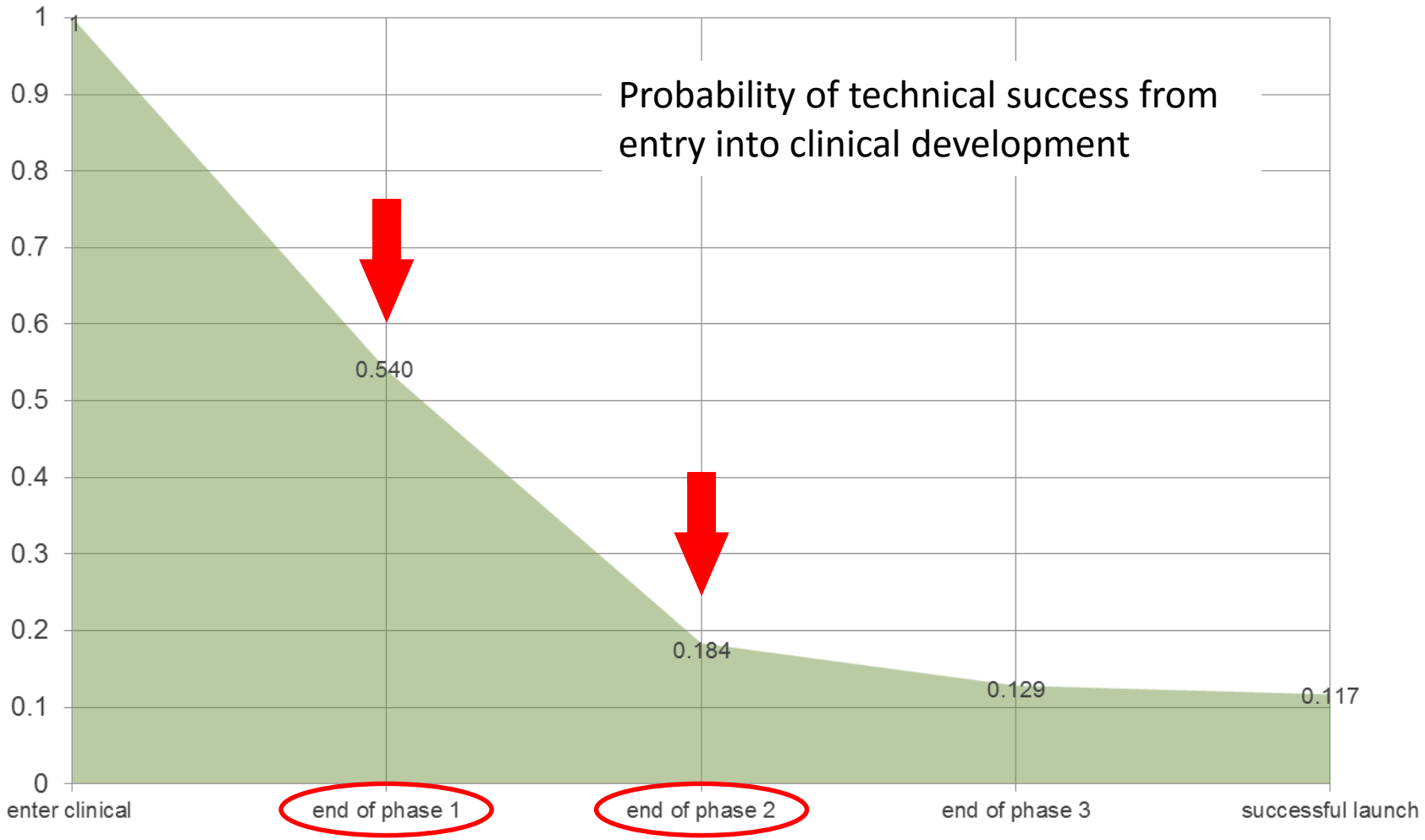


p(TS)	80%	75%	85%	69%	54%	34%	70%	91%	
***WIP* needed for 1 launch**	24.3	19.4	14.6	12.4	8.6	4.6	1.6	1.1	1
Cost per WIP per Pha									
Cycle time (years)									
Cost per launch (out									$873
% Total cost per NMI									
Cost of capital									
Cost per launch (cap									$1,778

Probability of Technical Success



HOW SUCCESSFUL IS CLINICAL DEVELOPMENT?



QUICK WIN, FAST FAIL

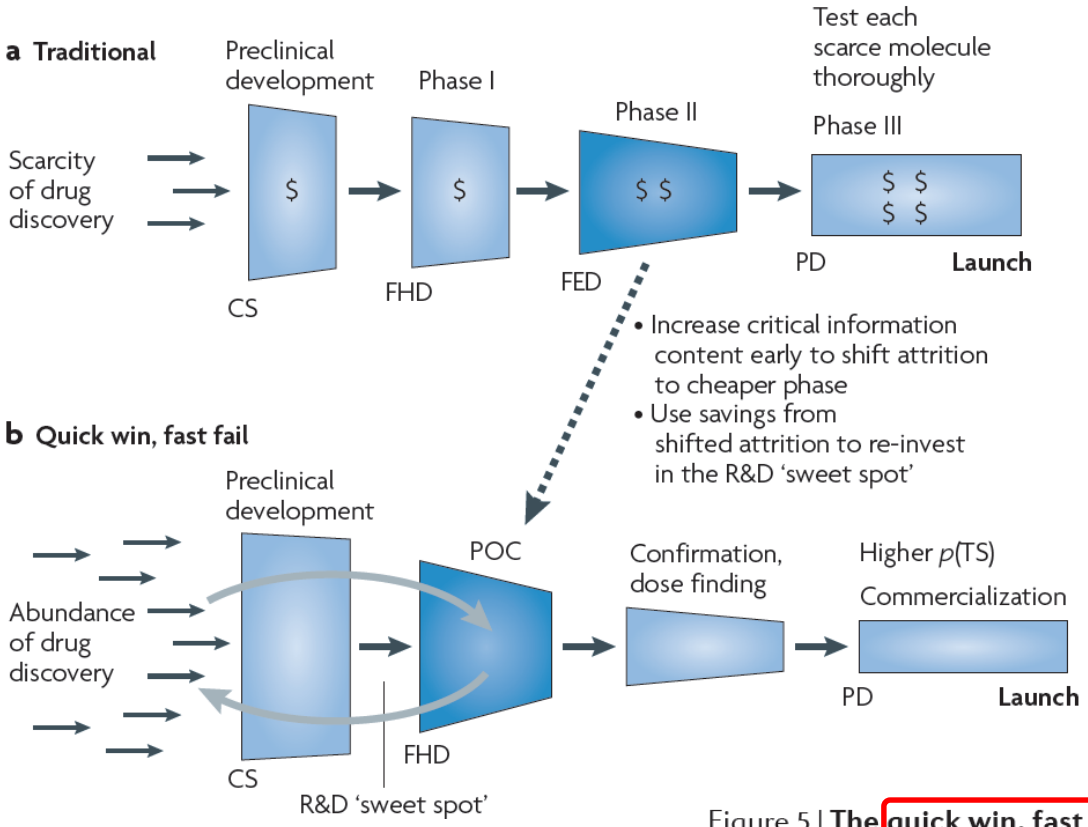
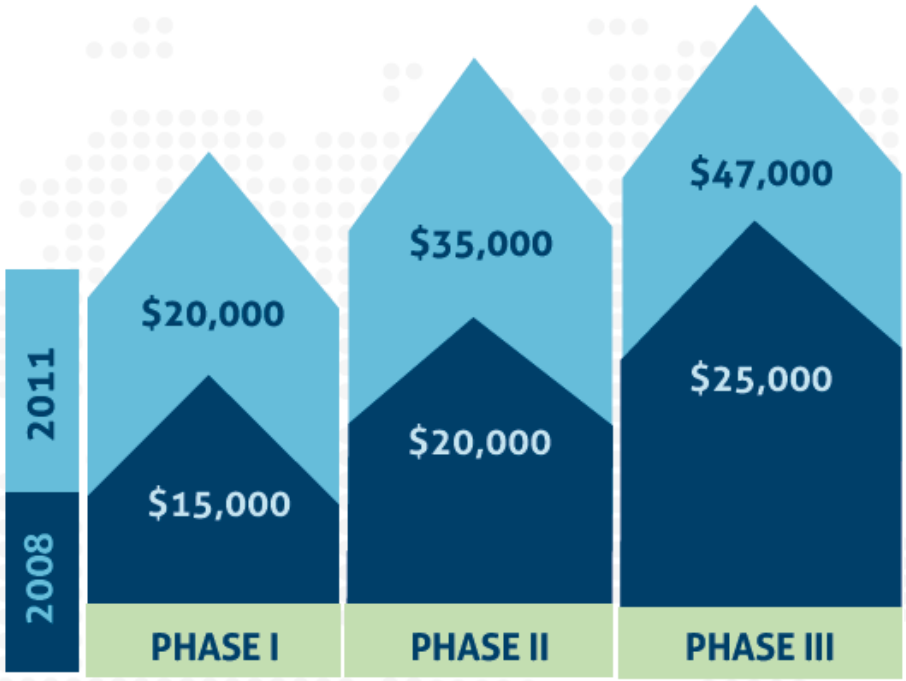
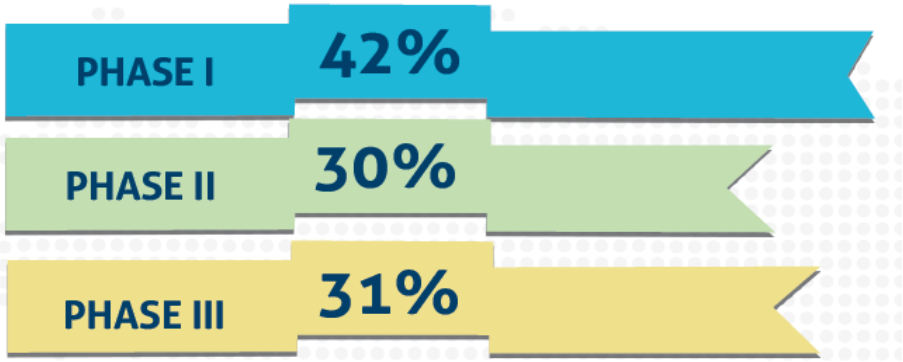


