DRUG DELIVERY EXPERTS

Contract Drug Product R&D | **Complex Injectable Formulations** | **Clinical Trial Materials**

www.ddelabs.com

PHARM R&D CENTER OF EXCELLENCE

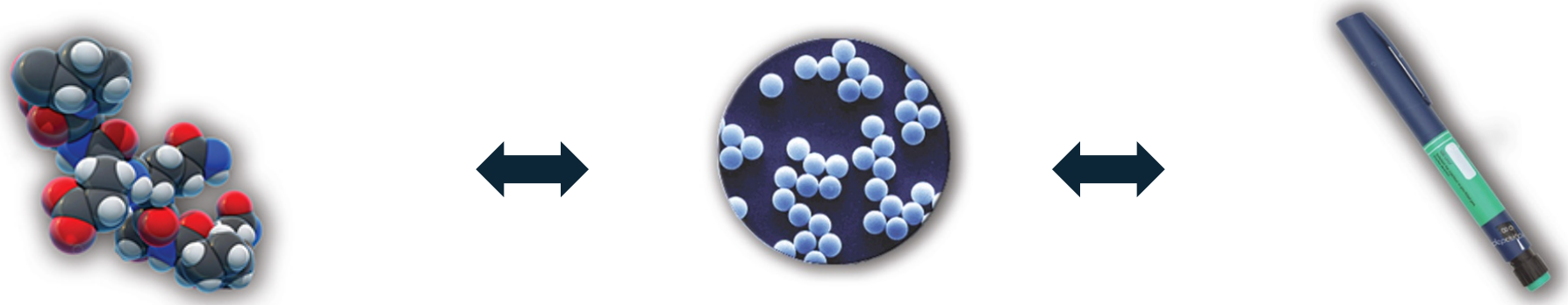
DRUG DELIVERY EXPERTS

- Specialists in injectable drug formulations and combination drug product development
- Injectable solution to complex formulation
  - Immediate to extended-release
  - Small molecule to antibody
- GMP clinical trial material manufacture for early phase clinical development
- Extensive experience in biologics, drug development, device, and delivery systems
- Highly-qualified Ph.D. scientists working in state-of-the-art R&D lab in heart of San Diego

CONTRACTED DRUG PRODUCT R&D

DRUG DELIVERY EXPERTS

- Leveraging a deep understanding of molecular properties, formulation, device
  - Integrating delivery system R&D projects into your development program
    - Optimizing target product profile to enhance value proposition



Discovery Support

- Lead molecule profiling
- Clinical candidate evaluation
- Biologic half-life extension

Drug Product Development

- Formulation design
- Drug product development
- Analytical methods

Integration with device

- Device identification
- Formulation compatibility
- Device product development

DDE LABS CAPABILITIES

DRUG DELIVERY EXPERTS

Pharmaceutical R&D Laboratory

- Formulation, analytical, process, chemistry, device development
- Specialists in complex drug product development
- Peptide and small molecule chemistry, conjugation (e.g., PEGylation)
- Lead candidate selection for peptide and small molecules
- Crystal and salt form selection for small molecules

GMP Fill Finish for Injectable Formulations

- Parenteral facility and quality system approved by the California Department of Public Health Food and Drug Branch
- Clinical trial materials in vials
- QC and stability testing
- Test article for GLP toxicity studies

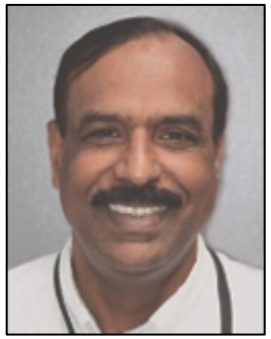
LEADERS WITH DEEP DOMAIN EXPERIENCE

DRUG DELIVERY EXPERTS

Chris Rhodes, Ph.D.
VP, Scientific Affairs
Founded Drug Delivery Experts in 2014 after 20 years in biotech and drug delivery companies in both technical and executive leadership roles.

Randall Freund
Director Quality Assurance
Randall has over 40 years experience in the pharmaceutical and medical device industry overseeing Quality and Production groups to implement or improve Quality Management Systems.

Lawrence D'Souza, Ph.D.
Scientific Director Discovery, Chemical and Process Development, Formulation
Organic chemist with discovery and early development experience in small molecule, peptide, and protein synthesis



Laxma Reddy, Ph.D.
Scientific Director Formulation and Process Development, Small Molecules and Biologics
Protein biophysical chemist with experience in extended-release drug delivery product development

Franco Ferrari, Ph.D.
Scientific Director GMP Operations and Manufacturing
Over 30 years of experience in quality system regulations, GMP facility management, and product development

Becky Bader, Ph.D.
Associate Director Formulation for Pharmaceutical and Device Applications
Polymer chemistry, synthesis, and characterization. Nanoparticles, microspheres, micelles, conjugates and hydrogels

05/23

LEADERS WITH >150 YEARS EXPERIENCE

DRUG DELIVERY EXPERTS

Our Leaders Have Worked at These Companies

PersImmune

AMYLIN

Bristol-Myers Squibb

AstraZeneca

MannKind Corporation

3M

SurModics

OHR Pharmaceutical Inc.

