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CANADIAN CDMO IN A WORLD DOMAIN OF PHARMACEUTICAL DEVLOPMENT

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Recent Trends in Pharma Outsourcing

- Overall increase of outsourcing to CDMO across the industry
- Big Pharma shift their outsourcing from Asia back to NA and Europe
- Focus on QbD and DoE driven development
- One-site vs One-stop shop model of service
- Fast Track product development programs

Sources: C&EN, May 21, 2018
Contract Pharma, January11, 2019

Why CDMO?

- Economical incentives
- Operational flexibility and responsiveness
- Increasing segment of virtual pharma
- Vast expertise in variety of pharmaceutical products
- Adoption of new technologies for development and manufacture

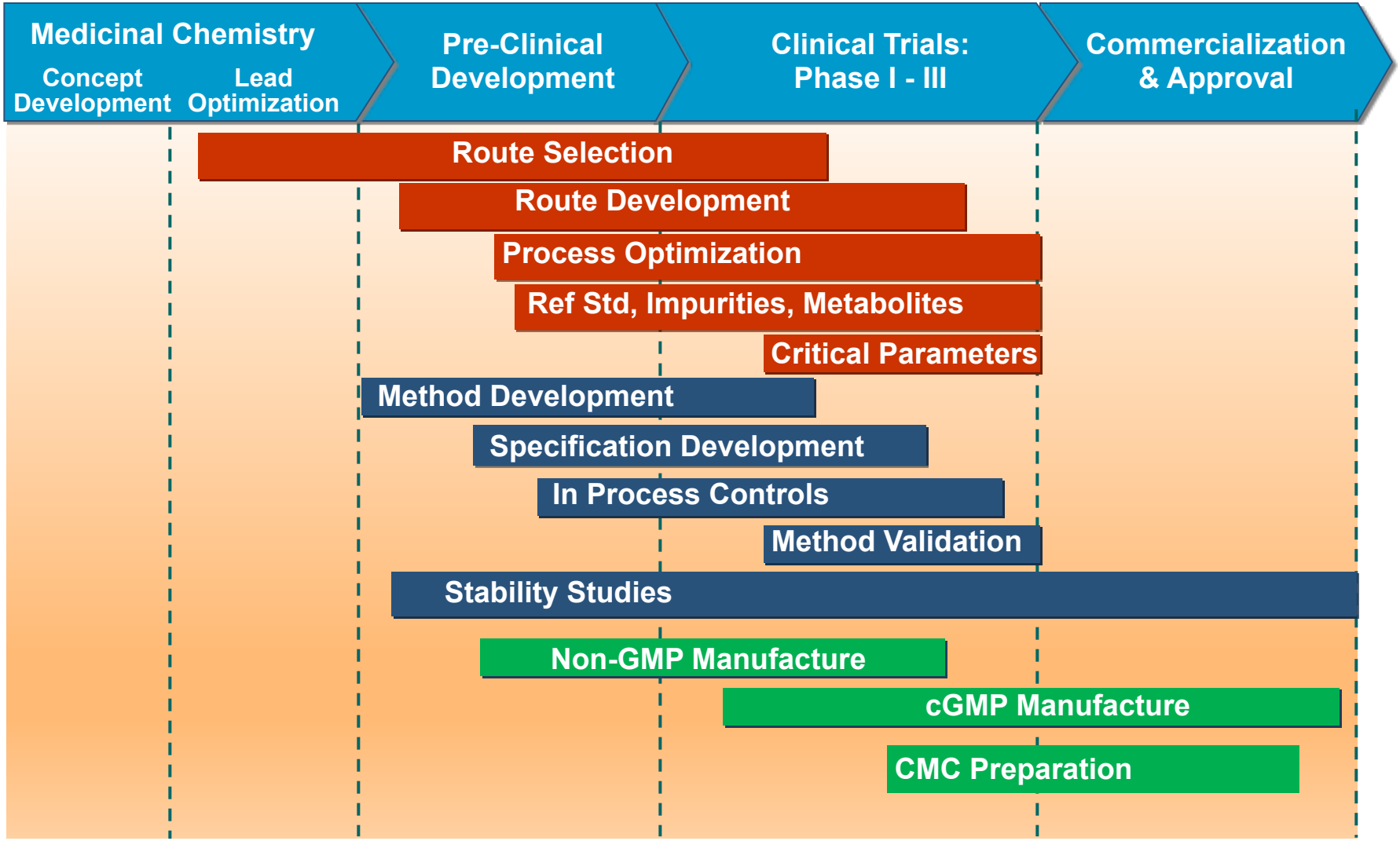
Eurofins Alphora

Our mission:

