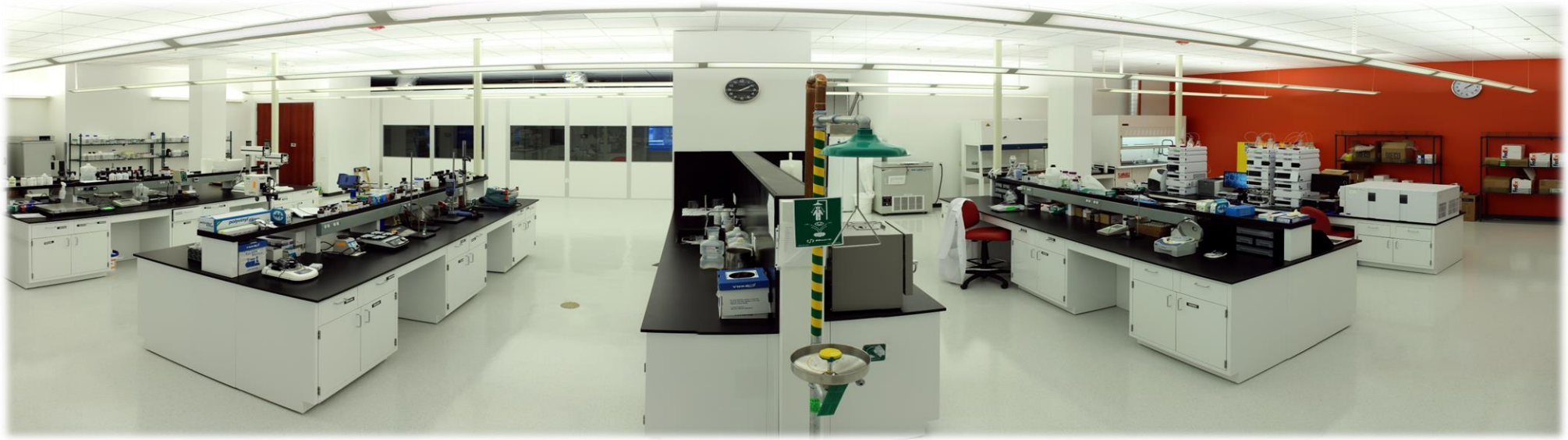
DOW DEVELOPMENT LABORATORIES, LLC

About Dow Development Labs

DOW DEVELOPMENT LABORATORIES, LLC

- **Development, testing and manufacture of semi-solid and liquid drug products**
- **FDA registered & GMP compliant facility located in Northern California (~23,000 sf)**
- **Subsidiary of Symbio, a global dermatology-focused clinical CRO founded 2002**
- **Clients range from start-ups and early stage companies through mid-sized and large pharmaceutical companies**

R&D Formulation Development Laboratory



Recent Client Success Story: Zoryve® Cream

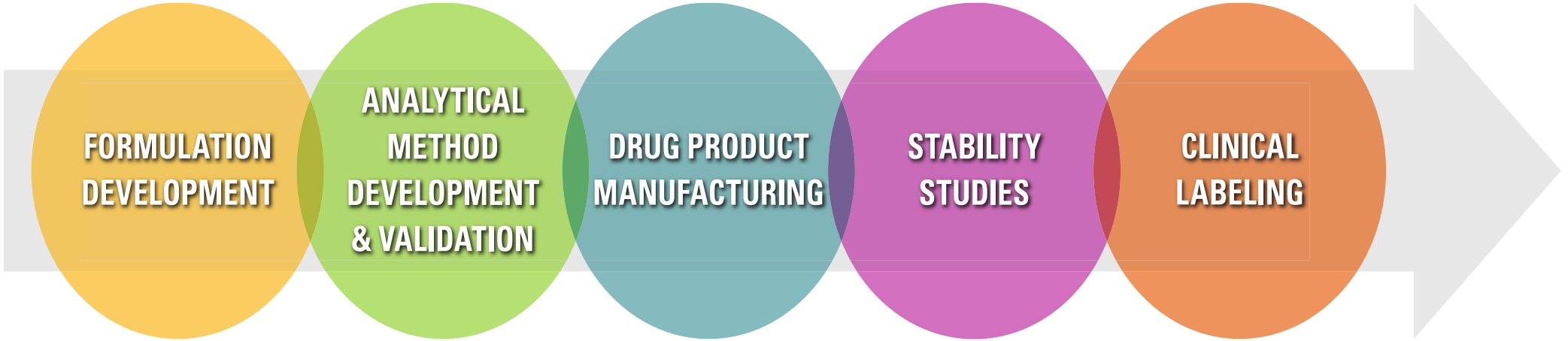
Successful Topical Product Development Provided by DDL:

Dow Development Labs provided support for the development of Zoryve® (roflumilast) cream 0.3% for plaque psoriasis from inception through to FDA approval in 2022, including formulation optimization, analytical methods development and validation, manufacturing of drug product batches for GLP non-clinical studies, and manufacture, fill, release and stability testing of GMP clinical batches.