GUILFORD PHARMACEUTICALS

DIOMICS

WomanCare GLOBAL | dkt INTERNATIONAL

daré bioscience

CardinalHealth™

eurofins | Advantar

Protein Polymer TECHNOLOGIES

MITOKOR the MITOCHONDRION COMPANY

Our Leaders Developed These Products

SymlinPen (pramlintide acetate) pen-injector

afrezza (insulin human) Inhalation Powder

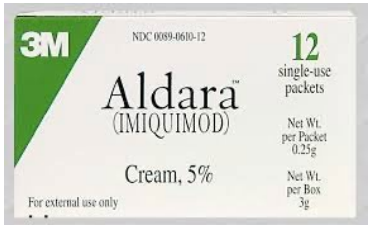
LUSEDRA (fospropofol disodium) Injection

BYDUREON exenatide extended-release for injectable suspension

Byetta (exenatide) injection

GLIADEL WAFER (carmustine implant)

myalept (metreleptin) for injection 11.3 mg per vial



OVAPRENE

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SUPPORT ACROSS DRUG DEVELOPMENT

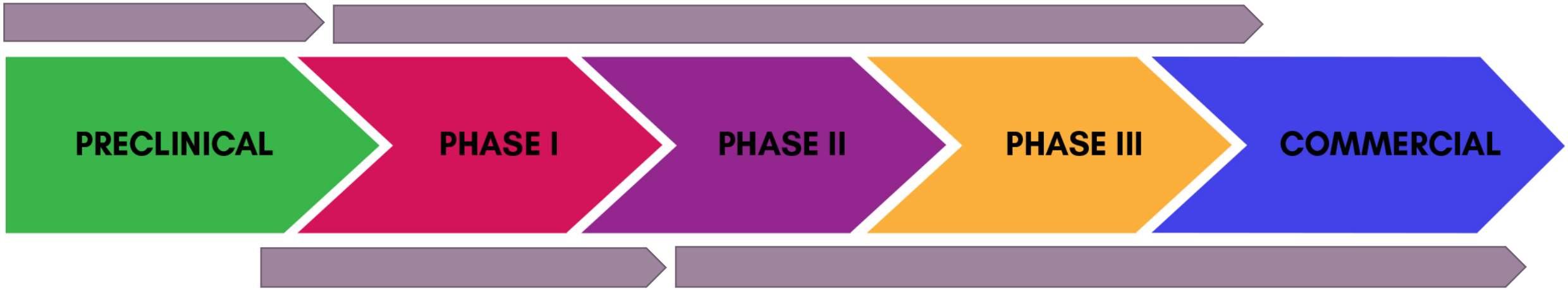
DRUG DELIVERY EXPERTS

LEAD MOLECULE SELECTION

- *Peptides*
- *Small Molecules*
- *PEGylation*
- *Salt & Cocrystal Selection*

INJECTABLE and LIQUID FORMULATIONS

- *Solution in a Vial / Bag*
- *Lyophilized Powder for Reconstitution*
- *Suspensions (Aqueous & Oil), Emulsions, Micelles, Liposomes*
- *Gel-Forming and Particle Systems for Extended Exposure*



GMP MANUFACTURING

- *Toxicity Test Articles*
- *Clinical Trial Materials*
- *QC Release*
- *Stability Testing*

DEVICE INTEGRATION

- *Pre-filled Syringe*
- *Cartridge*
- *Pen*
- *Auto-Injector*

LIFE-CYCLE MANAGEMENT

- *Reformulation*
- *Long-Acting Systems*
- *Non-Injectable Delivery (Oral, Nasal, Pulmonary)*

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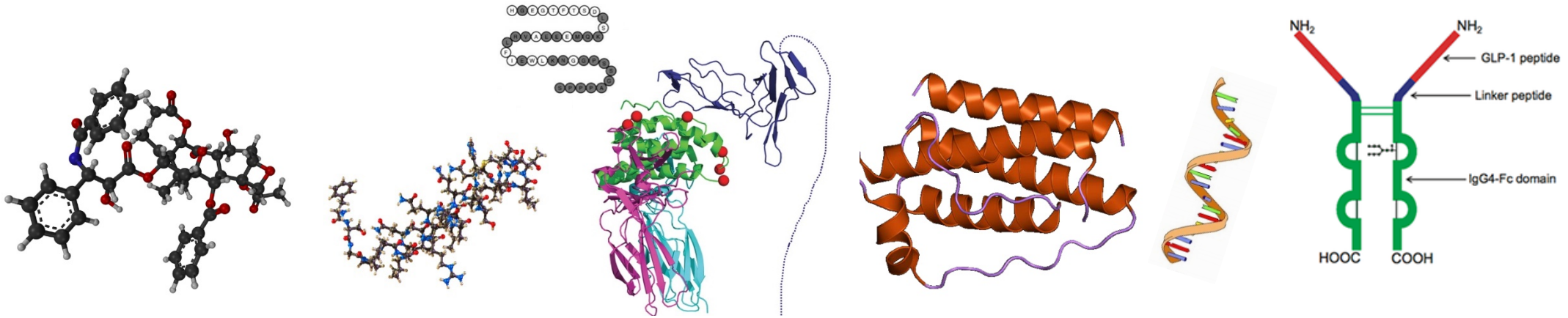
MOLECULE AND DELIVERY EXPERIENCE

DRUG DELIVERY EXPERTS



~ 1K Da

~ 10K Da

~ 100K Da

Small Molecules

- IV, SC, IM
- Nasal
- Oral

Peptides

- SC
- Inhalation
- Nasal
- Ocular
- Oral

Proteins

- SC
- Nasal
- Inhalation

Oligos

- SC

Antibody

- SC

COMPONENTS OF TYPICAL LAB PROJECTS

DRUG DELIVERY EXPERTS

Lead Molecule Selection

- Analytical Research
- Development Assessment
- Lead Molecule Design

Delivery System Selection

- Analytical Development
- Preformulation
- Delivery System Feasibility
- Formulation PK Screening

Drug Product Development

- Formulation Development
- Device Selection & Development
- Process Development Scale-Up
- Development Stability
- Analytical Methods Qualification
- Technology Transfer GMP Mfg.