Innovation-driven contract development and manufacturing organization (CDMO) focused on developing technologies for manufacture of pharmaceutical substances and drug products

- **History**
  - ➢ Established in 2003 as private enterprise
  - ➢ Acquired by Eurofins in June 2017
- **Team**
  - ➢ Total of approx. 170 people
  - ➢ 30 Ph.D. chemists
  - ➢ 115 scientists, engineers and support staff
- **Experience**
  - ➢ Developed hundreds of unique processes for making Active Pharmaceutical Ingredients for pre-clinical, clinical and commercial

Right Development at Right Time



Process Chemistry

Process R&D Expertise

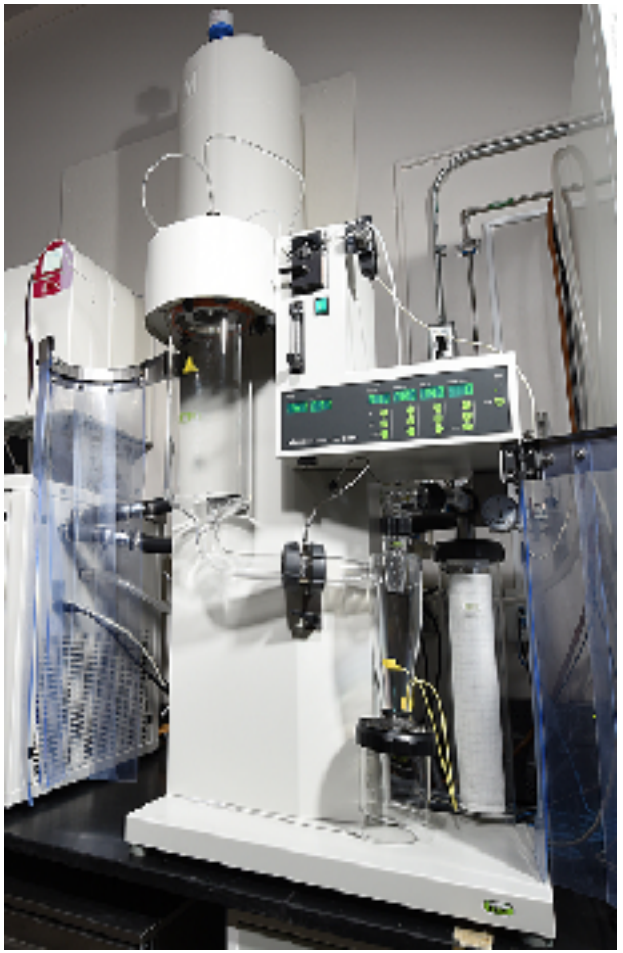
- ✓ Route Scouting
- ✓ Process Scale-up Development
- ✓ Design of Experiments (DoE)
- ✓ Critical Process Parameter Study
- ✓ Validation Preparation
- ✓ Impurity Marker Synthesis
- ✓ Fate and Purge Studies
- ✓ Process Safety Evaluation
- ✓ Structure Elucidation
- ✓ Solid Forms Study

Process R&D Technologies and Tools

- **High Throughput Screening**
  - Unchained Junior™ 96 wells HTS
- **Parallel reactor systems**
  - HEL Polyblock™ 8 wells system
  - Mettler EasyMax 420 and EasyMax102

Process R&D Technologies and Tools

- Preparative Chromatography (mg to kg)
- 0.5 – 4 L Parr™ Hydrogenetors
- Wipe-Film Distillation
- Spray and Freeze Drying



Process R&D Technologies and Tools

Flow Chemistry

- Vapourtec™ plug-flow reactor
- Labtrix™ for R&D Scale microreactor
- Kilotrix™ for cGMP Kilolab Scale

