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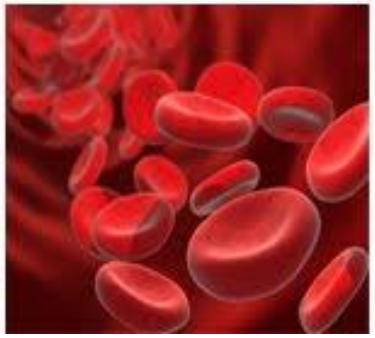

Dr. Olivier Loget DVM ERT
CEO & Founder

Gaëlle Vacher PhD, PharmD Associate Professor Expert Partner	Graham Scott PhD MRPharmS Dpt Dir Julie Balland PharmD	Camille Cadoret BSc Pharm Amandine Rey MSc Océane Vendrasco MSc	Yewon Ha MSc Rita Morkos
Pharmacology Toxicology	Expert Partner ADME PK	Toxicology Formulations	International Business Dev.

www.capeval-pharma.com

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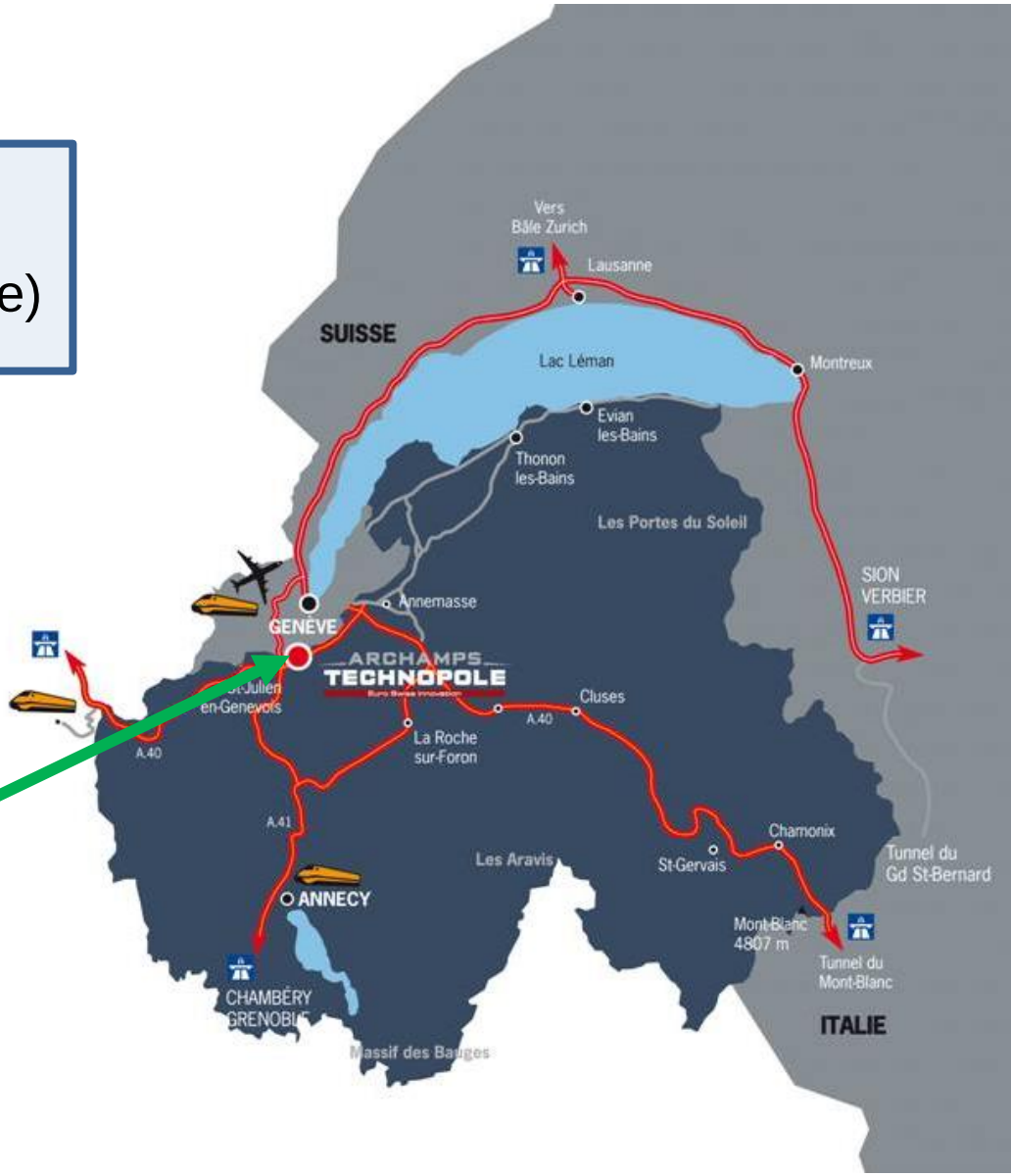
CapEval Pharma: Location