DDL Services Overview

DOW DEVELOPMENT LABORATORIES, LLC

- Full spectrum of services from pre-formulation studies through packaging, labeling and distribution of clinical supplies



Product Development

DOW DEVELOPMENT LABORATORIES, LLC

- **Liquid and semi-solid drug products (gels, creams, ointments, solutions, sprays, suspensions)**
- **Experienced with new chemical entities (NCEs), approved drugs, combination products, small molecules, oligos, peptides and proteins**
- **Rx, OTC and generic products**

Typical Therapeutic Indications

Acne	Atopic Dermatitis	Onycho-mycosis	Psoriasis	Wound Healing	Rosacea	Anti-infectives	Ophthalmics	Women's Health

Initial Steps of Formulation Development

DOW DEVELOPMENT LABORATORIES, LLC

- **Based on the physio-chemical properties of the molecule, development of Target Product Profile:**

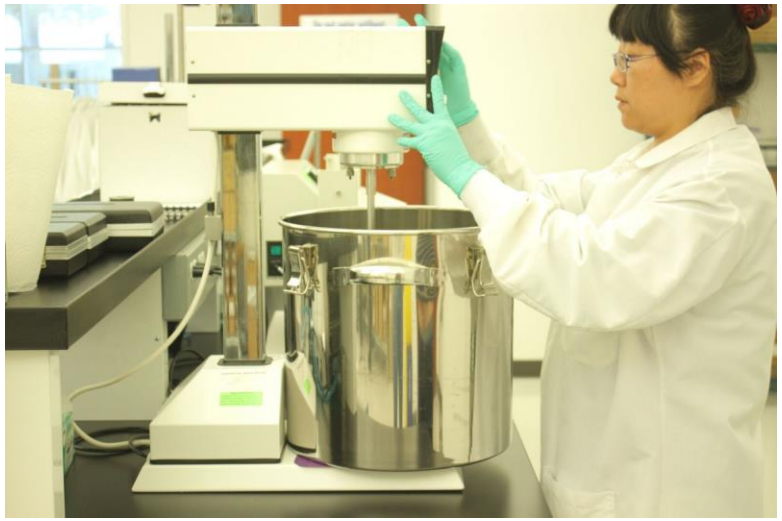
  - **Cosmetically elegant/aesthetically pleasing**
  - **Excipients and dosage form compatible with the therapeutic indication**
  - **Appropriate tissue penetration (or residence time and tonicity, if ophthalmic)**
  - **Chemical stability of the API in the product**
  - **Physical stability of the drug product for desired shelf life**
  - **Excipients and their levels selected from FDA's IID so as to be compliant from a regulatory perspective**
  - **Appropriately preserved**
  - **Scaleable process leading to robust product**

Formulation Development

Following QbD principles and with the patient in mind

- **Pre-formulation studies** - single and binary solvent solubility studies; pH profile; excipient compatibility

- **Formulation development** – prototype design including excipients such as anti-oxidants, gelling agents, emulsification systems, surfactants, emollients, preservatives



- **Screening** of prototypes for lead selection:
  - accelerated R&D stability evaluations
  - use partners for *in vitro* skin penetration studies and/or *in vivo* animal models (irritation, efficacy)

- **Optimization/process/scale up**:
  - Identification of CMAs, CPPs based on QTPP

Analytical Services

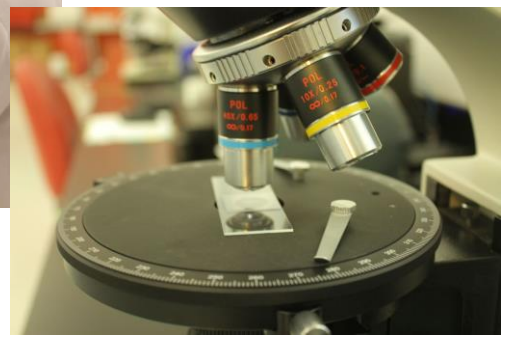
DOW DEVELOPMENT LABORATORIES, LLC

Methods and Testing

- API and drug product method development and validation to support testing of toxicology supplies and release of GMP supplies (HPLC, UPLC, LC/MS, GC, IR)
- Stability Testing (R&D, ICH)
- Raw material testing and release

Product Testing

Appearance
pH
Microscopy
Viscosity
Osmolality
Weight loss
Water content
Package integrity
IVRT
Conductivity
Assay



In Vitro Release Testing (IVRT)

- Assess release rate of the drug from the formulation over time
- Support product scale up or process changes
- Compare formulations