Process R&D Technologies and Tools

❑ HPAPI Isolators

- Compounds to Safebridge Class 4, OEL's <30 ng/m³
- Isolator containment, Bag-in-bag-out technology
- Air Monitoring / surrogate testing

Process Safety Assessment Tools

- **Calorimetry**
  - HEL Thermal Screening Unit
  - Phi-Tec™ Adiabatic calorimeter
  - Simular™ reaction Calorimeter

Process R&D scale-up capabilities

Kilo Labs

- 20-30-50 L Glassware
- 30 L Buchi reactors
- -80 to 200°C
- 4-20 L Hydrogenators
- 5-kg cartridge Biotage LC
- 2'-3' Prep-HPLC

Solid State Analytical

Solid Form Characterization:

- Polymorphism and crystallinity study
- Particle size distribution
- Thermogravimetric analysis
- Dynamic Vapour Sorption
- Light and Electron microscopy

Bruker D8 DISCO

Solid State Development

❑API Solid Form Development:

- Polymorph screening and development
- Pharmaceutical salt screening and development
- Solvates and co-crystals screening
- Particle size engineering
- Crystallization scale-up development

Unchained Labs Junior™ HTS robot

Analytical Development

GMP Analytical Services

- Method qualification and validation
  - ➢ Phase appropriate
  - ➢ Forced Degradation Studies
  - ➢ Photostability Studies
  - ➢ QbD Method Development - FUSION software
- Identification, Characterization, & Qualifications
  - ➢ Starting materials, intermediates, impurities & API's
- In-Process Controls
- Fate of Impurities Study
- Reference Standard Preparation and Qualification
- Development of methods for pGTI's (ppm & ppb levels)
  - ➢ GCMS
  - ➢ LCMS
- Non-Chromophore API's and intermediates
  - ➢ Evaporative Light Scattering (ELS)
  - ➢ Mass Spec
  - ➢ Flame ionisation detector (FID)
  - ➢ Electron capture detector (ECD)
  - ➢ Charged aerosol detection (CAD) (2018)
- Method Transfers

GMP Stability

- ICH Stability Studies – all Climatic Zones, (I – IVa)
- Photo Stability (ICH Q1B)
- Accelerated Stability
- Forced Degradation Studies
- Trending Studies and Reporting
- Vaisala Central Monitoring System
- Our stability programs are strictly controlled using 21CFR, part 11

Kilo Lab & Manufacturing Plants

Kilo Labs - GMP

2 Kilo Labs (up to Cat 3b)

1 Kilo Lab (Cat 4):

- 2 X 50L Glassware
- 2 X 60L Glassware
- -80 to 200°C
- 20L Hydrogenations
- Enclosed Filtration & Drying Systems
- Biotage
- Prep-HPLC

Manufacturing Plant - GMP

2 Manufacturing Suites (up to Cat 3b):

- 3 X 200L Reactors
- 3 X 500L Reactors
- -80˚C to 200˚C
- Hydrogenations
- Enclosed Filtration & Drying Systems
- Biotage
- Prep-HPLC
- Vaisala Central Monitoring System

API Commercialization Support

- CMC Gap Analysis and Risk Assessment
- Impurities Markers Synthesis
- Fate and Purge Studies
- Full Structure Characterization and Elucidation
- Process Optimization
- Critical Process Parameters Assessment
- Design of Experiments; QbD
- Supply Chain Management
- Preparation for, and execution of process validation
- Continuing CMC support during and after market launch