Clinical Trial Materials

- Formulation Process
- GMP Fill & Finish
- Analytical & QC Release
- Stability Testing

Molecule Design
Peptide/Protein
Conjugates for Half-Life
Small Molecule

Delivery System Design
Aqueous or Non-Aqueous Vehicle
Sustained Release Formulation
Triggered or Targeted Systems

Drug Product Design
Pen/Auto-Injector
Pre-Filled Syringe
Nasal/Ocular Drops/Spray

GMP Manufacture
Clinical Trial Materials
QC Release Testing
Stability Studies

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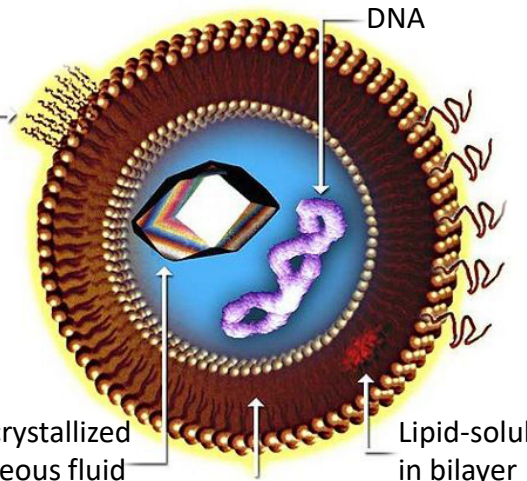
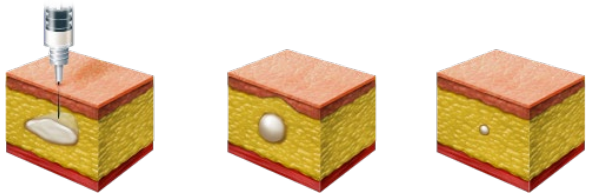
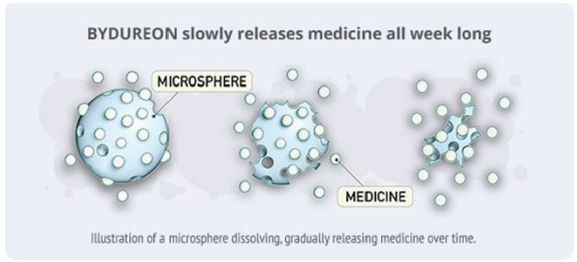
EXTENDED-RELEASE INJECTABLE APPROACHES

