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PQRI Workshop:
Managing Excipient and API Impact on Continuous Manufacturing
May 17 – 18, 2022

A CDMO Perspective on Continuous Solid Dose Manufacturing Process Development

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Outline

- Continuous Solid Dose Manufacturing at TFS
  - Line 1 existing capabilities
  - Line 2 coming capabilities
  - Future capabilities
- Development Approach
  - When to explore/transition to CM
  - Benchtop → full line development work
- Material Handling Considerations for OSD CM

Continuous manufacturing at Thermo Fisher

CM Program Highlights

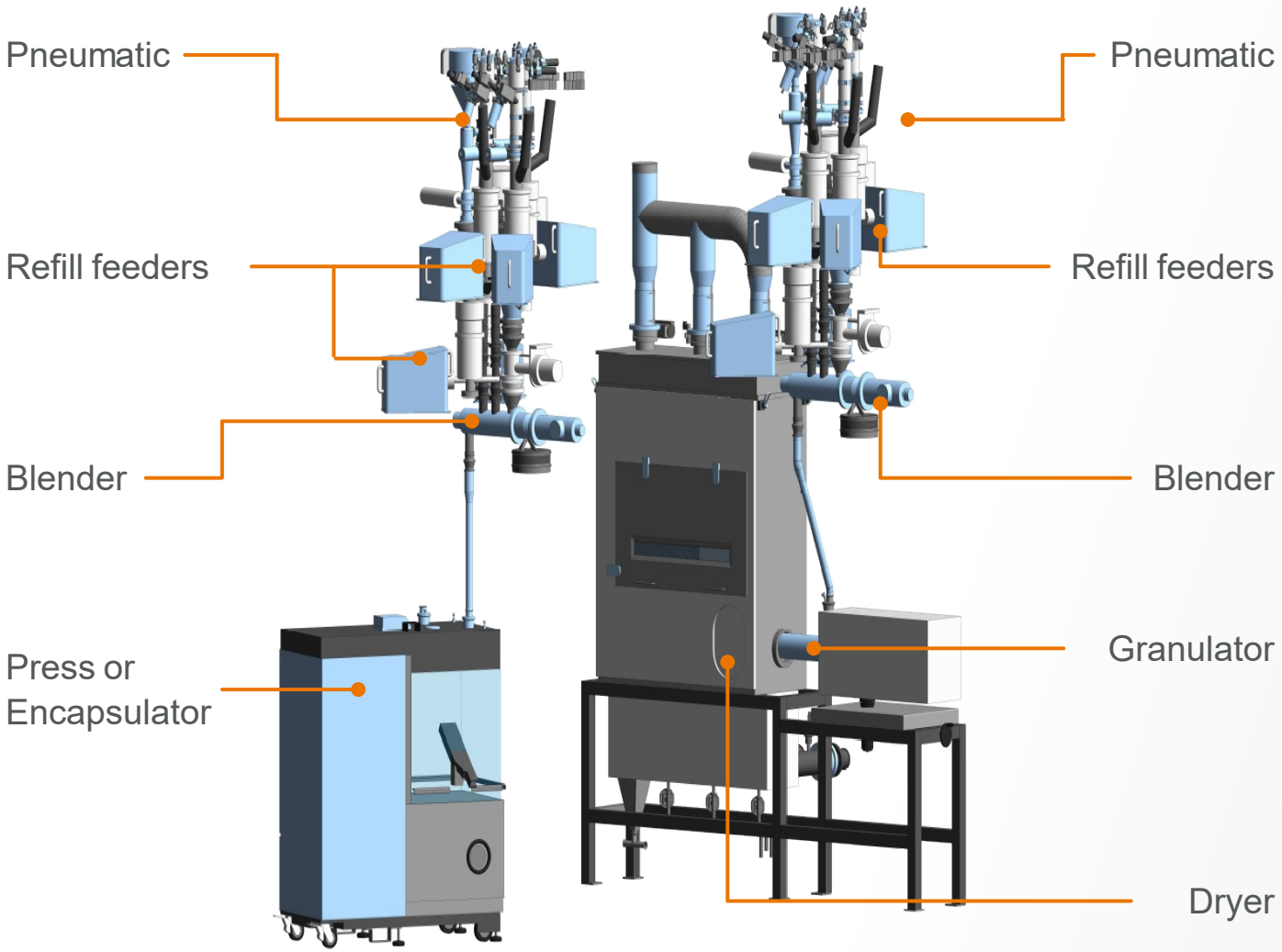
- TFS has made a commitment to Solid Dose Continuous Manufacturing – 1st line fully validated and producing clinical material, 2nd line buildout in progress (customer ready Q1 2024)
- Customizable full service offering available from early stage feasibly, through process development, Phase 2/3 clinical supply (packaging and distribution available), regulatory support, commercial manufacturing and packaging
- Experienced development team (5 PhDs) with multiple customer programs completed or in progress including low dose (tablet and capsule) and SDDs
- Technology roadmap includes continuous coating and real-time release

