Accelerate and achieve an optimal IND for your project

～Smart-IND®～

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Confidential

Contents

Questions & requests from our customers for IND-enabling studies

IND

API manufacturing:
Development of manufacturing process, non-GMP batch synthesis

- CMO selection and schedule arrangement
- Synthesis of clinical batch and calculation of required amount

Batch evaluation
(analytical method, crystal form etc.,)

- Setting more attractive TPP (target product profile)
- Estimation of human effective doses

Non-GMP batch quality test and method validation

Additional PD study

Bioanalytical method development & validation

- Evaluation of non-small molecule, new modalities
- Proposal of minimum IND package for a particular indication
- Dosage setting with limited GLP batch amount
- Proposal of exposure coverage methods in tox studies
- Analysis of human-specific metabolites in *in vitro* metabolic study for small molecules

DMPK study

Tox study (Non-GLP/GLP)

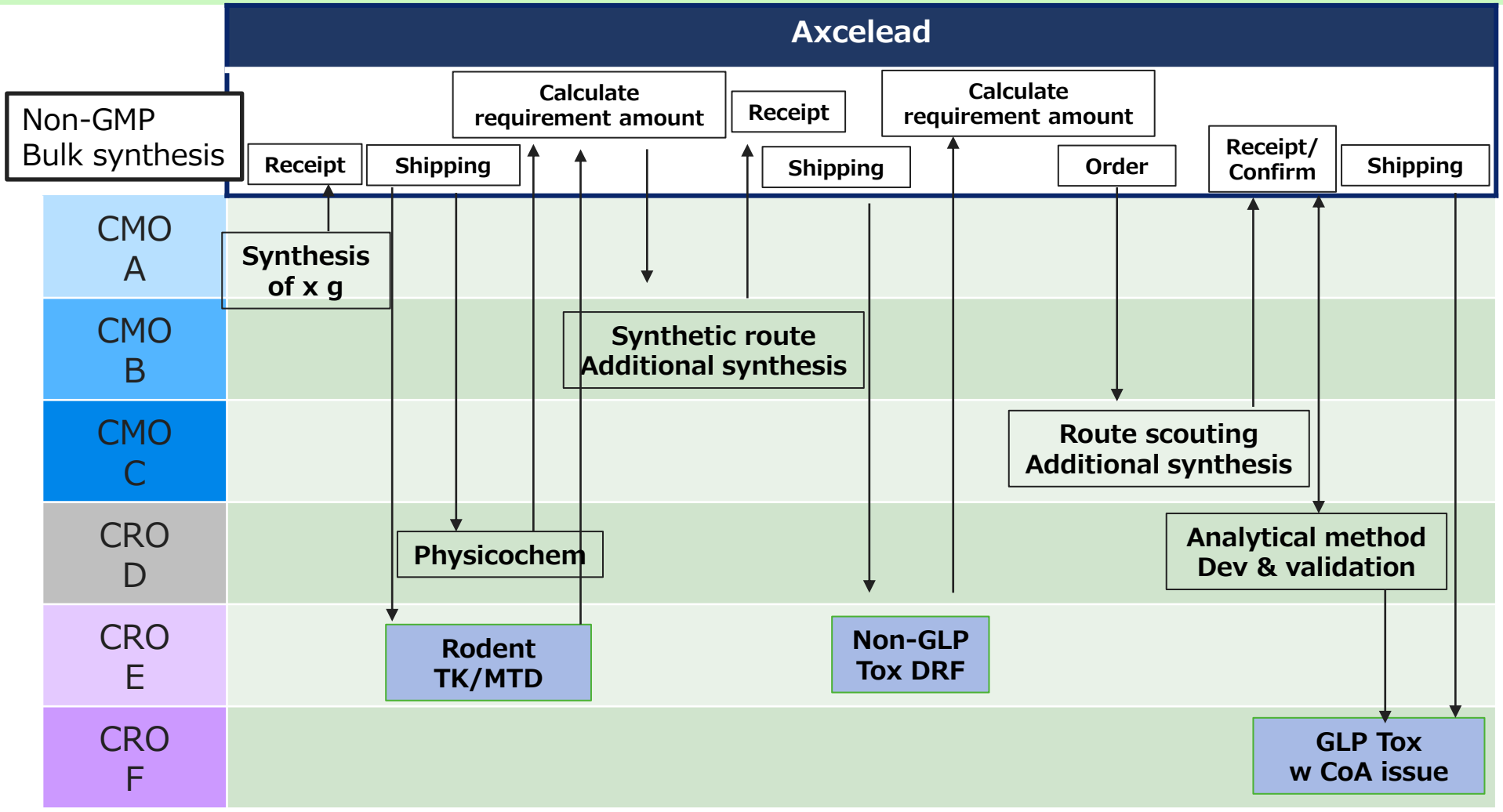
- Summarizing consultation items in regulatory agency meetings
- Supporting clinical trials and selection of clinical CRO