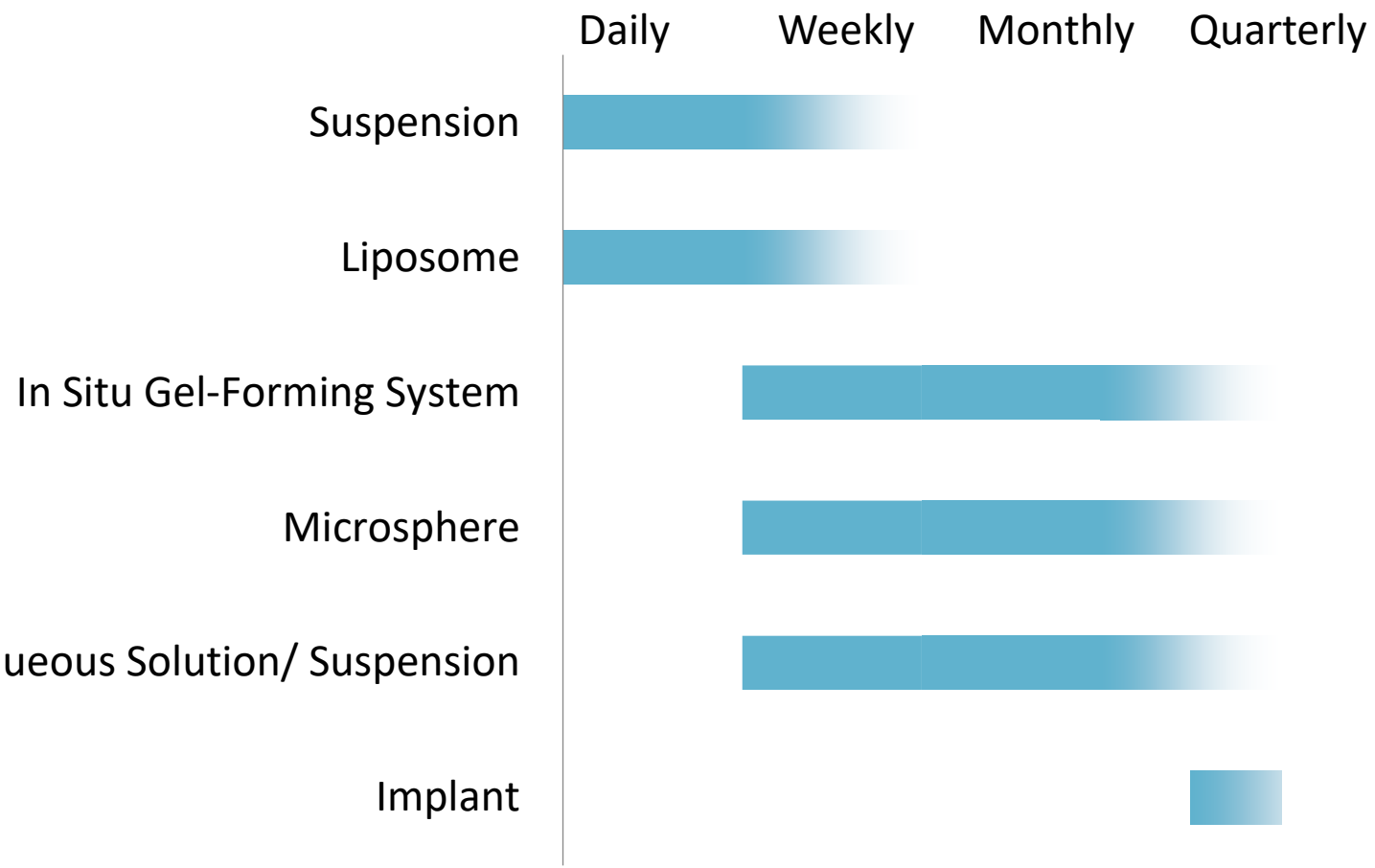
DRUG DELIVERY EXPERTS

Liposome for Drug Delivery



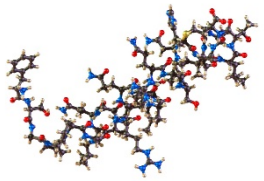


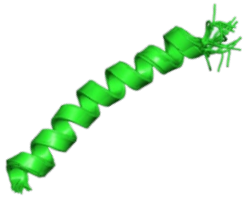


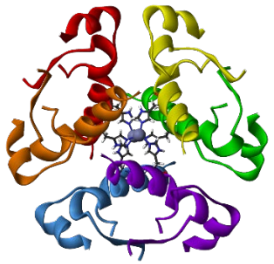


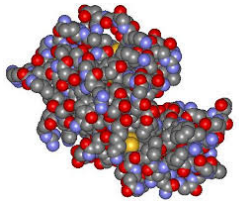
EXTENDED-RELEASE INJECTABLE PROGRAMS

DRUG DELIVERY EXPERTS









Compound Type	MW (kDa)	Injection Frequency	Liposome	Salt	Gel	Microsphere	Suspension
Small Molecule	<1, several	Monthly and longer		✓	✓	✓	✓
Peptide	1	Weekly to Monthly		✓	✓	✓	
Peptide	2	3 to 4 Months		✓	✓		
Peptide	3, 4	Daily		✓			
Peptide	4	Weekly to Monthly		✓	✓		
Peptide	4, 5	Weekly to Monthly		✓	✓	✓	
Insulin	6	Daily to Weekly	✓	✓			
Oligonucleotide	8	Daily to Weekly		✓			
Oligonucleotide triple combination	10	Daily to Weekly				✓	
Protein	15	Weekly		✓	✓		
Protein	50	Weekly	✓		✓		
Antibody	150	Weekly to Monthly		✓			

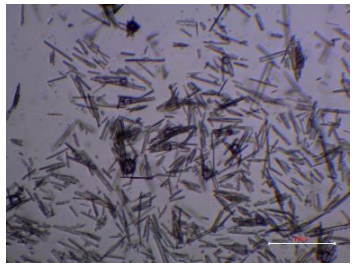
FORM SELECTION & PARTICLE SUSPENSION

DRUG DELIVERY EXPERTS

Drug Substance:
Free base or acid

Salt or
Co-crystal

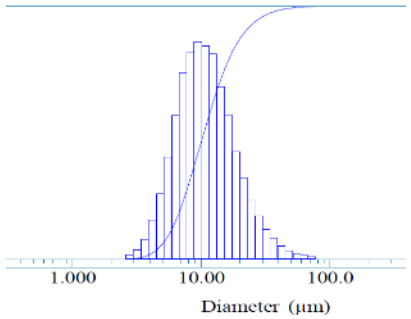
Form
Selection



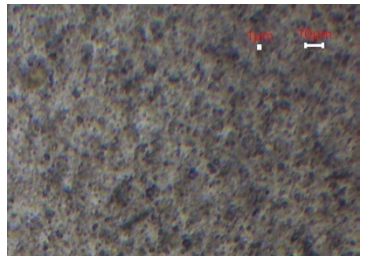
Insoluble Crystal Form
<0.01 mg/ml at 37°C PBS
Low rate of saturation solubility