Pre-formulation and Formulation Development

Bridging the gap

SSRD & Pre-Form: Synergy & Overview

API Physical Property Engineering

API Development & Manufacturing

Drug Product Dev. & Clinical MFG

Solid State Chemistry
Physicochemical Characterization

Solid State Screening
Salt, Solvate & Polymorph Screening/Optimization

Pre-Formulation
Solubility/Absorption/
/Excipient Compatibility/Stability

SSRD Capabilities

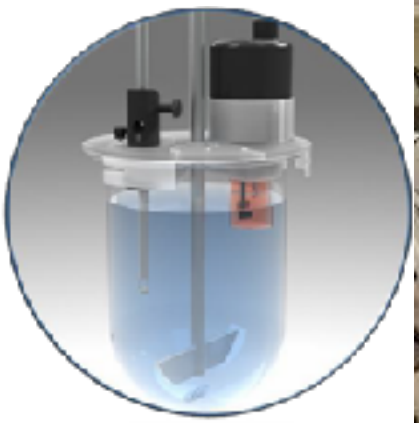
API Solid Form R&D

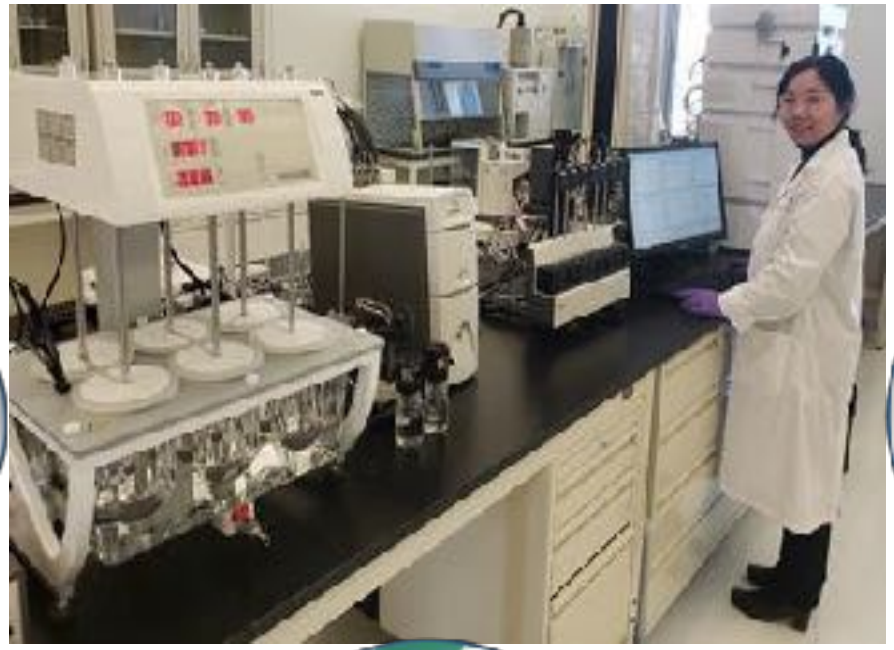
- High-throughput Screening for Discovery
  - Polymorph
  - Salt
  - Solvate
  - Co-crystal
- Solid State Characterization
  - PXRD
  - PSD
  - SEM
  - DVS
  - FT-IR
- Crystallization Process Development
  - Solubility
  - Metastable Zone
  - FBRM

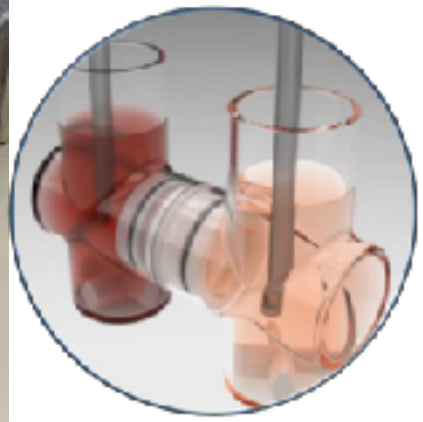
High-Throughput Screening (HTS)

- High-throughput allows quick execution of hundreds of tests using minimum amounts of chemicals
- Screening for salts and co-crystals
- Crystallization and polymorph screening
- Robotic equipment capable of liquid transfers, hot filtration, temperature cycling, stirring and grinding

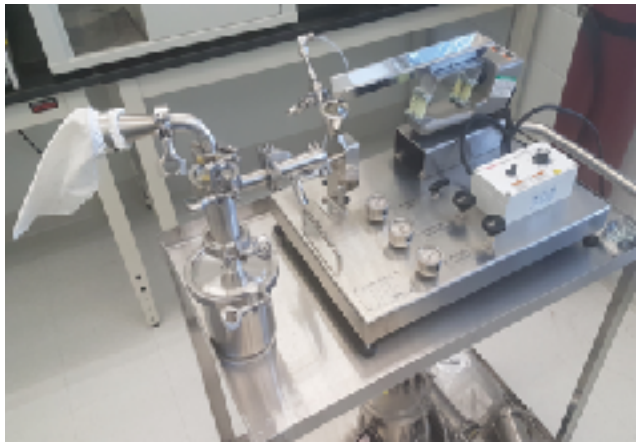
Candidate Ranking
PION: Solubility & Permeability