- 15 min from Geneva airport
- Archamps Technopole (France)

CapEval Pharma
Le Forum 2
218 ave Marie Curie
74160 Archamps
+33 612 13 29 72
capeval-pharma.com



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CapEval Pharma: The Know-How you need

Mostly pharma (in blue)

Audits	ADME/PK/DDI	Analytical Development	Acquisition Assessment	CMC-Regulatory Affairs
Development Partnership	Dossier and Registrations	Due Diligence	Pharmacology	Ophthalmology
CRO/Project Management	Quality Assurance & Compliance	Toxicology	ERG Assessment	Training
Agrochemicals	Industrial Chemicals	Veterinary Drugs	Cosmetics	Medical Devices

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CapEval Pharma: Our Strength

Team of highly qualified pharmaceutical consultants

- Several Decades of international experience; fluent in 3 languages
- Experience working in Biotech, Pharma and CROs

Our combined experience covers “overlapping areas”

- Pharmacology depends on pharmacokinetics and bioanalysis
- ADME/PK and toxicology are closely related
- No proper CMC-regulatory strategy without non-clinical input
- Uniquely qualified to offer complete outsourcing management services

Working closely with clients

- Help manage key objectives
- Assessment of major risks and regulatory hurdle

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CapEval Pharma: CEO

Dr. Olivier Loget DVM ERT

Expert Toxicology/Pharmacology

- More than 30 years of experience in pharma industry
- Worked in toxicology departments since 1988

✓Sanofi-Synthelabo SD (Paris area)
✓Hazleton/Ricerca/CRL (Lyon), CIT Tox Dpt Dir (Evreux)
✓Roche (Basel), Addex Pharma NCD Dpt Dir (Geneva)
✓OriBase Pharma CSO (Montpellier)
✓CapEval Pharma CEO (Geneva area)

- Founded CapEval Pharma in 2010
- Author or co-author of more than 20 publications
- Co-founder of the European Society of Laboratory Animal Veterinarians and board director of the International Society of Ocular Toxicology. He is a lecturer teaching preclinical R&D, toxicology in drug development and ocular examination in several Research Institutes (INSERM, INRA), Universities and Veterinary Schools.

Expert Partner

Dr. Gaëlle Vacher PharmD, PhD, Associate Professor

Toxicology/Pharmacology

Committed pharmaceutical formulation scientist with more than 10 years of experience in various dynamic, multicultural and challenging environments.

Peer Reviewer of European Journal of Pharmaceutics and Biopharmaceutics since 2010

Specialized in formulation, nanovaccins, molecular biology and cell culture

✓ Novartis Consumer Health (Nyon, Switzerland)	Development scientist & QA support in R&D
✓ University of Geneva (Geneva, Switzerland)	PhD in Biopharmacy, “Potential of a virosome-based vaccine in mucosal immunization”
✓ IST/CHUV (Lausanne, Switzerland)	Post-doctoral researcher
✓ CapEval Pharma (Archamps, France)	Project leader assistant

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ADME PK Department Director

Dr. Graham Scott PhD MRPharmS

Expert Toxicology/Pharmacology

- More than 30 years of experience in pharma industry
- Pharmacist with ADME PK expertise
- Worked in toxicology departments since 1984 (Inveresk/CRL, Pharmacia/Upjohn, Novartis, Takeda, Certara, CapEval Pharma)
- Experienced in clinical pharmacology and pre-clinical drug disposition
- Passion: to see clinical pharmacology skills applied in conducting efficient decision-making studies in early clinical development and effective drug labelling studies later
- Modelling and simulation approaches as key in delivering cost-effective successful drug development programmes.