Figure 5 | **The quick win, fast fail drug development paradigm.** This figure illustrates the traditional paradigm of drug development (**a**) contrasted with an alternative development paradigm referred to as quick win, fast fail (**b**). In this alternative, technical uncertainty is intentionally decreased before the expensive later development stages (Phase II and Phase III) through the establishment of proof-of-concept (POC). This results in a reduced number of new molecular entities (NMEs) advancing into Phase II and III, but those that do advance have a higher probability of success (*p*(TS)) and launch. The savings gained from costly investment in late-stage R&D failures are re-invested in R&D to further enhance R&D productivity. CS, candidate selection; FED, first efficacy dose; FHD, first human dose; PD, product decision.

Hurdles to Overcome



Length of trial **delay** due to **patient recruitment**



Rising cost of a patient in clinical trials

Source: Trends in clinical trial site selection and patient recruitment by CLINIPACE, 2014

WHAT TO EXPECT FROM INVESTIGATIVE SITES

ADAPTIVE

- Changing needs and demands
  - Pharma's fail fast strategies to save resources:
    - early critical go/no-go studies;
    - increasing demands and larger phase 1 studies;
    - more complex, labor- & technology-intensive
- Changing roles
  - Changes in structure, composition, and functions
  - Full-services capabilities
    - ARO
    - Strategic alliances or partnerships with CRO's

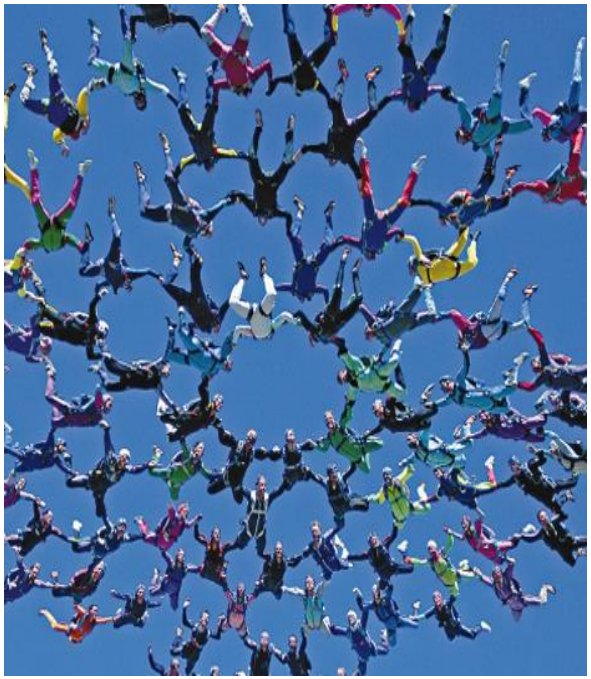
RESEARCH GOVERNANCE

- GCP Compliance and Ethical Conduct
  - Oversight measures
  - Education
  - Outreach

- Efficiency and Promotion
  - Operational systems
    - IT-integrated convergence technologies
  - Services
  - Marketing
  - Awarenes

INTEGRATIVE

- Hub for clinical trials
  - Connect with experts
    - Experts in discovery, nonclinical/preclinical and clinical development, regulatory sciences, and utilization
    - Specialists in various therapeutic areas
    - Database for translational and clinical research
    - Interactions and cross-talks
    - Intermural connections
  - Connect with resources
    - Secure resources necessary for special functions studies
    - Collective utilization of scattered resources
  - Connect with funding
    - Especially for venture companies and individual investigators



STREAMLINING

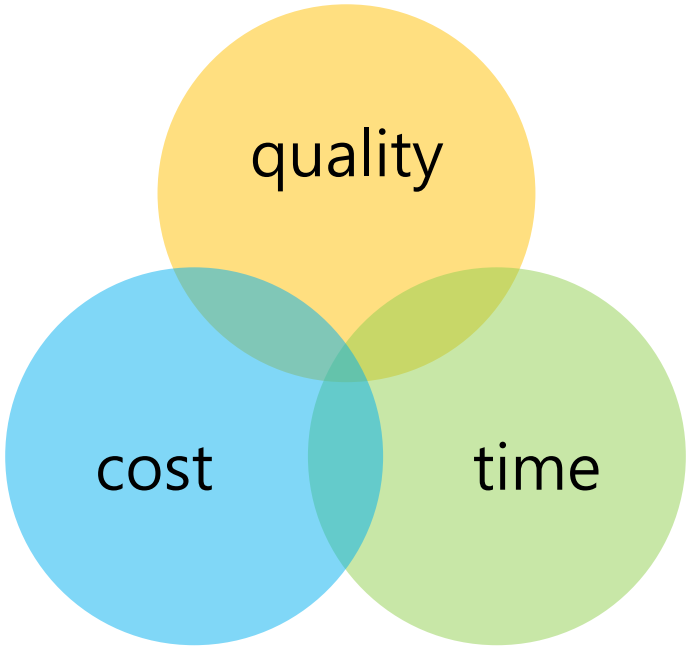
- Critical path initiatives emphasize the importance of streamlining in drug development processes
  - Finding the gaps in all stages and filling in
  - Critical and fast decision-making
  - Involvement from very early stages of development, even into discovery and preclinical stages
  - Operational aspects: cross-talks among relevant members