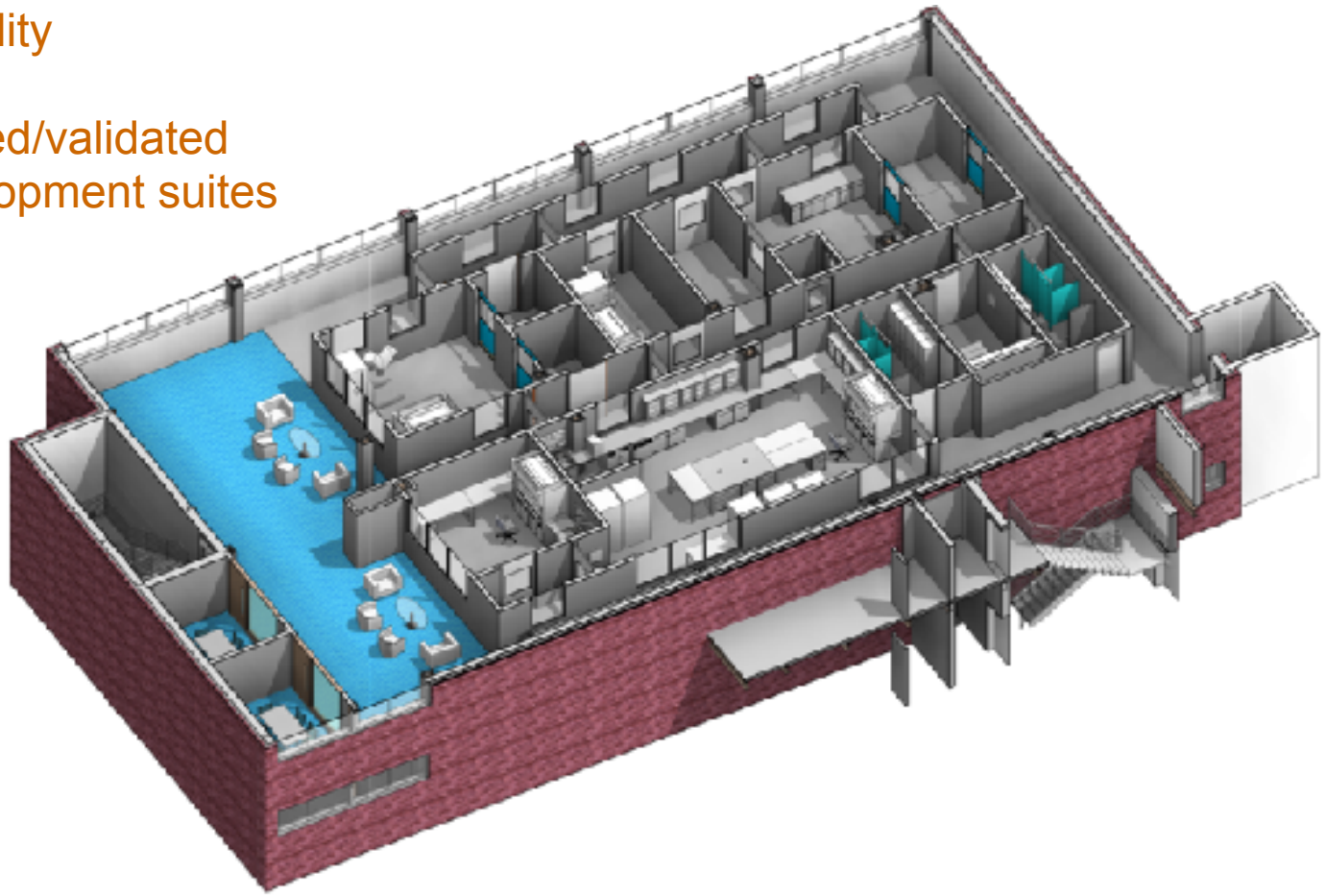
Drug Product Operations
- Formulation Development