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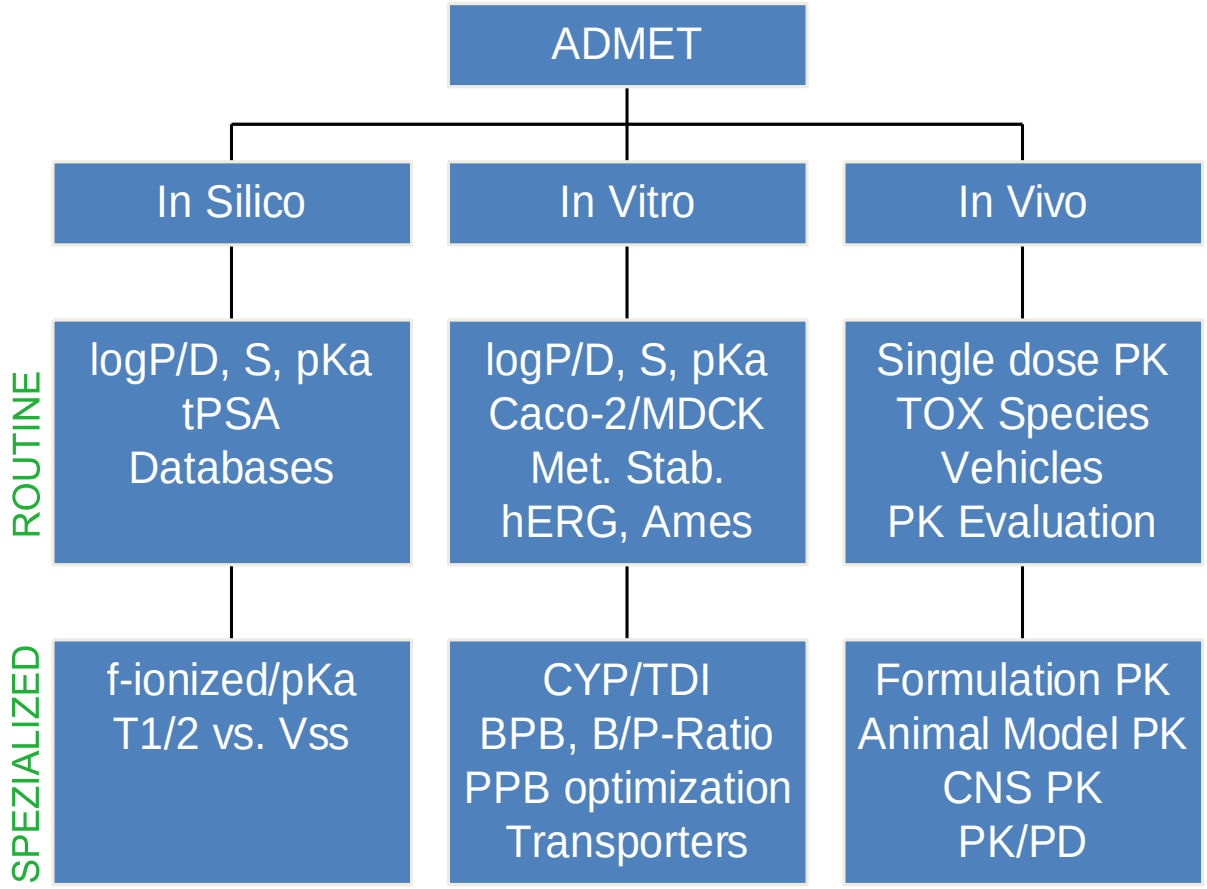
Expert Partner

Dr. Julie Balland

ADMET/DDI/PK Support



KEY CHALLENGES

- **Assay conditions**
  - ✓ Few are standardized
  - ✓ PK and formulation?
  - ✓ Dog or monkey?
  - ✓ BBB penetration?
- **“One Size Fits Nothing”**
  - ✓ Many CYP/TDI formats
  - ✓ Many PPB assays
  - ✓ GSH adduct thresholds?
- **New Assays**
  - ✓ Hepatocytes?
  - ✓ High content screening?
  - ✓ Transporters?

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PK, Human Dose and PK/PD Support

Absorption
(dose, species, first pass)

Distribution
(PPB, logP, pKa, V_{ss})

Metabolism
(Phase 1 to 3)

Excretion
(^{14}C, urine, feces)

KEY CHALLENGES

- **Prediction of human PK**
  - ✓ X-species allometry?
  - ✓ Rat for %F?
  - ✓ CNS penetration?
- **Prediction of human Dose**
  - ✓ Potential for once daily?
  - ✓ Multiple dose (C_{ss})?
  - ✓ PK/PD: Animal to Human?
- **Metabolism/Transporters**
  - ✓ Reactive intermediates?
  - ✓ Relevant phenotyping?
  - ✓ How many transporters?