SPECIALIZED

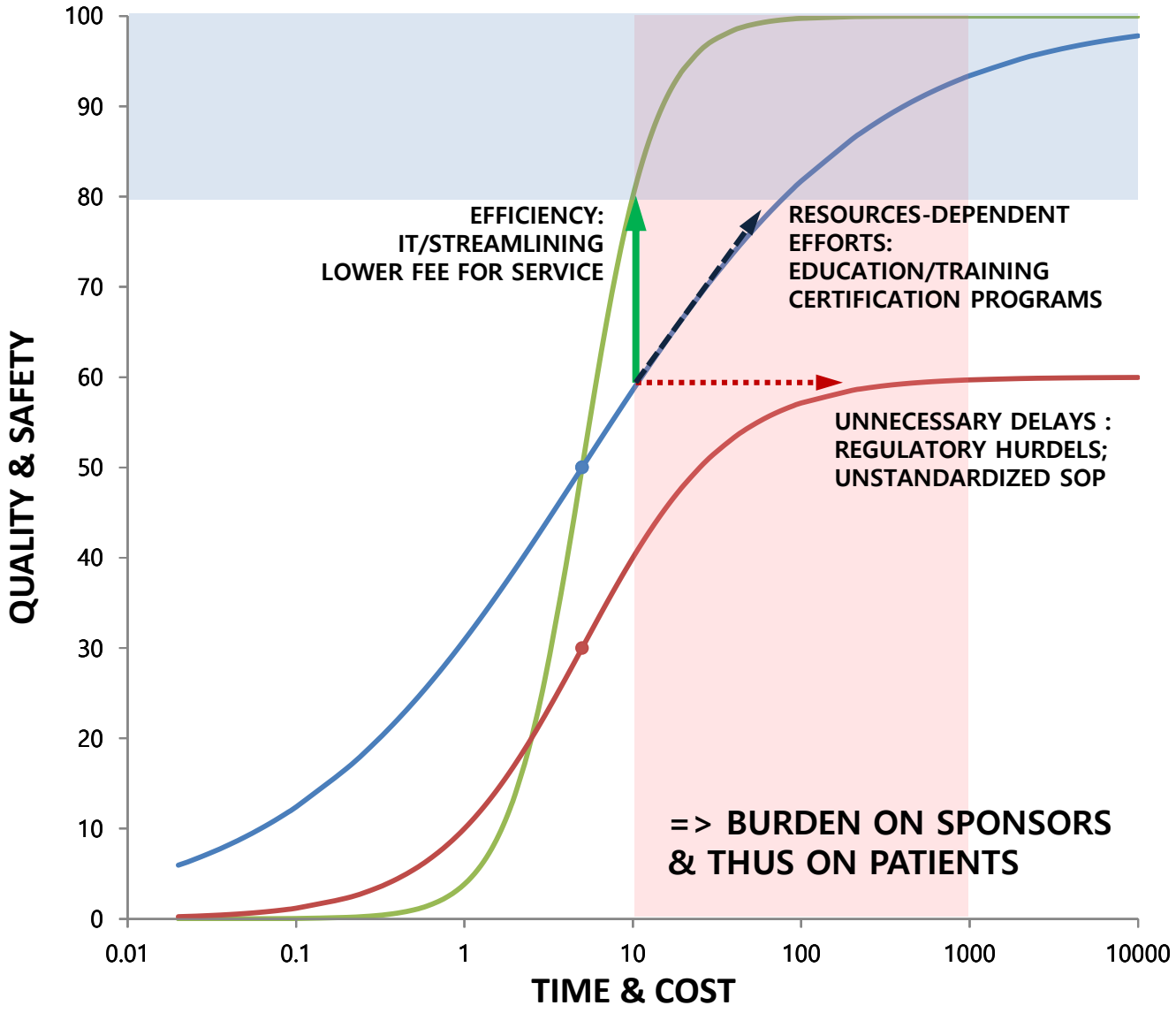
- Select and focus
  - In areas of excellence and expertise
  - In niche areas
  - In therapeutic areas with difficulty recruiting patients
  - Upcoming and evolving technologies
    - Biomarker development
    - Metabolomics
    - In-silico trials

CHANGING PARADIGMS, UNCHANGING VALUES

- No one-size-fits-all model for CTC's.
  - Tailored for purpose based on institutional policy
  - For science, IP generation, commercialization, academic achievements, etc…
- To uphold unchanging values associated with clinical research

