Choosing the right CDMO for late-phase clinical trials

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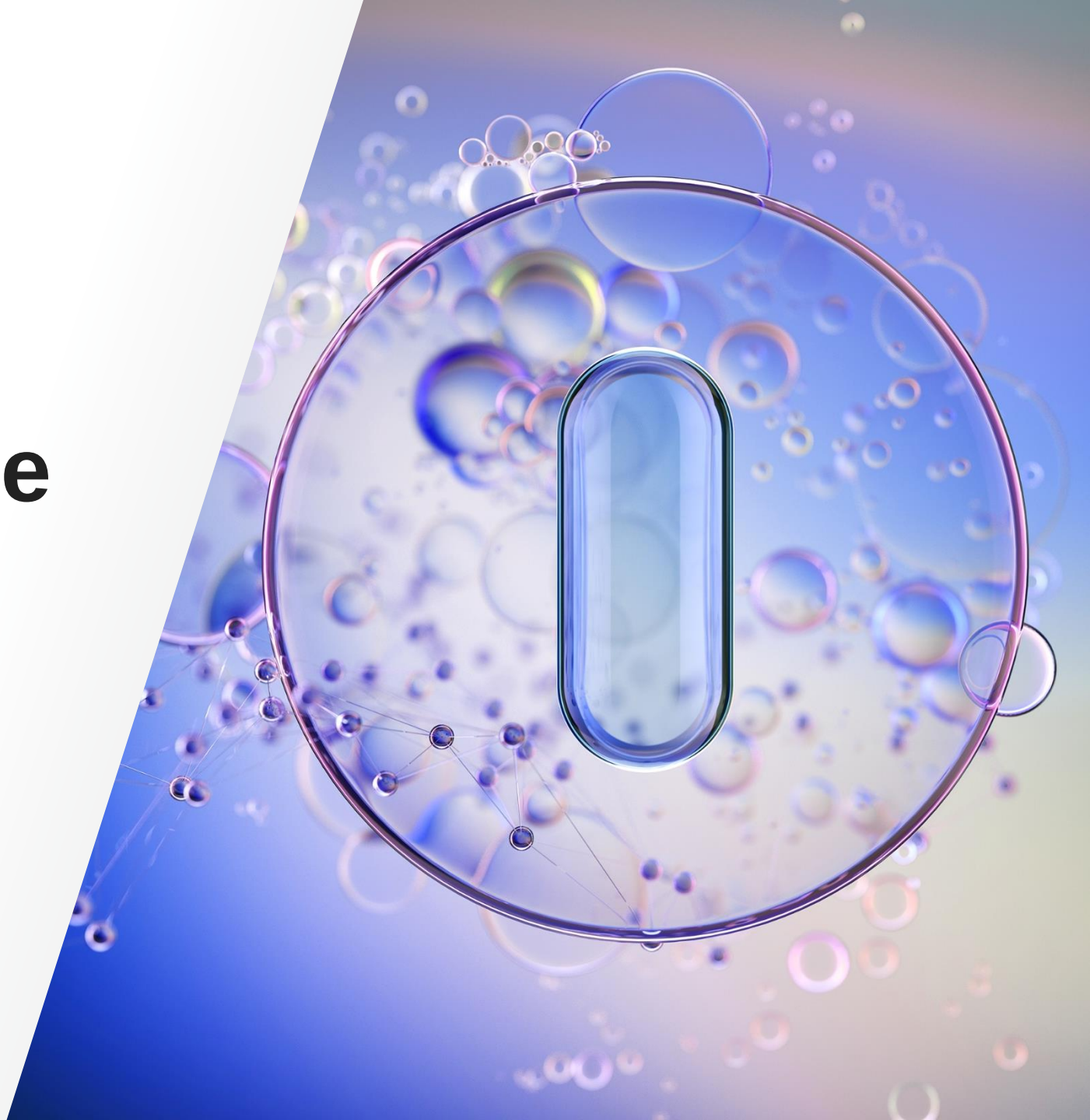

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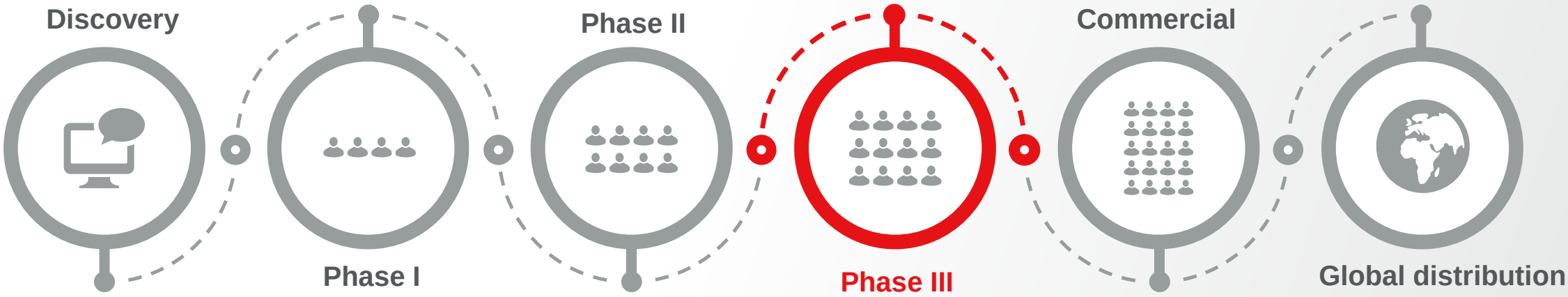
Product life cycle – Defining phase 3



Phase 3 statistics

Phase	Patient Enrollment	Length of Study	% of Drugs that move to next phase
1	20-100	Several Months	70
2	Several hundred	Several Months – 2 years	33
3	300-3000	1-4 years	25-30

Cost in Millions $

	Phase 1	Phase 2	Phase 3
Oncology	4.5	11.2	22.1
Pain/Anesthesia	1.2	17.0	52.9

The work completed by phase 3

At the initiation of Phase 3, an enormous amount of work has been done!