Continuous manufacturing at Thermo Fisher

Current state

- Single line, innovative modular line in Greenville, NC
- Validated for direct compression and encapsulation, roller compaction and wet granulation available
- Contained up to 3a
- Multiple projects initiated (as of Jan 2022)
  - Multiple feasibility studies with clients engaged in CM
  - Line fully validated Q4 2021
  - 2 Phase 3 development/clinical programs in process
- Multiple interactions with FDA
  - Initial meeting on March 10th of 2017
  - Joint Client visit for product specific talks May 30th 2018
  - FDA ETT Site Visit January 14th, 15th, 2019

TFS Line 1 Capabilities



Technical specifications

Default configuration:

- ≤6 direct blending components
- ≤11 components for granulation pathway

Capacity is formulation dependent:

- Minor component feed rate limits overall capacity
- Maximum capacity limited by tablet press/ encapsulator capacity
- Capacity for most products: 15 to 50 kg/hr

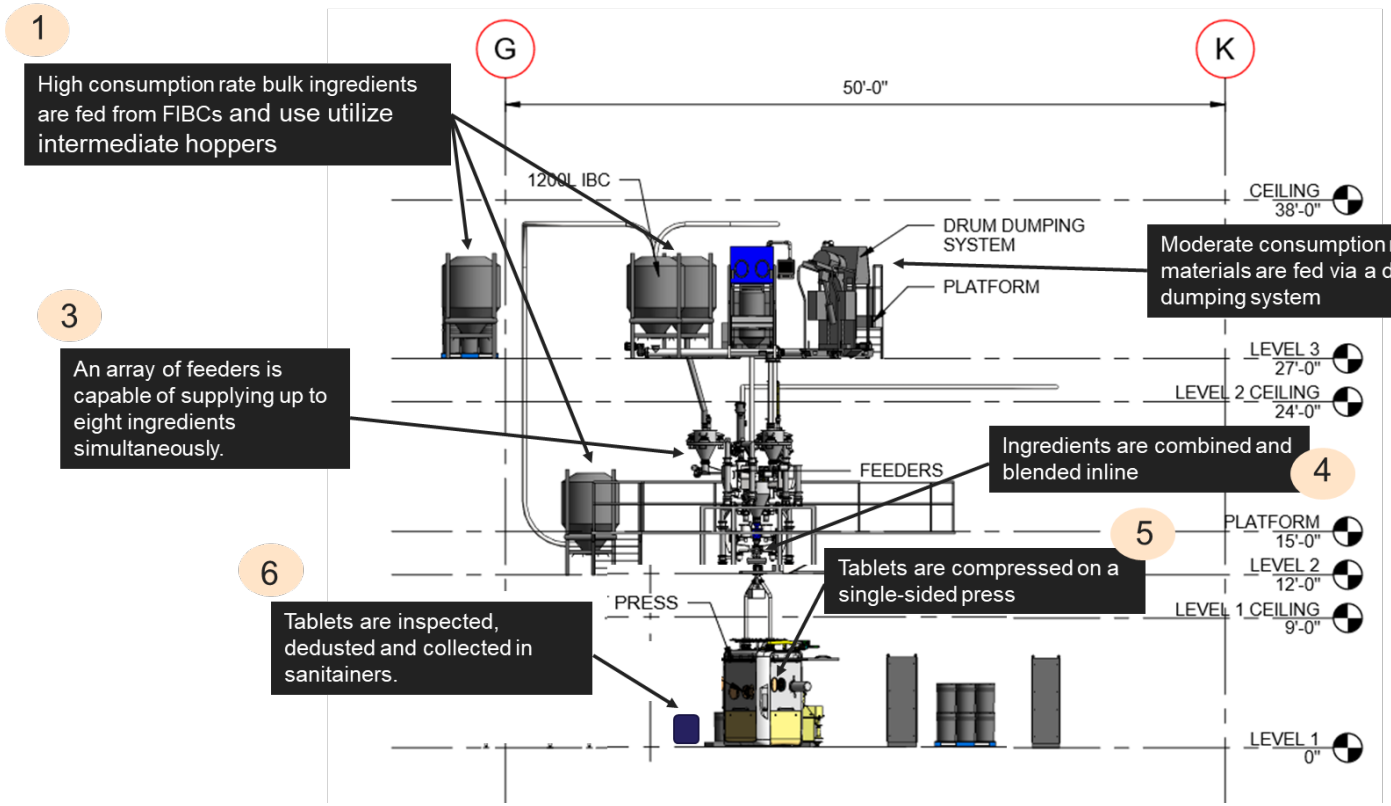
3a containment (1-10µg/m^3)