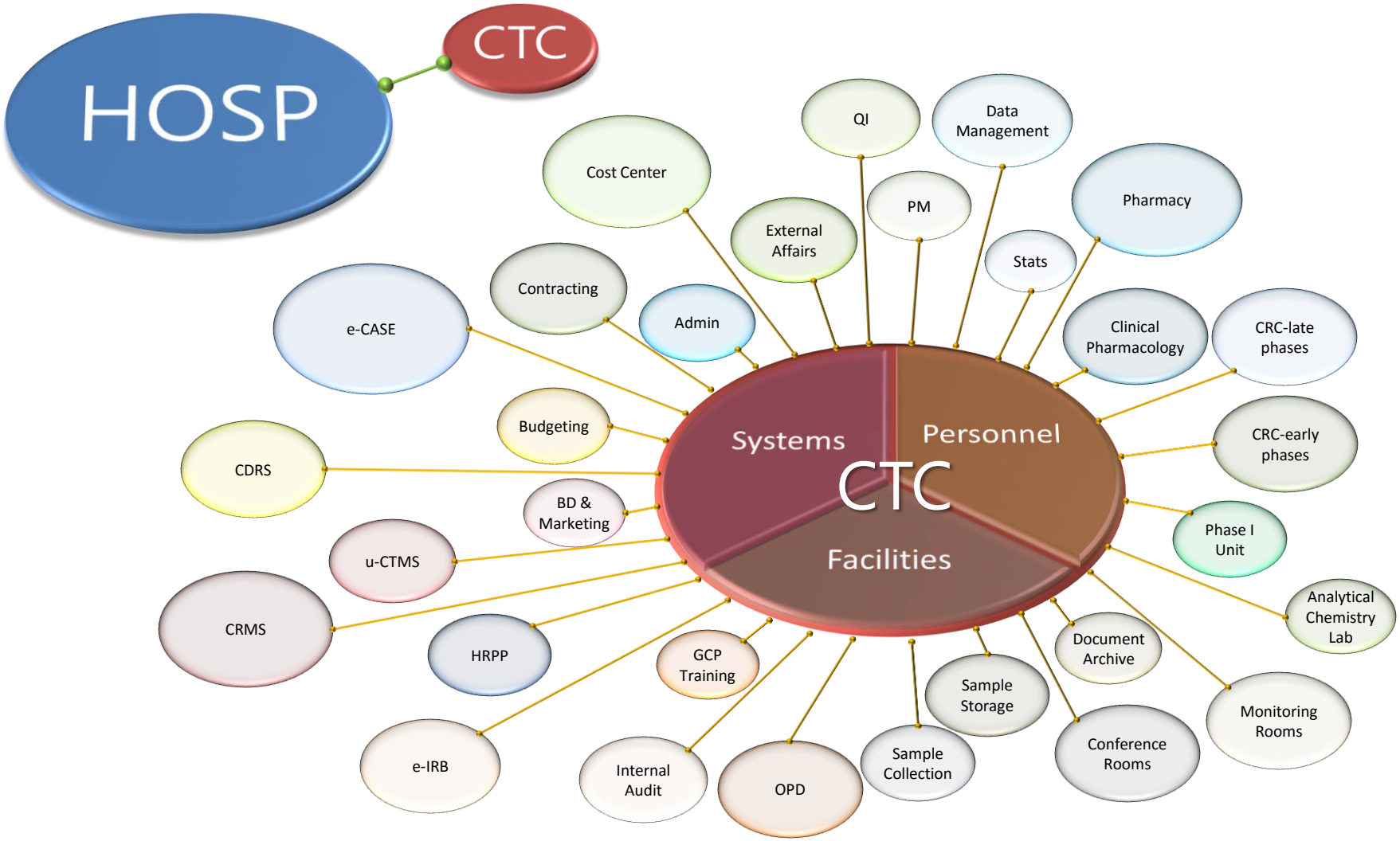


Q-S-T-C RELATIONSHIP

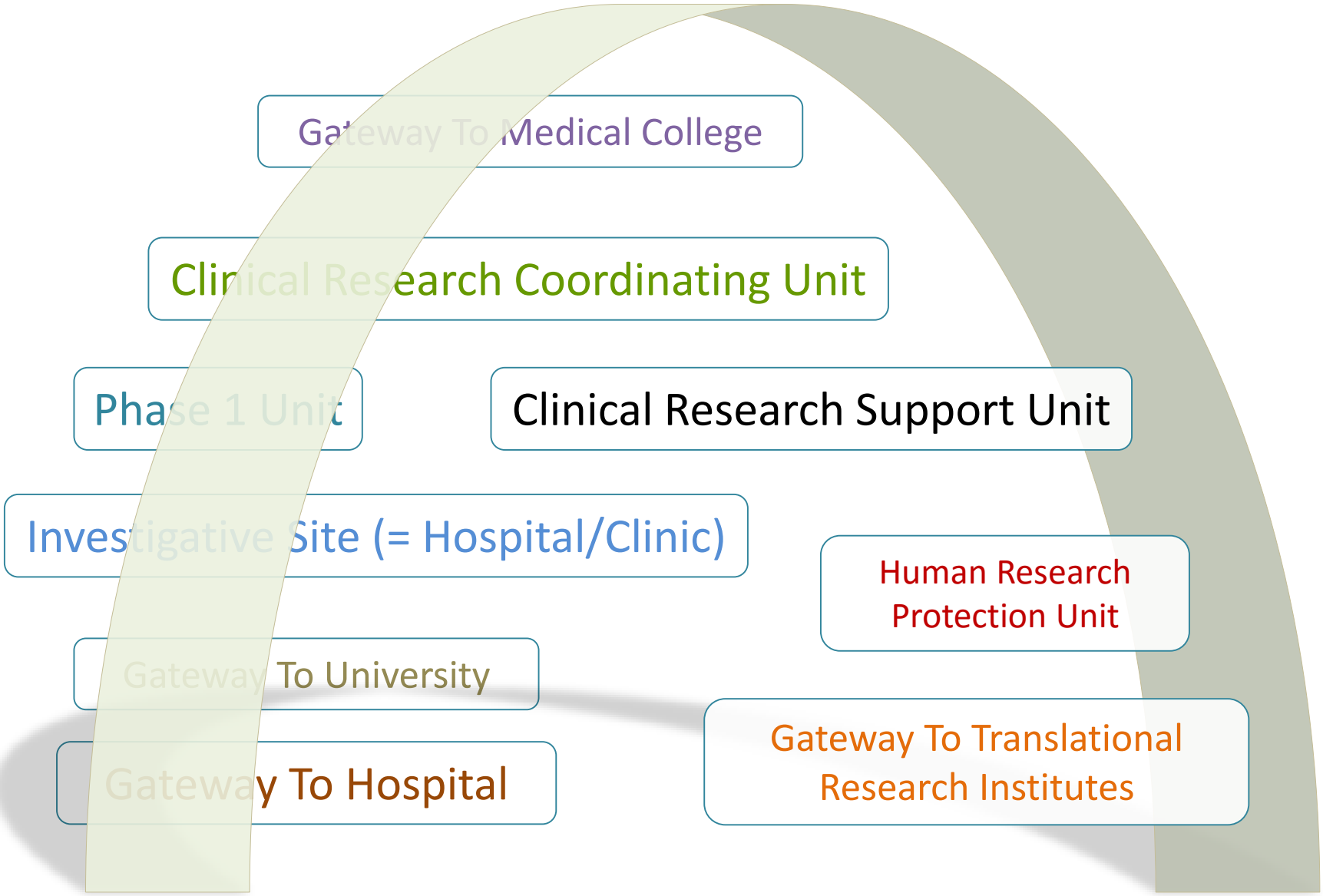


Clinical Trials Center As Infrastructure

Infrastructure: The basic physical and organizational structures and facilities needed for the operation of a society or enterprise.



Roles Clinical Trials Center Plays



LAUNCH OF KCGI

Where to Go?

- **DIRECTIONS**
  - Innovate clinical trials centers to attain global competitiveness in clinical trial industry
  - Develop new trial technologies to lower cost and shorten duration of clinical trials
- **VISION**
  - To become one of the global leaders in clinical trials and to contribute to global new drug development
- **GOALS**
  - Attract highly value-added early phases clinical trials from global pharmaceutical companies
  - Help domestic pharma's develop new drugs and go global

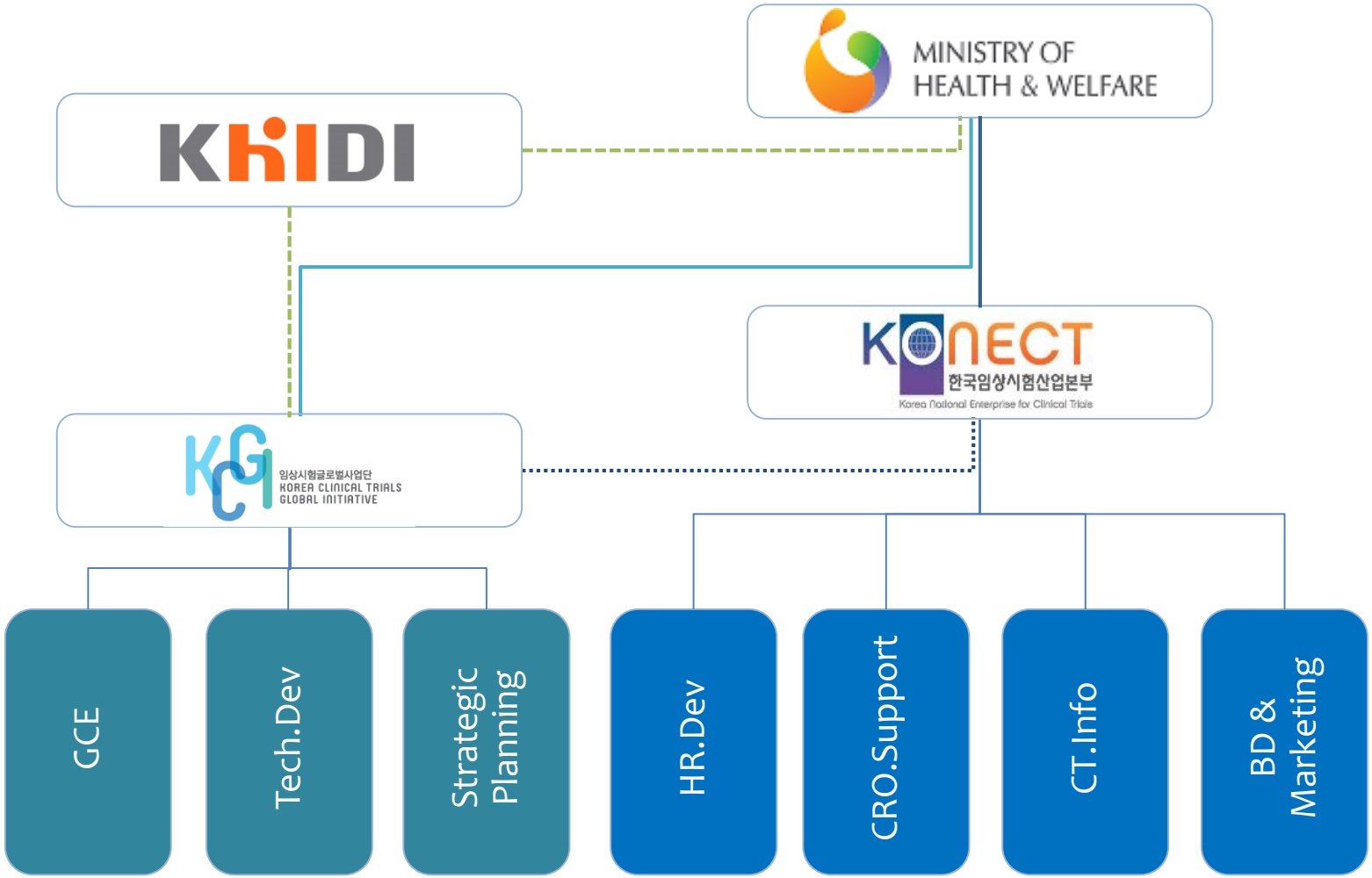
KEY SUCCESS FACTORS

- Specialization and differentiation of Global Centers of Excellence; Global business development
- Foster convergence technologies
- Sharing of information and experience as well as connecting the dots between academia and industry
- Mutual collaboration with KoNECT2.0 for infrastructure building, external affairs, and global marketing
- Activation of clinical trials policy-making and planning for open innovative R&D

OVERVIEW OF KCGI PROGRAM

- Duration: 2014. 9. 1 ~ 2019. 3. 31 (4 yr 5 mo)
  - Phase 1: 2014. 9. 1 ~ 2017. 3. 31 (2 yr 5 mo)
  - Phase 2: 2017. 4. 1 ~ 2019. 3. 31 (2 yr)
- Budget: 42 billion KRW
  - Phase 1: 33 billion KRW
  - Phase 2: 9 billion KRW
- Projects
  - Infrastructure & Systems Support Project: Global Centers of Excellence for Clinical Trials
  - New Technologies Development Project: Development of Convergence Technologies for Clinical Trials
  - Clinical Trials R&D Policy-making & Planning

ROLES & RESPONSIBILITIES SHARED



Projects and Plans

1. Global Centers of Excellence for Clinical Trials

- While each GCE having uniqueness of its own through specialization and differentiation, together GCE's will cooperate and act in unity for joint global marketing and strategic collaboration to attain global competitiveness

2. Convergence Technologies for Clinical Trials

- Newly selected projects will have to combine cutting-edge technologies of multiple disciplines that are clinically valid and can be applied in clinical trials for more efficient and relevant development

3. Clinical Trials R&D Policy-making & Planning

- Projects will be utilized to gather and process information regarding open and innovative models of new drug development and come up with strategic plans supporting policy-making and project planning

Global Centers of Excellence for Clinical Trials

Budget & Evaluation

- Budget: 45 billion KRW
- Staged evaluation as well as yearly evaluation
- 5 projects ongoing (2 in 4th year, 2 in 3rd year, 1 in 2nd year)

Growth Phase (2014.09 ~ 2017.03)

- Efficient management of R&D resources within consortia and improvement of infrastructure and systems
- Increase in contracts of studies from global pharma's (esp, sophisticated early phases trials)
- Focus on high-tech trials, unmet needs, and international networks

Fruition Phase (2017.04 ~ 2019.03)