Work Completed:

- Formulation Development
- Process Development
- Animal studies
- Safety Studies
- Stability Studies
- Dose Escalation
- Analytical Method Development
- Phases I and II

Decisions Made:

- Presentation
- Dose
- Components
- Clinical Trial Study Design
- Commercial Supply Strategy

Work Ahead:

- Phase 3 Study
- Method Validation
- Risk assessment
- Identify CPPs
- Scale up
- Registration
- Process Validation
- Packaging Design
- Regulatory Submission

Phase 3 will build on the previous results and compare efficacy with similar products

Why move to a new CDMO at phase 2b/3

Most common reasons for transitioning to a new CMO at phase 3 include:

Scale
Current CMO has batch size limitations

Commercial Capability
Current CMO supports clinical only

Experience
Current CMO does not have experience with PV

Multiple Vendors
Desire to simplify for long term partnership

Presentation change
Current CMO supports vials only and PFS is desired

Flexibility
Options for dual sourcing, global presence

Regulatory Track Record
Relationship with agencies and successful launches

Expertise
Technical support to ensure smooth transfer

Price
Larger batch sizes decrease the per unit cost

End to End Service
Ability to perform multiple services under one roof

Important criteria to consider during CDMO evaluation

Regulatory Support and Track Record

Redundancy In Network

Technical Expertise

Process Validation Support

Global Footprint

Scale and Options

Relationship

Culture

Regulatory support and track record

Consider the site and company track record:

- How often is the site inspected?
- Does the site have any 483s? If so were they addressed?
- What regulatory bodies have visited the site?
  - Do those bodies align with intended markets?

Consider the level of regulatory support you need:

- How many other similar products has the site moved from late phase to commercial?
- Does the site have a local team dedicated to regulatory support?
- Can the site provide all the required information to support your filing?

Validation support and technical expertise

Project team

What does the core team look like that the site?

Does it include representatives from validation and process engineering/operations?

Technical Expertise

Has the team ever worked on a similar program?

What is the approach to technology transfer?

Has the CDMO demonstrated successful Tech transfers?

Processes

Are standard practices in use?

How does the partner de-risk new programs?

Efficiency

Is the CDMO implementing process improvements?

Can the team be flexible and creative to meet required timelines?

Collaboration

Does the CDMO encourage communication directly between functional groups?

Are persons in plant encouraged?

Questions worth asking the intended CDMO before you sign on the dotted line

Defining a technical match

Capacity, scale, timeline and cost are all important to consider; but a technical match is critical for success.

Things to consider include:

- Expertise with product type – small vs large molecule, lyo vs. liquid product
- Is the tech transfer process clear?
- Can the CMO either match or improve on the equipment and process design.
- Do the analytical services offered match the required product testing?

Scale and options

1

Does the CDMO have the ability to **scale up**? Have they presented **options** if the scale increases?

2

Does the CDMO have the **capacity** to meet the commercial demand?

3

Is the site **flexible** in terms of processing and making adjustments required for your specific product?

4

Does the CDMO have built in **redundancy** in the case that a second source is needed?

Relationship and culture

1

How does the project team work internally and externally?

2

How accessible and involved is the management team?

3

Does the site value the expertise of the client's technical counterparts?

4

Does the site see the customer as a critical partner?

Technology transfer: A case study

Background

Clinical batches were successfully completed at another in-network site at small scale.

Process knowledge:

Well defined parameters, however, difficult to manage at scaled-up batch size.

Project risks:

- Critical hold times put batches at risk
- Additional validation required for PV

Technical challenges:

Sensitivities:	Hold times:	Batch processing:
• Oxygen • Stainless Steel • Heat • Hygroscopic API	• 6 hours from API addition to completion of pH adjustment • 20 hours from API addition to Lyo start w/ IPC • Filling line hold time of 30 hours from SIP to end of fill	• Nitrogen Sparging In disposables • DO measurements • Localized high pH • Temperature Monitoring/Active Cooling

Case study results

Outcome

Three registration batches were successfully completed

Process improvements were made along the way, with a robust process designed and executed prior to PV batch production.

Commercial launch from an additional network site was completed in the following year.

Keys to successful registration/validation:

Constant updates and good communication between operations and QC labs

Customer on site during production allowed for expedited decision making

Very specific batch record instructions and operator training for highly technical batch

Summary and key takeaways

Leverage product and process knowledge

- Adopt scientific and risk-based approach
- Identify CPPs and CQAs
- Utilize early development data

Align with expectations and regulatory requirements

- Complete all required stage gates before moving on to PPQ
- Risk-based process evaluation, data driven improvements

Plan and execute

- Define requirements at each project phase
- Implement proper documentation throughout development and clinical phase work
- Finalize production strategy

Thank you