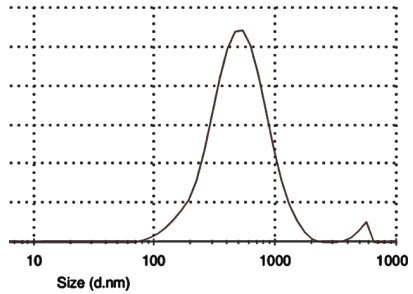
Dry Ball mill

Or Wet Bead mill



Micro-particle Suspension



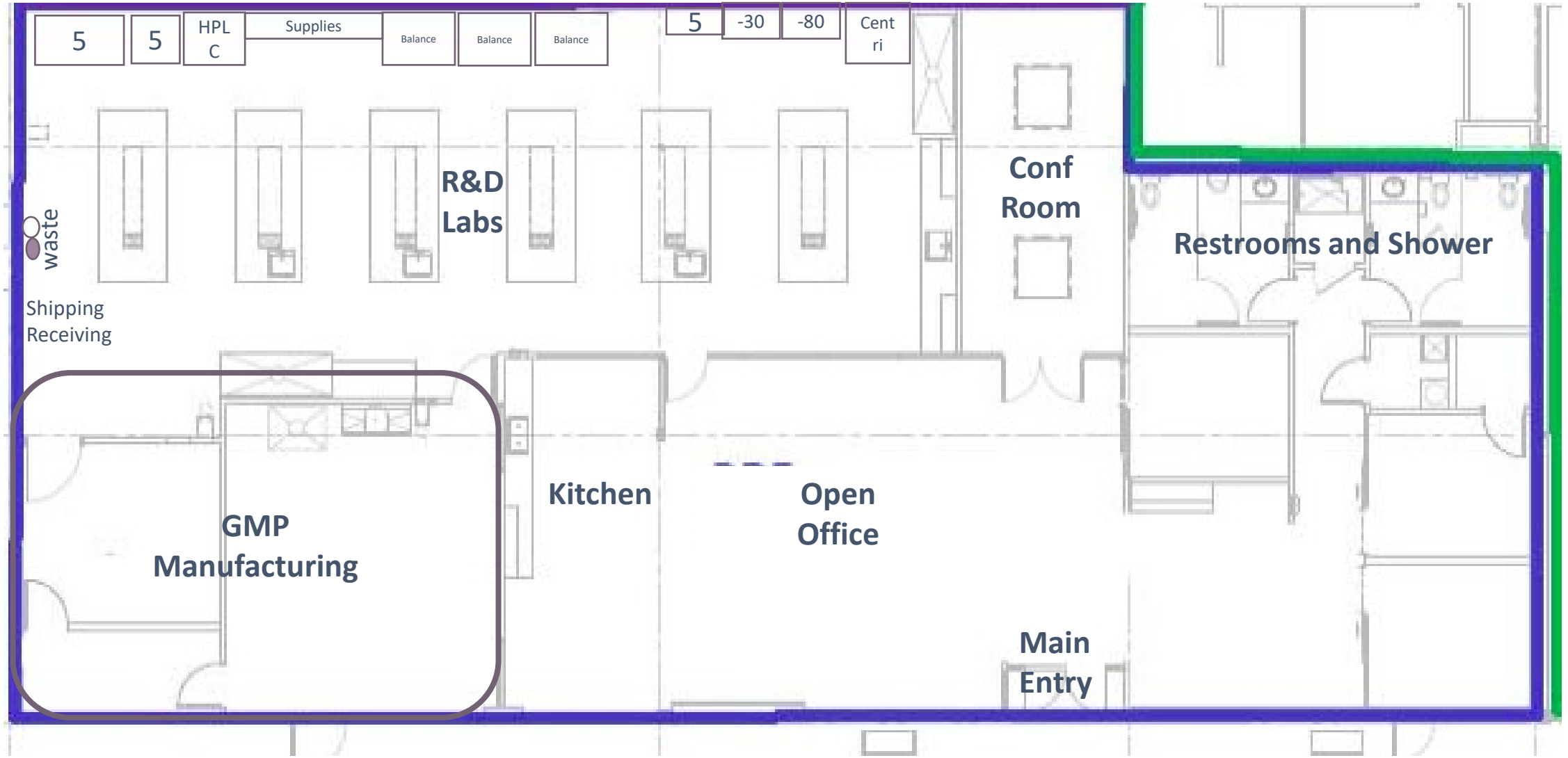


Nano-particle Suspension

Horizontal oscillatory ball mill for small scale grinding
Tube Roller for low energy grinding
Vertical planetary ball mill for high energy grinding

STATE-OF-THE-ART DRUG PRODUCT LAB

DRUG DELIVERY EXPERTS



DDE LABS DEVELOPMENT CAPABILITIES

DRUG DELIVERY EXPERTS

Formulation and Process Development

- Homogenizers, emulsifiers
- 37°C incubators for In vitro release testing for extended-release injectables (water bath and shake-flask)
- Instron Injection force measurement
- Nano assembler for nanoparticle & liposome
- Shelf–stoppering lyophilizer for cycle development
- Ball mill, tube roller, planetary ball mill for grinding
- Capsule hand-fill for powder and liquid formulations
- Laminar flow hoods for preclinical supply / stability

Chemistry and Chemical Development

- Organic synthesis reactors, jacketed reaction vessels
- Rotary evaporator
- Manifold lyophilizer
- FPLCs for protein purification
- Salt, co-crystal synthesis and form selection
- Prodrug design and synthesis
- Polymer synthesis