- Global competitiveness through specialization and differentiation
- Joint cooperation among consortia
- Provide open platforms for late comers

Global Centers of Excellence for Clinical Trials

Specialization and Collaboration

	Capabilities	Environment	BD	Network
Specialization	• Early phases special studies • Experts and staff specialized in certain areas	• Specialists in selected TA • Special functions, facilities and equipment	• ARO services • IIT support (incl. RA) • Comprehensive consulting services for drug development	• Expand overseas network • TA-specific collaborative models
Collaboration	• Multicenter trials infrastructure and systems • SOP standardization (harmonization) • Feasibility DB	• Support of acquisition of international HRPP accreditation • QM(QA/QC) • IRB review processes	• Industry-academia collaboration ecosystem • PM reinforcement	• Global marketing • Joint effort at a national level

Global Centers of Excellence for Clinical Trials

Strategy 1: Operational Management

Operational Excellence

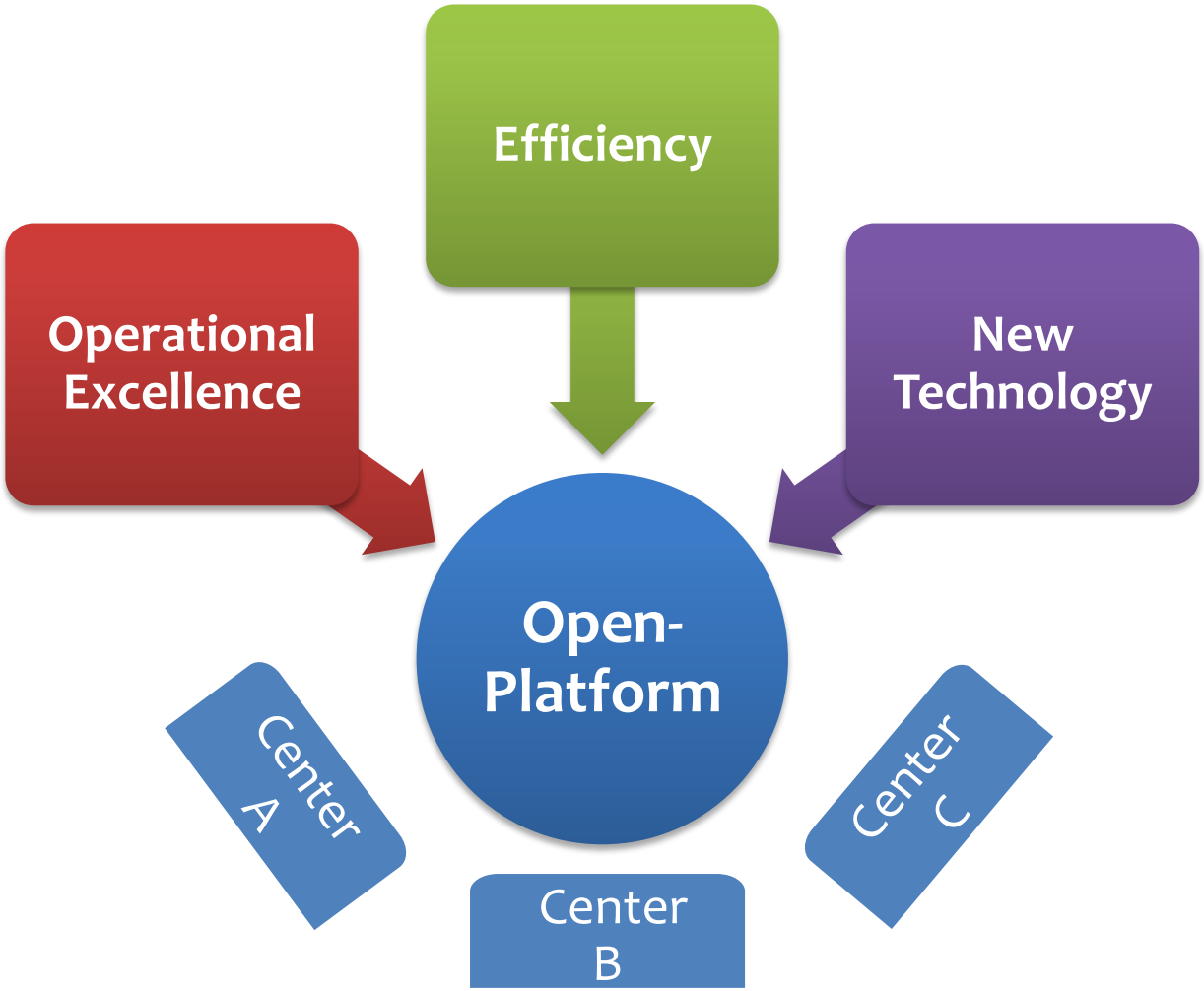
- **Quality Management:** QC/QA, HRPP structures and functions
- **Safety Management:** safety reporting and monitoring
- **Performance Management:** IRB approval process and PM function

- **Integrated Resource:** investigators, patients, experts, knowledge and experiences
- **Standardization & Harmonization:** SOP, procedure, Data and statistical management (CDISC)

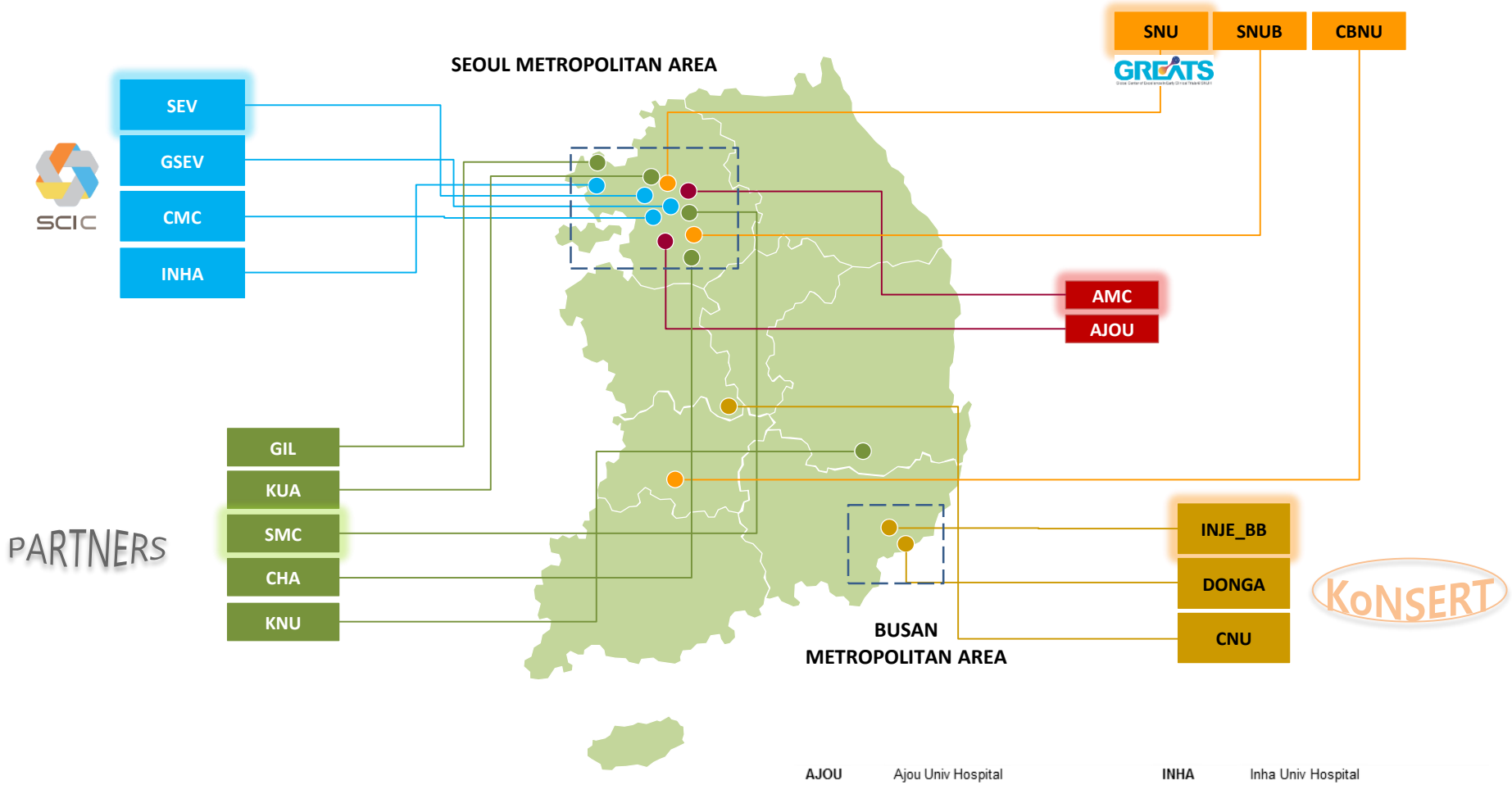
Efficiency

Global Centers of Excellence for Clinical Trials

Strategy 2: Open-Platform for Sharing Best Practices



GLOBAL CENTERS OF EXCELLENCE



AJOU	Ajou Univ Hospital	INHA	Inha Univ Hospital
AMC	Seoul Asan Hospital	INJE_BB	Inje Univ Busan Baik Hospital
CBNU	Chonbuk Univ Hospital	KNU	Kyungpook National Univ Hospital
CHA	Cha Univ Bundang Cha Hospital	KUA	Korea Univ Anam Hospital
CMC	Catholic Univ Seoul St. Mary's Hospital	SEV	Yonsei Univ Severance Hospital
CNU	Chungnam Univ Hospital	SMC	Samsung Seoul Hospital
DONGA	Donga Univ Hospital	SNU	Seoul National Univ Hospital
GIL	Gachon Univ Gil Hospital	SNUB	Seoul National Univ Bundang Hospital
GSEV	Yonsei Univ Gangnam Severance Hospital		