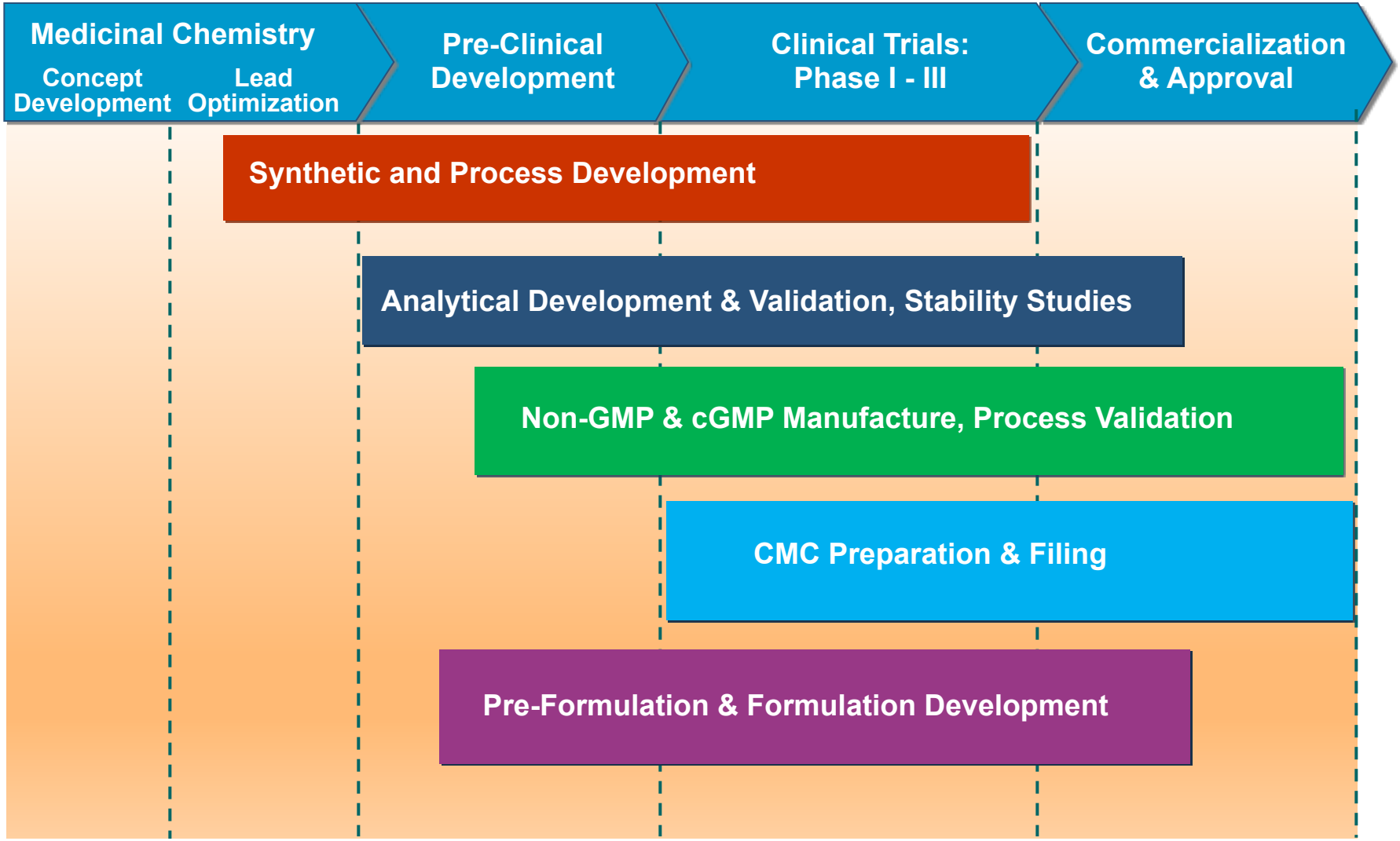
Drug Product Facility (2020)

Key Features

- High potent capability
- Humidity control
- ISO Class 8 certified/validated
- Independent development suites



Fully Integrated Service one-site CDMO




gratitude
strength
leadership
grateful
guidance
mentors
think
effort
path
thank you
strategy
real
success
business
learn
partnership
believe
big
strive
friends
time
grow
enrich
attitude
team
dream
potential
develop
choices