Analytical Development

- 15 HPLC (diode array UV Vis, fluorescence, ELSD, RID)
- HPLC – MS
- UPLC
- UV/Vis & fluorescence plate readers and nanodrop
- Particle size analyzer (laser diffraction, 1µM – 500 µM)
- Dynamic light scattering / zeta potential (1 nm – 10 µM)
- Stability Chambers certified and monitored (ICH 25°C/60RH, 40°C/75RH, 2-8°C, -20°C, -80°C)
- Osmometer and Viscometer for characterization
- Endotoxin testing for preclinical / development stability samples
- Scanning electron micrograph
- Visual microscopy

Bioanalytical Development

- MSD ELISA for bioanalysis
- Gel electrophoresis imager for imaging protein gels

PRECLINICAL PARENTERAL FILL EXPERIENCE

DRUG DELIVERY EXPERTS

Manufactured over 250 stability and preclinical batches in the past 6 years

Batch sizes up to 2 liters historically in process suite

Batch records signed off ahead of fill

Batch release with analytical test results

- Concentration, purity, pH, osmolarity, endotoxin, and others

Formulation composition and process methods

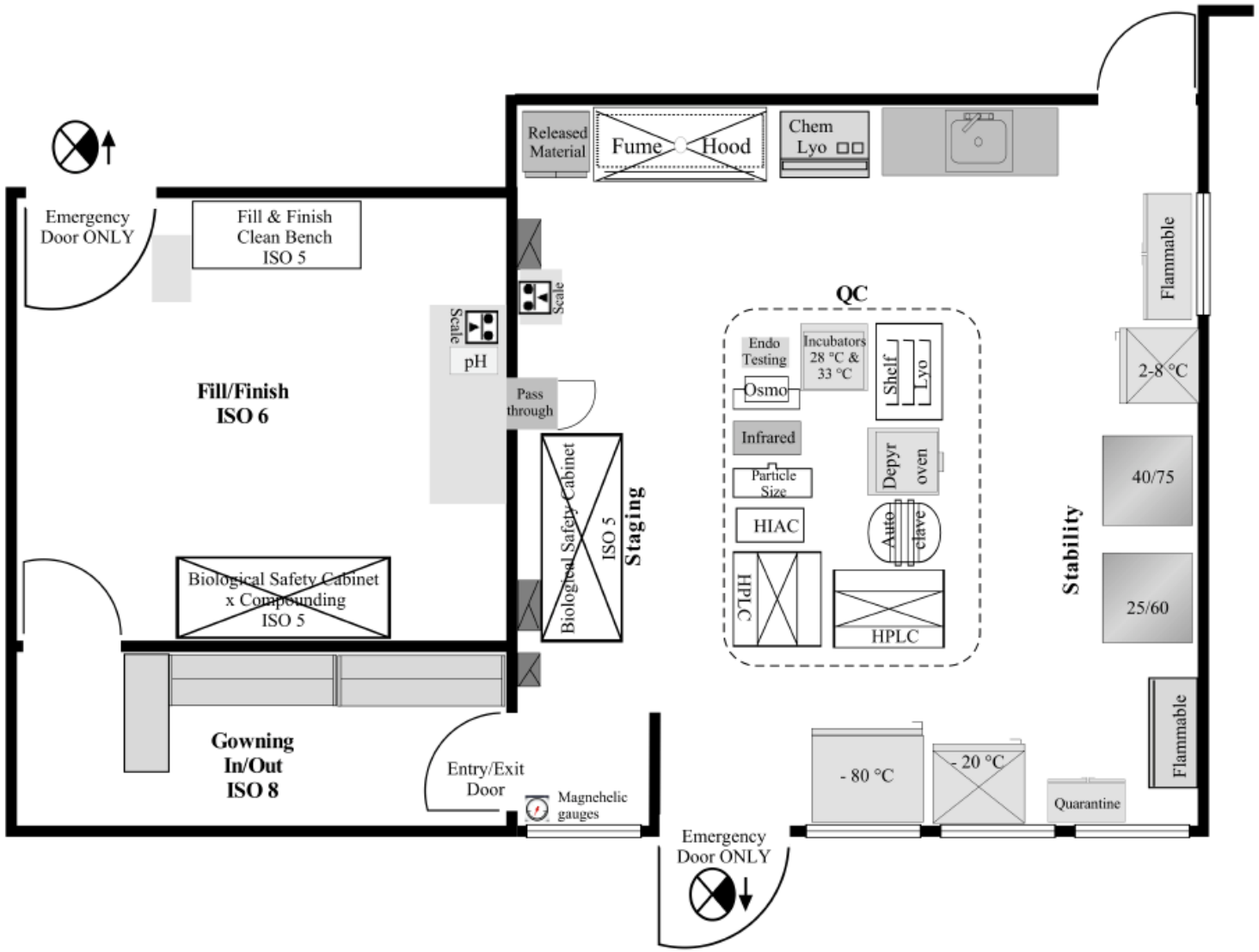
- Aqueous and non-aqueous solutions and suspensions
- Liposomes, microspheres, gels, salts, and others

Formulation and development stability manufacturing

- 24 month shelf-life now supporting phase 2 program
- Stability studies to support ANDA filing
- Several development studies for toxicology and clinical formulation selection

GMP FILL FINISH, QC & STABILITY TESTING

DRUG DELIVERY EXPERTS



Vial Fill and Finish for Clinical Materials

Media fills for 2 ml to 10 ml vials

Fill / Finish Suite (ISO 6) with Hoods (ISO 5)