Continuous coating (planned with line 2)

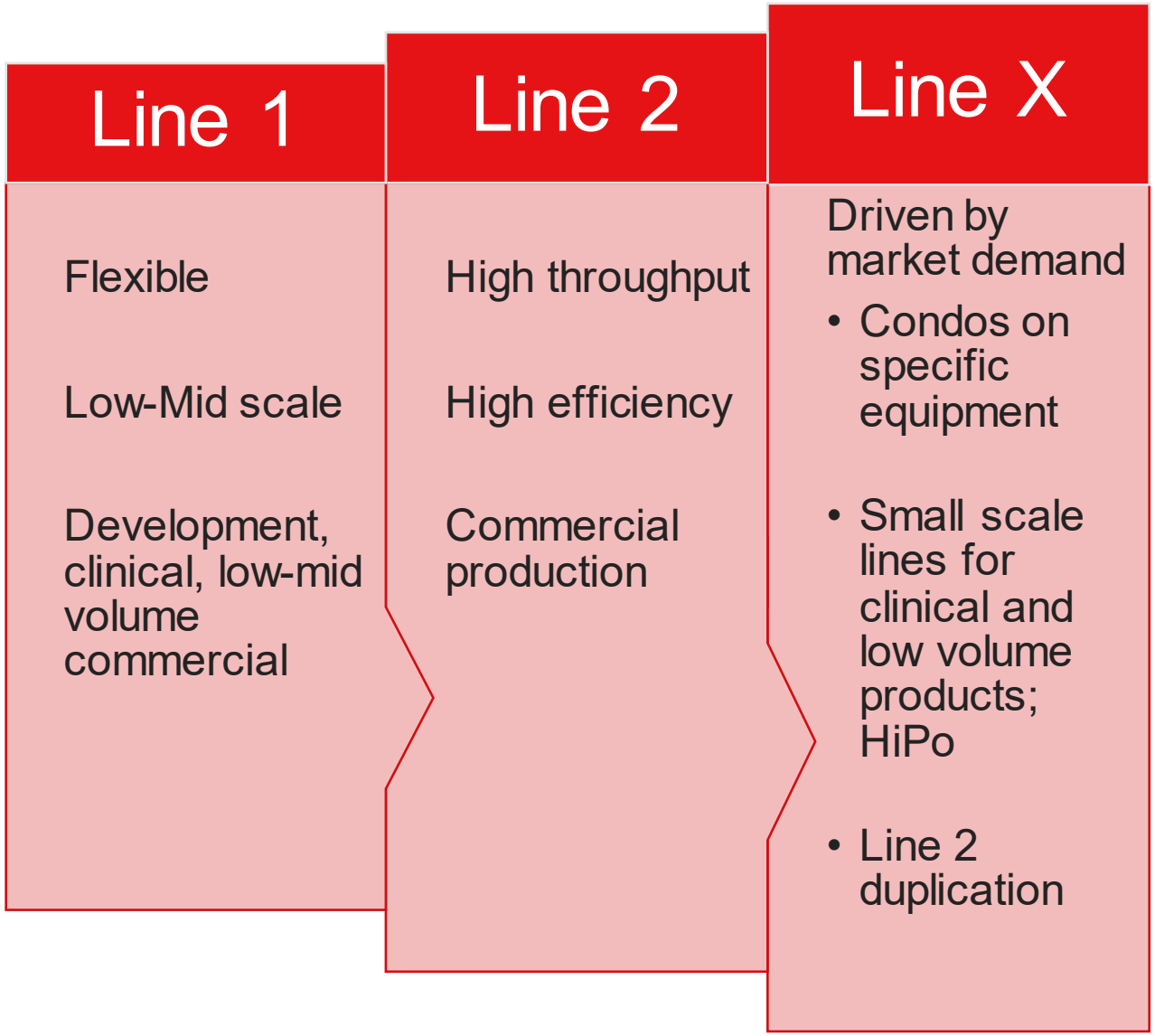
Continuous manufacturing at Thermo Fisher