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CMC-Regulatory Affairs

- Support for product development specifically in CMC & analytics
- Author IMPDs, INDS, DMFs, briefing documents, amendments, annual reports
- Resolve regulatory questions: Author responses to agency questions
- Regulatory due diligence for in & out-licensing: Gap analysis, key questions, risks

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Regulatory Strategy

Develop phase appropriate CMC strategies resulting in cost effective production & control activities

Develop and apply analytics to understand manufacturing performance & reduce end-product testing

Develop control strategy for genotoxic impurities & apply staged TTC

Set specifications based on process understanding and toxicology qualification limits

Develop specifications for key materials to ensure production of API meeting quality attributes

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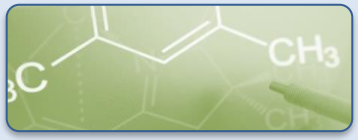
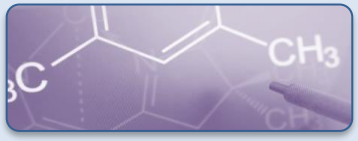
Quality Assurance and Compliance


Respond to compliance issues


GMP & GLP audits


Quality agreements, SOPs


Analytical methods and validation protocols and reports


Manufacturing records

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Supplier Selection & Outsourcing Management

Manage outsourced projects from start to finish

Contractor selection for chemical synthesis and analytical development

Tech transfer to plant scale & transfer of analytical methods

Ensure correctness and quality of documentation from CROs

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Non-Clinical international CROs
Non GLP/GLP audits
(more than once a month)

Pre-audit

Informing
Preparing
Organizing

On-site facility qualification

Study documentation
Animal facilities/Laboratories
Archives/CSV…

Post-audit

Reporting
Checking answers
Checking changes/improvement

Assessment

Rating quality
Rating responsiveness
Selection confirmation

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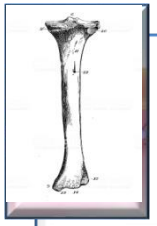
Pharmacology to Regulatory Tox Support and Monitoring

Various therapeutic areas, including, but not limited to:

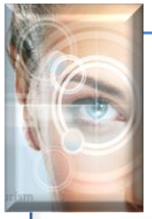

Cardiovascular

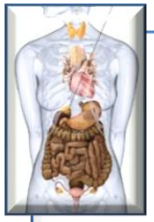

Bones


Dermatology


Inflammation


Oncology


CNS/**Ophthalmology**


Metabolic Diseases


Antibiotics, Antivirus etc…

Small (NCE's) as well as large molecules (biomolecules, mAB, biosimilars…) or cell therapy

Efficacy and safety studies can be followed by CapEval Pharma or outsourced

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Classical NCD Drug Safety Studies

Our Expertise

- Strategic expertise in preclinical efficacy & safety assessment
- Scientific expertise in tox design & interpretation of Non-Clinical Safety aspects of Drug Development
- Project and program management
- Regulatory knowledge & official document writing: IMPD, IND
- Scientific network
- Participation in international regulatory steering committees and to boards of international societies

Genotoxicity Studies
Safety Pharmacology Studies
Dvpt & Reproduction Toxicity
Acute to chronic toxicity
Carcinogenicity

>20 projects managed

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“A la carte” Services
NCD Strategy & Support

- Phase zero prerequisites
- Exploratory/mechanistic experiments and regulatory studies implementation
- Data analysis: interpretation and reporting
- Report writing, reviewing, and supervising
- Advise & support projects teams
- R&D programs coherent with regulatory constraints
- Flexible project management adapted to findings:
  - mechanistic studies target organ-oriented
- Monitoring studies
- Lead selection
- Target organ identification

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Ocular Safety Assessment of NCEs and/or NBE's Focus on ERG

PCL Safety Testing in a Global Regulatory Environment

Drug safety including ocular safety testing:

extraordinarily driven by global regulatory constraints

- OECD / ICH guidelines
- GLPs National legislation
- Animal welfare laws

Increasing pressure from Health Authorities:

especially the US-FDA as the World leader in setting the standards

More Sophisticated Methods in classical PCL needed

ERG can be one of those used for extrapolating to human.

Spectrum of toxicity

Detection of adverse ocular effects in selected laboratory animal species and description of the dose-effect relationship over a broad range of doses.

Extrapolation and Prediction of adverse effects

to other species, and particularly, Man.