Pre-IND/IND meeting in US/JP

Proposal of pre-IND/IND strategy

The example includes GxP bulk preparation

Troublesome and time loss by outsourcing to multiple facilities (Example)



Safety

Integrated IND-enabling service

- **Optimal strategy:** Fit for your project/compound and a target product profile based on accumulated experience of >100 INDs and >20 NDAs

- **One-stop shop:** ADDP manages and executes all in-house and outsourced studies in collaboration with partner CROs

Smart-IND®

What is Smart-IND® ?

SMART

Timely
Proposal of a strategy
in line with the latest trends

Reduction
Reduced R&D costs

Acceleration
Shortened development time

Minimum
Application of the minimum necessary requirements for an IND

Specification
Proposal of a concrete plan, method, and goal

We propose the best way to success

Smart-IND®: One team for IND

One team in the one-stop shop

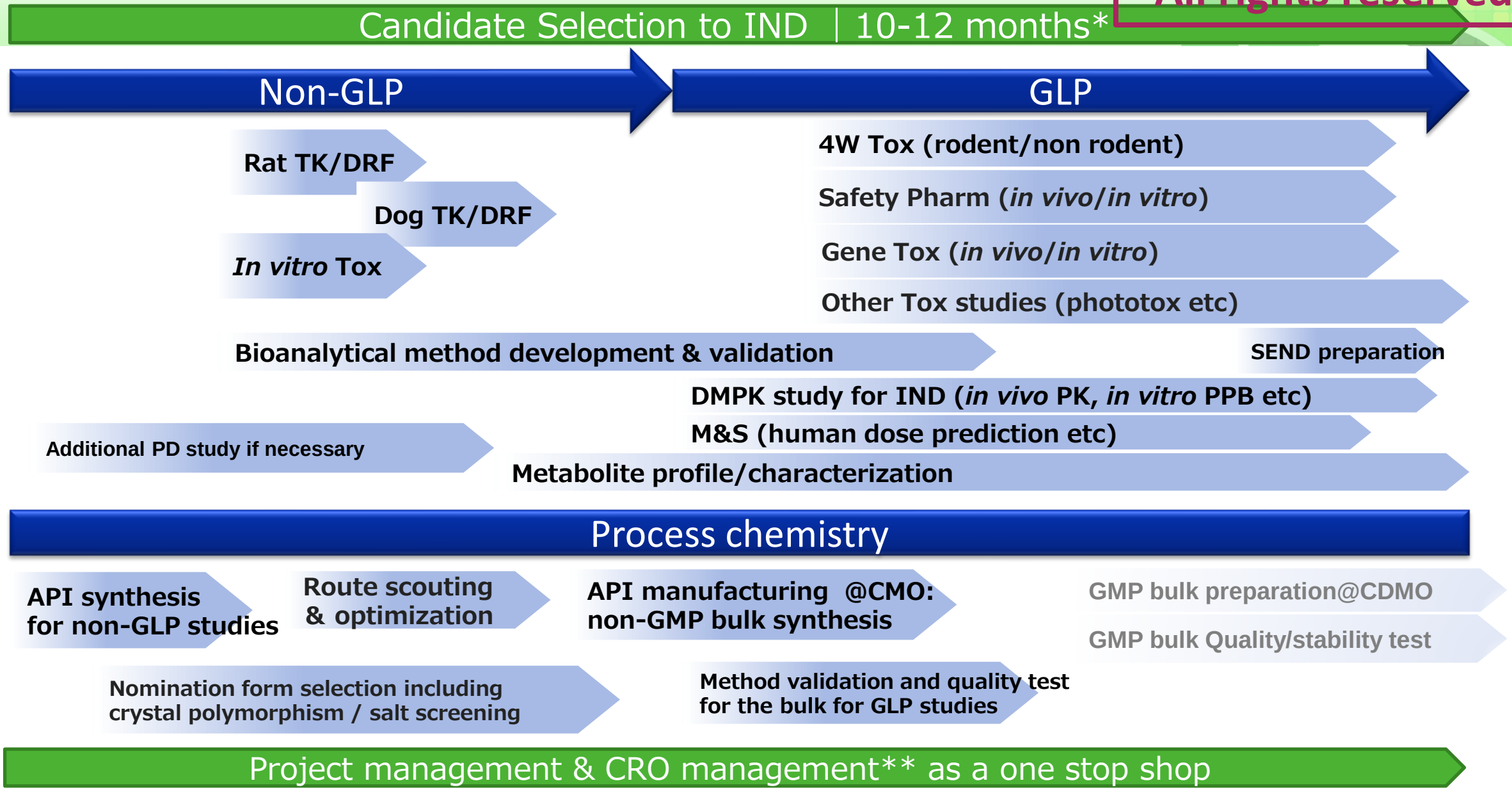
AXCELEAD Drug Discovery Partners ⟷ partnership