PARTNERS

PARTNERS

We are striving for PARTNERS to be a partner

PARTNERS stands for
Personalized and precision clinical trial consortium based on
Advanced **R**esearch **T**ools, **N**etwork in the biomedical **E**cosystem and
Robust **S**upport system

Advanced Research Tools

PARTNERS offers optimal personalized & precision clinical trial through multi-site collaboration and cutting edge technologies such as panomics based clinical trial, stem cell trial, image biomarker and metabolite biomarker.

Network in the biomedical Ecosystem

PARTNERS' open innovation and true collaboration is based on its hospital-based control tower, which organically connects various fields ranging from basic research to translational, clinical research.

PANOMICS BASED CLINICAL TRIAL

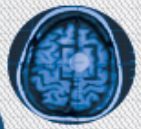


IMAGE BIOMARKER

STEM CELL TRIAL

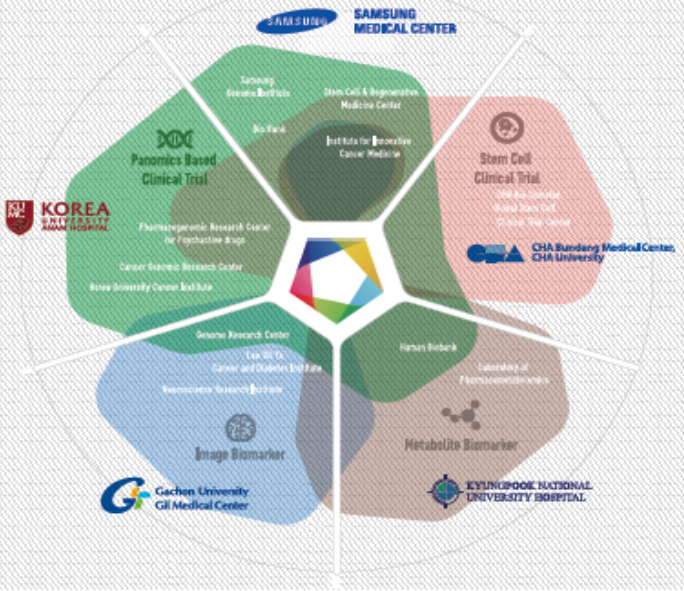
Robust Support system

PARTNERS has established an integrated support system that covers all phase of drug development from developing innovative pipeline to consulting, regulatory affairs, resource coordination and commercialization.

METABOLITE BIOMARKER

PARTNERS CONSORTIUM

We are committed to providing personalized & precision clinical trials with our specialized facilities & a team approach strategy

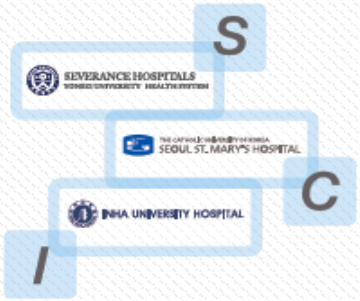


SCI CONSORTIUM

SCI C

Meet Your True Companion On the Way to Successful Drug Development

ABOUT SCI CONSORTIUM



The SCI Consortium (hereafter SCI-C), consisting of clinical trials centers (CTCs) of excellence from the three leading medical institutions in Korea

: Two **Severance Hospitals** of Yonsei University Health System, Catholic University Seoul St. Mary's Hospital, and Inha University Hospital, has set out to fulfill the unmet needs of our clients with drug development initiatives.

INTEGRATED FUNCTIONS OF SCI-C

1. Clinical Trial Operation

IT-driven feasibility DB, SCI-C IRB system, Phase I clinical trial, Patient-oriented early phase clinical trial, Late phase clinical trial, Project management.

2. Drug Development Support

Core disease investigators' networks, Design of early phase clinical trials, PK/PD modeling and simulation, Strategic consultation of drug development, Regulatory sciences.

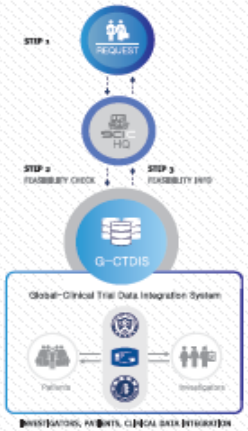
3. Business Development/Marketing

Trial budgeting and contracting, Service marketing and sales, Advertisement, New business development.

CORE SERVICES

SCI-C FEASIBILITY DB

Integration of resources such as investigators, patients, research staff, and experts and sharing of knowledge and experiences maximize productivity and increase the chances of success.
Three medical institutions (four hospitals) provide integrated data of investigators, patients and other research resources via a centralized data base.
For the study feasibility, relevant information can be obtained quickly and accurately. This allows much faster subject enrollment (for either normal healthy volunteers or patients).



SCI-C SALT

SALT (Strategic Advisory Leadership Team) that involves experts in drug discovery, nonclinical & pre-clinical development, clinical development, biomarkers including bioimaging, pharmacometrics, pharmacogenomics, biostatistics, regulatory affairs, and intellectual property & technical transfer.
Experts comprise academicians and clinicians from biomedical sciences backgrounds and provide professional consultations on issues ranging from early drug development through late stage of clinical drug development and to post-approval medical affairs in a multidisciplinary approach.

SCI-C IRB SYSTEM

In general, sponsors go through IRB review processing at each institution individually when conducting multicenter clinical studies. It leads to the burden, redundancy and delay. We provide a solution for improving the IRB process in multicenter studies settings.
SCI-C first introduces an alternative model of IRB in Korea, a modified "IRB Mutually Recognized System". Approval at one of the institutions in the consortium will be accepted by the rest of the institutions without delay.

SCI-C OPERATION

Patient-oriented early phase clinical trials (including phase I) can be conducted simultaneously at the hospitals of SCI-C.
All clinical trials centers systemically coordinate trials in terms of harmonized SOPs for the best performance.
This operational excellence in multicenter clinical trials with consistent procedures is a key factor for a successful clinical development.
The investigators, study coordinators, and clinical center staff all work towards the same goal of accelerating the process and increasing efficiency.

GREATS

GREATS
Global Center of Excellence in Early Clinical Trials @ SNUH

SNUH provides

- World-class medical care
- Huge patient volume
- Research-oriented environment
- Strong translational research capabilities
- Highly motivated and devoting investigators

Network

to create win-win results

- **Consortium :** 6 local hospitals
- **Domestic :** Pharmaceutical companies, CRO, Academia
- **Global :** Pharmaceutical companies, CROs, Academia

Core Values

Guiding
GREATS guides you through the maze of successful clinical trial projects.

Respectful
GREATS is respectful of your unique clinical trial needs.

Ethical
GREATS is ethical in every conduct of its clinical trial business; it always puts human rights first.

Adept
GREATS works skillfully to get the job done.

Trustworthy
GREATS is reliable, responsible, and can be trusted completely.

Sustainable
GREATS provides you with a sustainable clinical trials infrastructure.