Tasks of Experimental Ocular Toxicology and role of ocular electrophysiology

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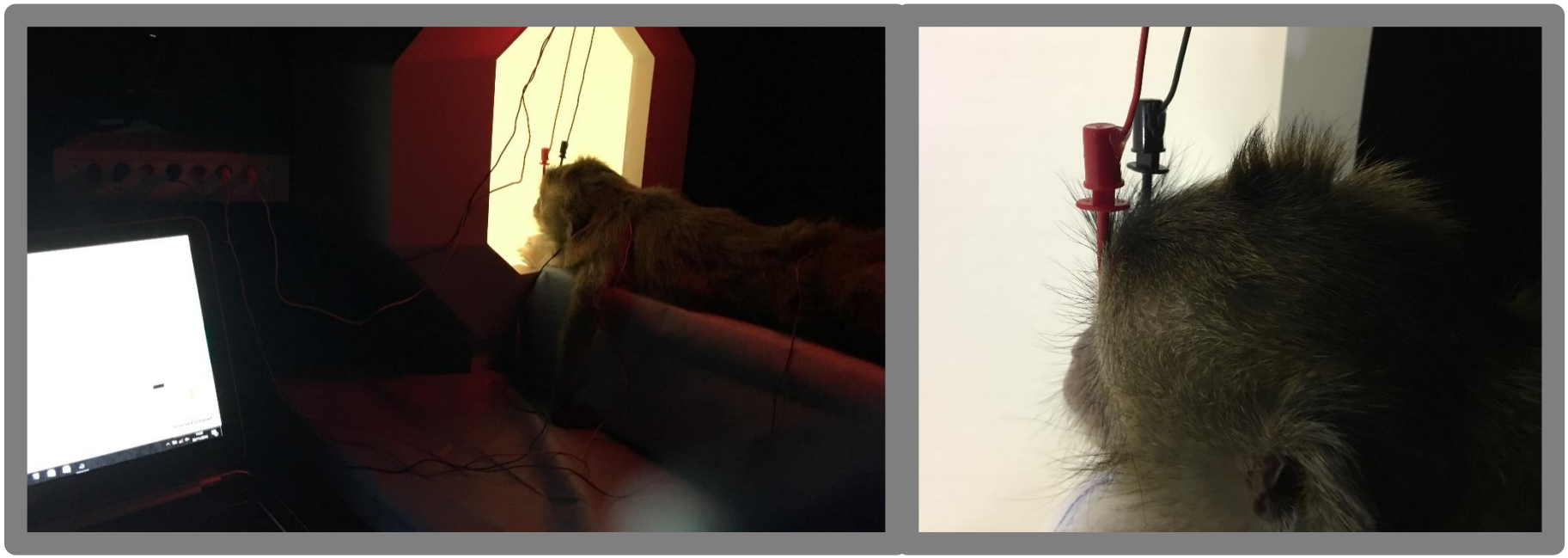
Expertise in Ophthalmology

ERG(Electroretinography) / FA(Fluoroangiography)

Efficient, unique platform for retinal toxicity assessment



- ✓ Contribution to laboratory animal ocular adverse effects interpretation
- ✓ Assessment of relevance for human species and related clinical risk
- ✓ Laboratory animal ocular examination

International Society of Ocular Toxicology

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Pre-Clinical CRO Partnerships

- Strategic assessment of CROs
- Early ADME package
- Selection, audits & monitoring
- Bridging client needs with CRO competencies

Strategic Assessment

Efficacy
ADMET
PK, PK/PD, TK
Safety
Adverse effects of various compounds

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Some of the selected CROs: Worldwide Non-Clinical Studies (non-exhaustive list)

Accelera	Advinus Eurofins	Aptuit	atlanbio (citoxlab/CRL)	Avogadro Eurofins
ERBC (CERB/RTC)	Charles River (CRL)	citoxlab/CRL	Covance (Envigo: HLS+Harlan)	Cynbiose
Histalim	KLC	MPI CRL	Pharmarom Quotient	Quintiles
Ricerca	RTC (ERBC)	SNBL	WIL (citoxlab/CRL)	Wuxi

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Due Diligence: Licensing and Partnership

Scientific assessment and contribution to negotiations

6 to 8 due diligence per year/per expert

Deep-fact finding in e-Room

Identify key safety issues and risk assessment

Evaluate regulatory dossier and perform gap analysis that may impact project worth

NCSD Consulting: start-ups to big pharma

From Discovery to the Market

Opening European & American Market to Asian Companies

- Decades of international experience; fluent in 3 languages
- Experience working in Biotech, Pharma and European, global & US based CROs
- FDA, EMA and National Agencies

Opening Asian Market to European & American Companies

- Asia based CROs
- Global CROs

Thank you

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