Line 2

- Continued Thermo Fisher investment in lines, technology and the people. **Line 2** scheduled to be customer ready Q1 of 2024.
- Direct compression
- Contained, 3A
- High throughput capable
- Highly similar to TFS line 1 to enhance TT



Continuous manufacturing at Thermo Fisher



When to Explore or Transition to CM

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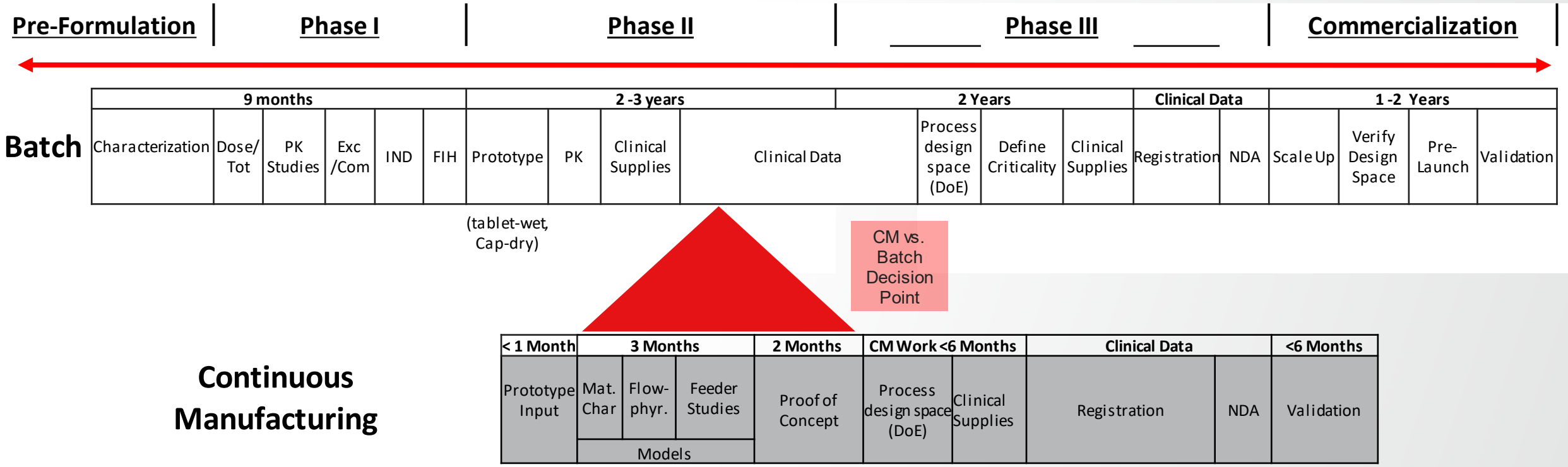

Early stage CM development available in both Greenville, North Carolina and Bend, Oregon

Process Development Approach

- Offline Development
  - Measures flow behavior such as bulk/tap density and FT4 shear cell analysis
  - Bench top feeder characterization
  - Compaction simulation

- Scale Development
  - Proof of concept (PoC)
  - Design of Experiment (DoE) runs
  - Clinical Manufacturing
  - Stability
  - Registration
  - Process Model Validation

Material Handling

CM lines need to be able to run for extended periods of time which requires a strategy for refill of the loss-in-weight feeders:

- Line 1 - Pneumatic conveying
  - Not all materials transfer easily
  - FF, FT4 used as a guide
- Line 2 – Gravity conveying
  - Enables higher throughput

Closing Remarks

- Thermo Fisher Scientific continues to expand capabilities for OSD continuous manufacturing
  - Line 1 serving customers, Line 2 customer ready 2024, Line 3 being planned
  - Open to further collaboration and co-investment with our clients

- Development programs are flexible and can be customized to the customer; we seek to work closely on the science and regulatory aspects of your product

- Contained development and manufacturing is available for HiPo compounds (1-10µg/m^3)

- Material properties are an important consideration for both the active and excipients throughout development and into commercial production

Thank you