- CMO/ CDMO
- CRO

- Project management
- Chemistry Physicochem
  - Route scouting & optimization
  - Polymorph & salt screening
  - Non-GMP bulk preparation
- Safety
  - Non-GLP DRF
  - GLP studies
  - Both on- & off-target tox evaluation w/ KI/KO animals
- DMPK
  - DMPK studies according to guidelines
  - Human prediction, M&S
  - Metabolite characterization w/o a radiolabeled compound
- Pharmacology
  - Discussion of target product profile
  - PD studies to increase project value

A team consisting of well-experienced scientists of necessary functions lead a project swiftly

Achievement of IND by Smart-IND®



Note *: Timeline is depending on a candidate profile and several factors on a project.
**: Depending on the studies, there are cases where it is carried out at partner CROs.

IND-enabling studies package

□ Questions to customer from Axcelead

What is your goal? Your goal is IND, POC or NDA?

The expected timing of the studies should be considered.
It will be thought strategically about whether to conduct studies earlier to increase value or backload it to be more cost-effective.

Axcelead supports you on a case-by-case basis with an effective plan tailored to your goals.

IND-enabling studies package

□ Questions to customer from Axcelead

What is indication of the candidate?

Anti-cancer drugs, drugs to treat lifestyle-related diseases or rare diseases, vaccines?

Different guidelines should be applied. It may be able to move forward faster with a risk-benefit approach. On the other hand, a longer treatment period may be required in non-clinical studies.

Axcelead proposes the most suitable studies and design according to the indication, guideline and the TPP.

Evaluation of toxicity and dose setting

☐ Questions to customer from Axcelead

What is observed in non-GLP tox studies?

How about on-target toxicity?

Can the NOAEL be evaluated?
Initial dose in first-in-human trials should be setting from the No observed Adverse Effect Level (NOAEL).

Axcelead proposes dose selection and appropriate animal species selection to clarify NOAEL and on- and off-target toxicity.

New modalities

☐ **General questions**

What is the modality?

What if guidelines are not yet available?

Some modalities do not have established ICH or local guidelines. The study package will be proposed based on existing guidelines and the latest information.
Axcelead proposes optimal package and design for modalities according to the latest information from FDA, EMA and PMDA.

Added value by collaboration with Axcelead

◆Implementation of the best package plan according to various modalities

Incorporating safety pharm and/or *in vivo* MNT to repeat tox studies

Animal selection for repeat tox (KI/KO animals, appropriate single species, etc.)

Omitting *in vitro* studies

◆Smooth transition to clinical development

Modeling and simulation

PK/PD assays and analyses

Our contribution for IND and out-license

Chordia Therapeutics Inc.
26-1, Muraoka-Higashi 2-chome, Fujisawa, Kanagawa 251-0012
info@chordiatherapeutics.com

March 29, 2019 3:00 PM JST

Chordia Therapeutics Raises Approximately 27 m

- Chordia Therapeutics Inc., an oncology resear in Kanagawa, Japan, closed the first tranche c USD) Series B financing.

Chordia Therapeutics

December 15, 2020

Chordia Enters into Exclusive License Agreement with Ono on CTX-177, a MALT1 Inhibitor, and its Related Compounds

Chordia Therapeutics Inc. (Kanagawa, Japan; President and CEO, Hiroshi Miyake; "Chordia") today announced that it entered into a license agreement with Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; "ONO") for CTX-177, Chordia's MALT1 inhibitor and its related compounds.

Our contribution

- Full support for IND and the license-out
  - ✓ Evaluation study results and proposal of successful strategy
  - ✓ Accompanying PMDA pre-IND meeting
  - ✓ Support for the scientific explanation to the licensed-out company

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- ☐ **Approved for clinical trials and successfully funded**
- ☐ **Successful license out!!**

Summary

Axcelead manages the entire preclinical studies and processes by serving as an operational hub to significantly reduce the client's burden for IND.

Smart-IND®

- Achieve an optimal IND based on the project goal and TPP by researchers who are well-experienced in pharmaceutical industry
- One-stop access to the necessary functions/technologies of Axcelead and partner CROs and CMOs
- Implementation of the best package plan according to various modalities such as peptide, antibody, gene/cell therapy