Gowning Vestibule (ISO 8)

QC Lab for Incoming / Outgoing Materials

GMP Stability Chambers Monitored 24/7

DDE LABS GMP CAPABILITIES

DRUG DELIVERY EXPERTS

GMP Manufacturing

- ISO 8 Gowning Vestibule
- ISO 6 Process Suite with pass through
- ISO 5 Laminar flow and biosafety cabinet in process suite
- ISO 5 Laminar flow hood in QC lab for compounding
- Depyrogenation oven, autoclave
- Chemical fume hood
- HPLC, osmometer, endotoxin, particle size, pH
- Incubators for environmental monitoring
- Semi-automated filler
- Semi-automated crimper

Formulation and Chemical Process

- Solution formulations
- Gel and viscous formulations
- Homogenization and emulsification
- Microparticle and nanoparticle manufacture
- Salt, prodrug, PEGylation, polymer synthesis

QC Testing and Stability

- HPLC (diode array UV Vis, others as needed)
- Microparticle size by laser diffraction
- Nanoparticle size by dynamic light scattering
- Stability Chambers certified and monitored (ICH 25°C/60RH, 40°C/75RH, 2-8°C, -20°C, -80°C)
- Osmometer and Viscometer
- FTIR for incoming raw material receipt and characterization
- USP particulate testing (HIAC)
- Environmental monitoring
- Endotoxin (Charles River Labs kit)
- Sterility / bioburden outsourced to qualified vendor

Current Media Fills

- 2 ml vials / 1 ml fill volume / 0.5 to 5 liter batch size
- 10 ml vials / 5 ml fill volume / 5 to 10 liter batch size

- Up to 20 to 40 liters batch volume
- Up to 3000 vials per batch

DDE LABS NOW 7 YEARS IN BUSINESS

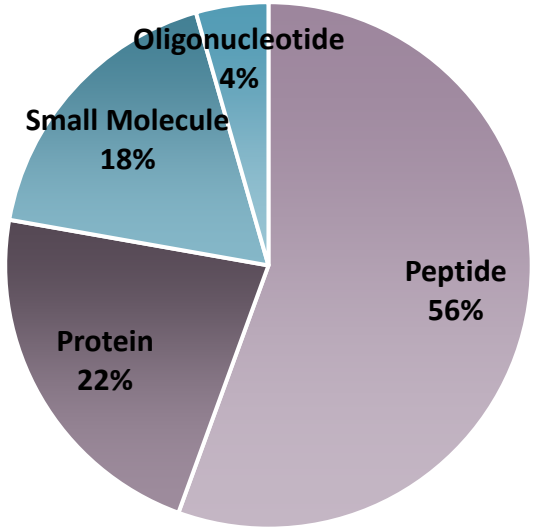
DRUG DELIVERY EXPERTS

- 88 DDE Labs clients and 150 lab projects over 7 years laboratory operations
  - 80+ consulting clients since business start 10 years ago
  - 90% of clients in US / remainder EU and JP
  - 15 multinational corporations
- Over the last 3 years (2018 to 2020)
  - 22 DDE Labs clients each year and growing
  - 50% of clients repeat business over 1 to 3 years
  - 80% business from clinical and commercial companies
- GMP sterile fill finish new offering in 2021