Quality

in Science, Ethics and Data management

- **No critical issues from Audit and Inspection**
  - Audits by the top 20 global pharmaceutical companies and CROs.
  - Inspections by KFDA, FDA, PMDA, and EMA
- **Accreditation**
  - AAHRPP accredited in December, 2012
  - SIDCER / FERCAP accredited in 2006, 2009, 2012
- **Training and Education**
  - Our staff members are quarterly trained with GCP and current regulation

Efficiency

by improving the facility and system

- **IT implementation**
  - Barcode for data and sample collection system
  - Electrical Medical Record(EMR)
  - Radio Frequency Identification (RFID)
  - Fully automated clinical research system using (TrialOne®) by OmniComm
- **IRB**
  - 8 per month of IRB regular review
  - 2 weeks from submission to initial IRB review
  - Web-based tracking system

ASAN - Ajou

ASAN FOUNDATION 아산재단

ASAN
Medical Center
Clinical Trial Center

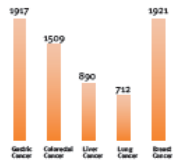
Ajou University
Medical Center

Our Strengths

1. **High volume center**
   - The highest patient volume in Korea
2. **Outstanding platform technology & infrastructures**
   - Advanced technology in radiopharmaceuticals
   - Bio Resource Center
   : vast amount of clinical information & specimens
3. **Qualified and experienced global investigators**
4. **Highly qualified staffs dedicated to clinical trials**

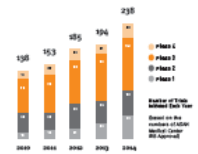
RANKED TOP IN NO. OF SURGERIES FOR 9 OUT OF KOREA'S 10 MAJOR CANCERS

AMC treats 10% of total cancer patients in Korea (Stomach, Liver, Colon, Rectum, Thyroid, Prostate, Uterine, Ovary, Breast)



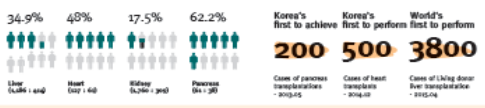
ASAN MEDICAL CENTER CLINICAL TRIAL CENTER
(GLOBAL CENTER OF EXCELLENCE IN PoC TRIALS)

ASAN Medical Center Clinical Trial Center has been designated as the Global Center of Excellence in Clinical Trials by the Korean Ministry of Health and Welfare in 2012, focusing on accelerated "Proof of CoNcept(PoC)" trials.



RANKED TOP IN NO. OF ORGAN TRANSPLANTATION

Organ Transplantation Asan Medical Center (~Dec. 2013)



Excellence in clinical trial

Phase I to IV clinical trials & IT supporting

Optimal research environment

Dedicated Phase I research unit

Reliable partner in investigator sponsored trial

Academic Research Organization Full Service

ANYCAP system development

Innovative coaching of pharmaceutical industry

Clinical development Accelerated center (CDAC)

Clinical Translational research services

We are always there for you.

We are committed to caring for you and your family

KoNSERT

INJE UNIVERSITY BUSAN PAIK HOSPITAL CLINICAL TRIAL CENTER

Cost effective, time efficient, well-orchestrated, and fully compliant clinical trials

Clinical and Non-Clinical Services

Conventional Phase 1 Trials

* First-in-human
* Bioavailability / Bioequivalence
* Drug-drug/food -drug interaction
* Special population
* Thorough QT

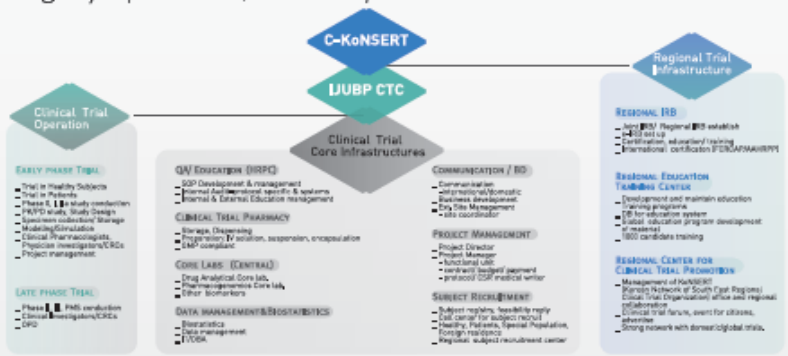
Technology Driven Clinical Trials

* Microdosing & human mass balance
* Cocktail studies for drug intar action potential
* Biomarker driven clinical studies (pharmacogenomics/metabolomics/imaging)
* ePOC translational research
* Phase 1 studies in target patient populations
* POC trial in treatment naive patients (KoNSERT; Korean Network for South East Regional Network)
* Platform for combining 'Bottom-Up' PBPK and 'Top-down' PopPK data analysis

Bioanalytical / Genomics analytical Core Lab Services

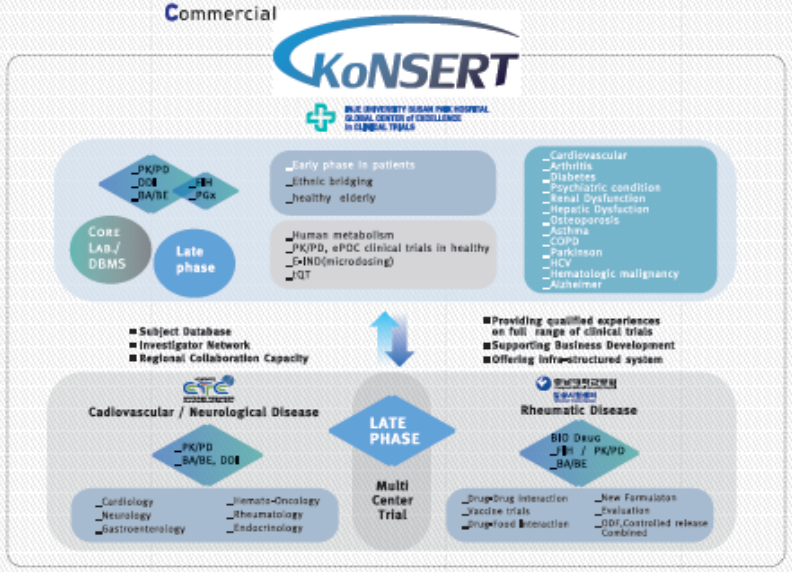
* Advanced bioanalytical method development
* Protein binding assay
* In vitro metabolism, in vitro permeability and transporters
* Metabolite identification
* Genotype method development
* Haplotype and LD analysis
* Functional analysis of SNPs and copy number variation
* Gene expression profiling