Manufacturing

DOW DEVELOPMENT LABORATORIES, LLC

Manufacturing and Filling Operations

- R&D batches for screening and stability testing
- Batch preparation for use in GLP toxicology studies
- GMP manufacturing & filling of clinical supplies (up to ~40 kg/batch), 4 compounding suites
- Filling into tubes (laminate, aluminum), syringes, vials, bottle, jars, sachets
- Tech transfer to CMO for large Phase III / commercial manufacturing

California FDA drug manufacturing license no. 74824

Four ISO 8 / Class 100,000
production rooms for GMP manufacturing and filling

Example of Dedicated Manufacturing Equipment: ~40L scale, jacketed glass reactors (ChemGlass) with VWR temperature control unit (R&D, GLP, GMP)

ICH Stability

DOW DEVELOPMENT LABORATORIES, LLC

Fully qualified temperature and humidity controlled stability chambers maintained at ICH conditions:

- Temperature- and humidity-controlled chambers for long term and accelerated stability evaluation
  (reach-in chambers and walk-in chambers)
- Shelf life determination in qualified ICH stability chambers
- Stability data tables and reports with QA review

ICH Conditions
5°C
25°C / 60% RH
30°C / 65% RH
40°C / 75% RH

Clinical Labeling & Distribution

DOW DEVELOPMENT LABORATORIES, LLC

Custom Packaging, Labeling, & Worldwide Temperature Controlled Distribution

- Custom label design, kit design, and distribution plan, any dosage form
- Packaging and labeling of clinical Phase I, II and III supplies
- Inventory management
- Temperature tracking during transit
- Destruction
- Dedicated GMP labeling suites

Qualified packaging
15-30˚C | 2-8˚C

Custom Kit Design

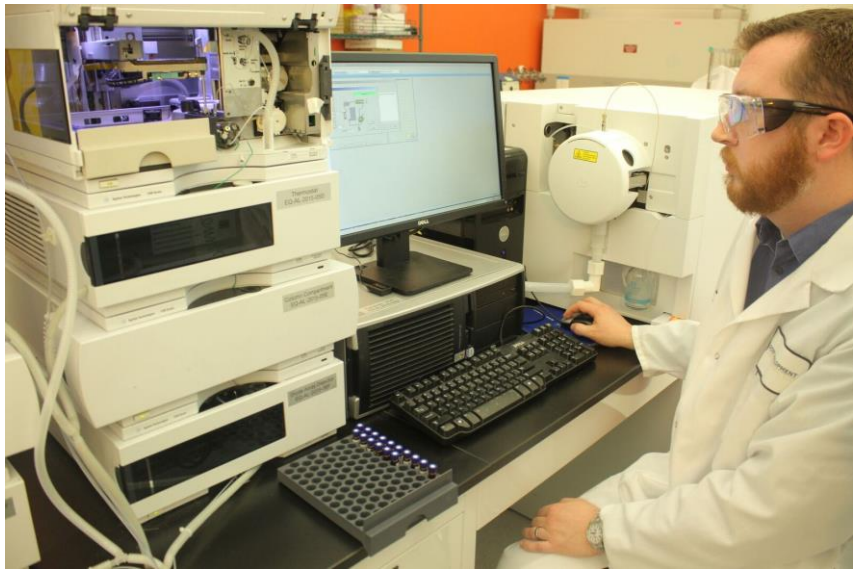
Random Code Generation

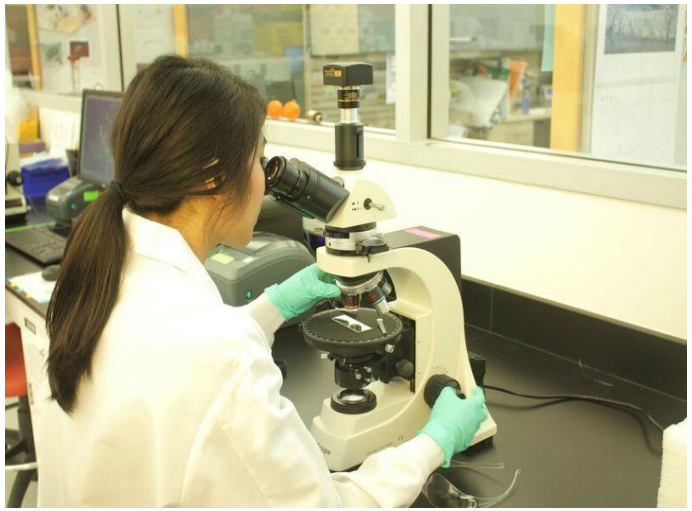
Dow Development Labs

DOW DEVELOPMENT LABORATORIES, LLC

Experienced, Focused, Flexible, Responsive

- Focused exclusively on topical drug products
- History of success
- Dedicated project teams meeting deadlines
- Project managers provide frequent communication
- Flexible, responsive and able to react quickly to the changing needs of our clients





Thank You

For additional information contact:

Karen Hanley, Senior Director of Client Services
KHanley@dowdevelopmentlabs.com
707-202-6965