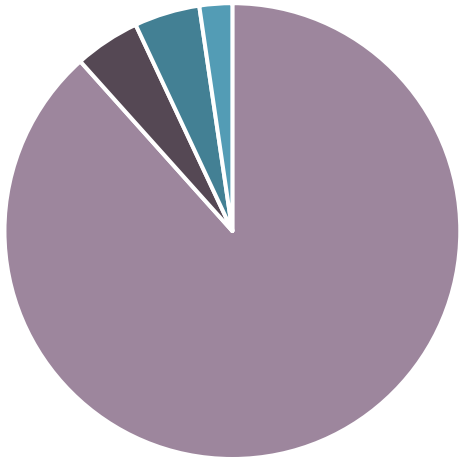
DISTRIBUTION OF PROJECT TYPE

DRUG DELIVERY EXPERTS

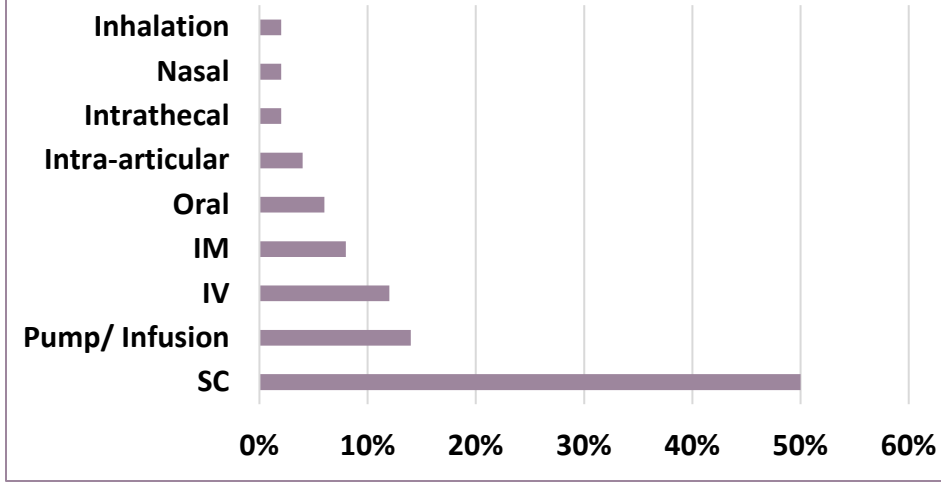
MOLECULE TYPE



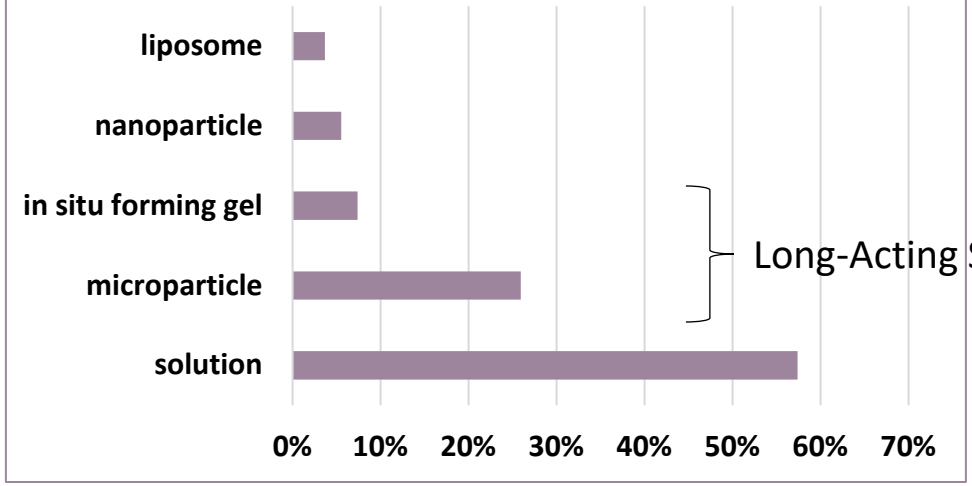
PROGRAM TYPE



ROUTES OF ADMINISTRATION



FORMULATION



PARTNERSHIP OPTIONS

Project Specific Work

- Shorter well-defined projects
- Typically 3 to 9 months
- Time and materials fee-for-service
- Payment milestones

Dedicated R&D Team

- Longer term and broader R&D programs
- Typically 1 to 3 years
- Dedicated resources for program
- Regular quarterly or monthly payments

PARTNER PATENT & PUBLICATION SUPPORT

DRUG DELIVERY EXPERTS

Veru Healthcare

- Compositions and Methods for Long Term Release of Gonadotropin-Releasing Hormone (GnRH) Antagonists, US 15/885,464
- ASCO presentation on preclinical results

Aileron Therapeutics

- Peptidomimetic macrocycles and formulations thereof, US 20160101145 A1

Abvance Therapeutics

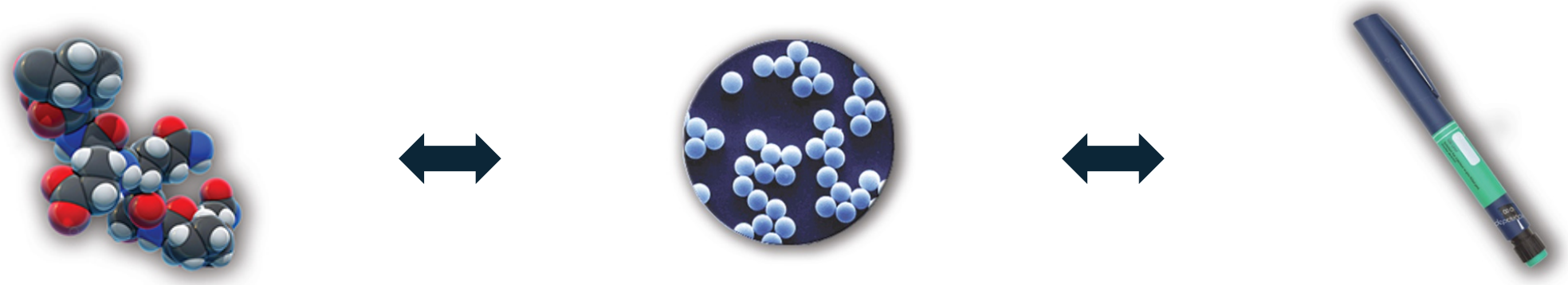
- Systems, Compositions, and Methods for Treating Diabetes, Allan Cherrington, Soumitra Ghosh, Christopher A. Rhodes, Jui-Chen Lin, Patent Application US2018016647 filed March 2, 2017

Iogen LLC

- Emolient topical disinfectants, WO 2018/017645 A1
- "Enhanced topical delivery of non-complexed molecular iodine…",*Intl J Pharm* 554(2019)81-86

OUR EXPERTISE

DRUG DELIVERY EXPERTS



Combination Drug Product Development and GMP Manufacturing

- Small molecule through peptide, protein, oligonucleotide, antibody
- Lead molecule profiling and half-life extension
- SC, IM, IV, topical ocular and intraocular formulation design and development
- Extended-release injectable and implantable formulations
- Translation from research through clinical trials and commercialization

DRUG DELIVERY EXPERTS

WE THRIVE ON SOLVING YOUR MOST CHALLENGING PROBLEMS