Highly qualified, and experienced staff

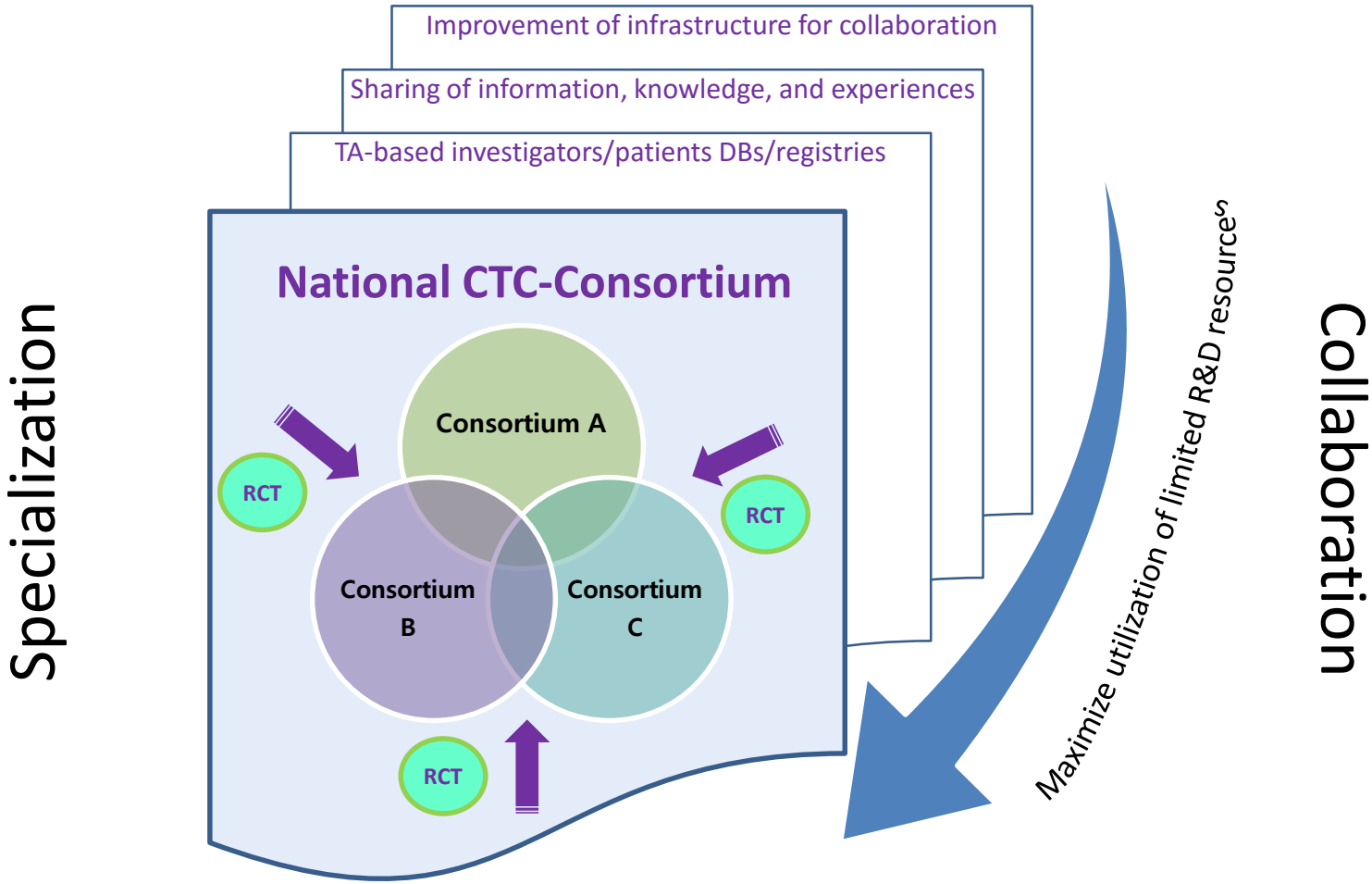


Communication
Collaboration
Cooperation
Contract
Corporation
Commercial

'SEE' KONSERT



Virtually Integrated National CTC-Consortium



Convergence Technologies for Clinical Trials

Stage 1 Projects Selection and Evaluation (2014.10 ~ 2017.03)

- High priority technology areas chosen based on strategic planning reports
- 2 projects will be selected (3.5 billion KRW per project ('14))

Stage 2 Projects Selection and Evaluation (2016.10 ~ 2019.03)

- High priority technology areas chosen based on ensuing strategic planning reports
- 2 projects will be selected (budgets TBD)

Application and Expansion of Utilization

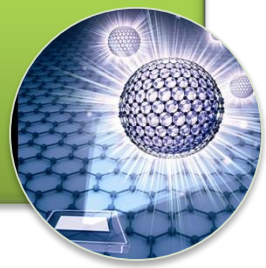
- Annual evaluation focused on feasibility of clinical application
- Primary objective is IND approval of clinical trial protocol for clinical validation of new technology; additionally publication

Convergence Technologies for Clinical Trials

Examples of Innovative Multidisciplinary Fusion Technologies

- OMICS (Genomics-Proteomics-Metabolomics) technologies
- Diagnostic methods for responses to personalized therapies and/or rare diseases
- New therapeutic response monitoring approaches such as biomarkers or surrogate endpoints

New Diagnostic Methods or Biomarker Development



- Streamlining and facilitation of data collection, management, patient allocation, drug accountability, etc (EDC, IWRS, PRO)
- Clinical trials management system (CTMS) and solutions for functional integration
- EMR-based big data application technologies

Improved Trial Efficiency through IT and Mobile Technologies

Convergence Technologies for Clinical Trials

Strategy 1: Choose and Focus, then Apply

Area of New Tech

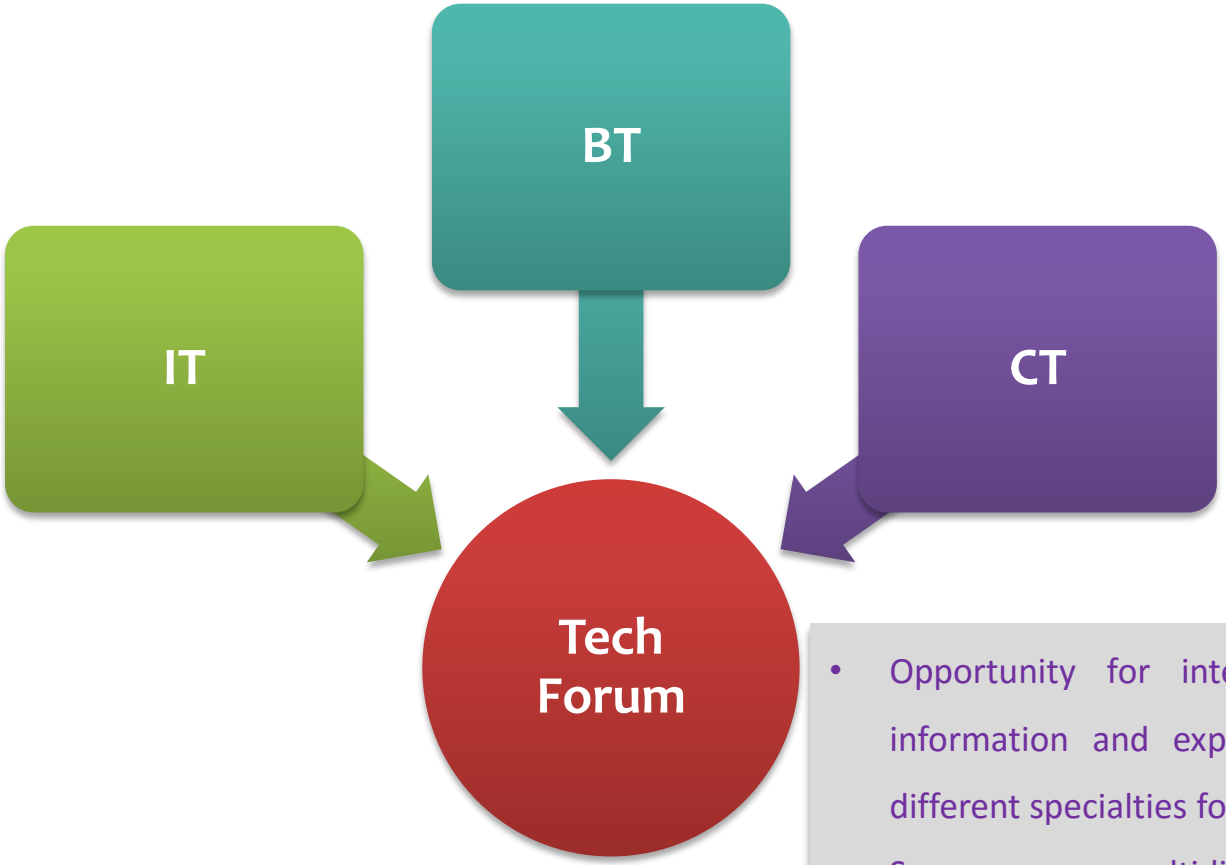
- Priority setting
- Choose and focus on select few projects

- Aim for clinical application of newly developed technologies
- IND approval of trial protocols and eventually clinical validation in ensuing years
- Minimum duration of 3 years up to IND approval

Clinical Validation

Convergence Technologies for Clinical Trials

Strategy 2: Interact and Exchange of Tech



- Opportunity for interaction and exchange of information and expertise among experts with different specialties for fusion and integration
- Synergy across multidisciplinary areas

Clinical Trials R&D Strategic Planning

Clinical Trials R&D Advancement & Support Models

- Develop new clinical trial R&D ecosystem model and plan support for global leadership
- Devise strategies to contribute to improved productivity in global drug development

Selection of RFP

- Refer to strategic planning reports and opinions from experts for listing up of focus areas
- Use variety of methods to gather info and opinions (e.g., focusing interview or survey or workshop)
- Prioritize areas of focus for final selection

Support for policymaking and strategic planning

- Secure data and evidence needed for policymaking and strategic planning through reports of these projects
- Follow-up projects based on newly developed policies and strategies

Clinical Trials R&D Strategic Planning

Strategy: Integrated Management

Open R&D Innovation

- Interactions of experts with different specialties in specific therapeutic areas (non-clinical, translational, clinical development specialists)
- Predict and prepare for new R&D ecosystem
- New business model development

- Exchange and interaction with leading instutitions abroad
- International clinical trials R&D collaboration
- Share new visions for stakeholders of clinical trials ecosystem

Network & Benchmark

ANTICIPATED OUTCOMES

- Improved global competitiveness of GCE's will provide opportunities for Korea to become a hub for clinical trials in AP region
- Convergence technologies for clinical trials will be used to bring down the cost and shorten the time for clinical development, and eventually contribute to improvement of productivity in drug development
- Well-developed infrastructure, shared resources and efficient operating systems for clinical trials as well as new technologies will be advantageous for
  - Global pharmas to conduct early phases global studies, and in turn late phases multinational studies
  - Domestic pharmas to grow drug development capabilities and contribute to Korea's becoming new drug development leader

THANK YOU FOR LISTENING.