CritiTech®
Pulmonary

Transforming Drugs Into Better Treatments for Respiratory Diseases and Conditions

Management Team

Sam Campbell
Chairman

Matthew McClorey
President

Jody Schrandt
Chief Operating Officer

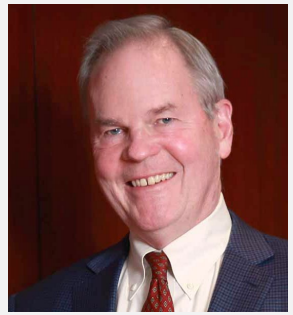
Mike Baltezor, PhD
Chief Scientific Officer

Mark Williams
Vice President
Technical Operations

Highly Skilled and Experienced Drug Development Leadership Team

- >150 years of experience in the pharmaceutical industry - early-stage drug development, particle engineering, formulation, material characterization, analytical testing, method development, clinical trial management, commercial manufacturing, quality operations, regulatory, and corporate management
- Previous positions held at Sanofi-Aventis, Merck, Sandoz, Marion-Merrill Dow, Cardinal Health, Celliance, Quintiles, CareFusion, and Plastikon
- Involved in the development of >100 drugs that have been tested in the clinic and >20 drugs that have been approved by the FDA
- Collectively, members of our team have been listed as inventors on >100 patents

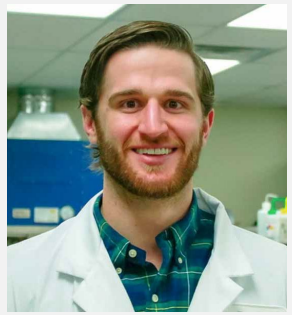
Michael Baltezor, PhD
Chief Scientific Officer



Gere diZerega, MD
Chief Medical Officer

Mark Williams
Vice President Technical Operations

Tracy Doty
Senior Director Quality Operations



Jake Sittenauer
Director Drug Development Programs

Purcision™ Technology is a Platform for Developing Drugs for Direct Delivery at the Site of Disease

CritiTech Pulmonary

Purcision™
DIRECT TO TARGET DRUGS

Platform for Oncology Drug Development

Partnered
5 Drugs
8 Phase I/II Clinical Trials

- Taxanes
- Kinase Inhibitors
- PARP Inhibitors

Platform for Respiratory Drug Development

Partnered
1 Drug
Preclinical Testing

- Antivirals
  - Respiratory Diseases (PAH, IPF, COPD, Asthma, CF)
- Antibiotics
  - MCM's for Chemical Warfare Agents (Lung Treatment & Protection)

Platform for Direct-to-Target Drug Development

Partnered
1 Drug (Phase I Trial)
1 Drug (Phase II(a) Trial)

- Pain Management
- Wound Healing
- Topical
- Bladder Infection
- IM or SC Injections
- Nasal MCM's

Developing Inhaled Drugs is Tough

Conventional drug development and manufacturing technologies struggle to produce the right mix of particle attributes necessary for safe and effective inhaled drugs.

Problems with Inhaled Drug Development

- Insufficient drug load
- Additives (sugars, stabilizers) hinder performance
- Inconsistent material
- Poor flowability – static charge
- Inadequate delivery of drug from a DPI
- Limited retention time in the lungs
- Side effects from faster than desired systemic uptake

Purcision™ Helps Overcome Challenges Associated with Developing Inhaled Drugs

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Attributes

- Crystalline powders
- Low density particles which reduce aerodynamic particle size
- High surface area
- 100% pure drug particles - no excipients necessary
- Uniform particle size distribution
- Improved flowability

Purcision™
DIRECT TO TARGET DRUGS

Performance

- High drug load
- Long duration in the lungs
- Avoid phagocytosis
- Highly stable
- Larger particles remain at the site of administration but release drug like smaller particles
- Maximizes flow from DPI

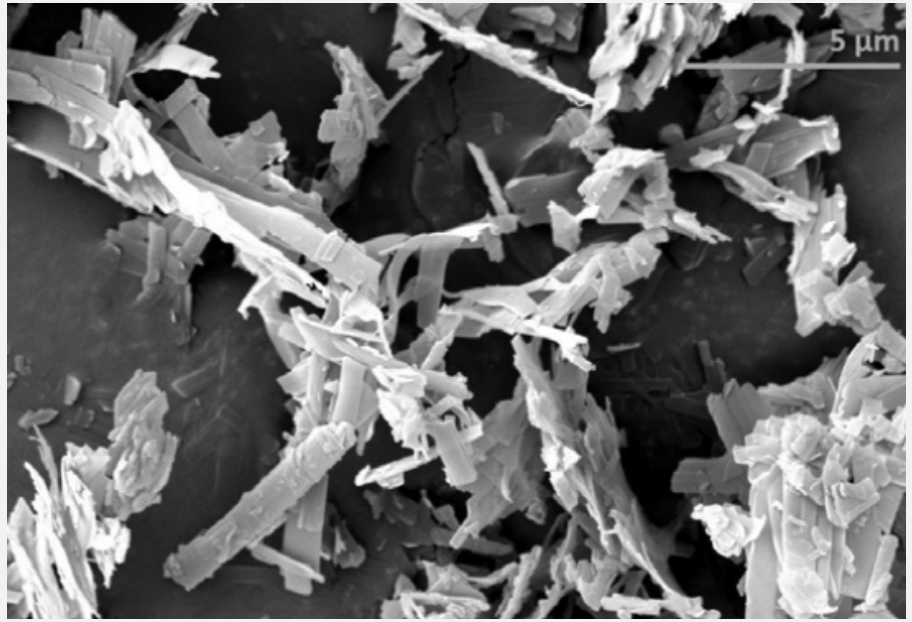
Purcision Creates Many Opportunities for Respiratory Drug Development

- **Second chance for "shelved" drugs**
- **Reformulations of current IV and oral drugs**
- **New drugs**

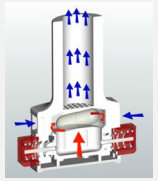
Purcision™ Particle Engineering & Production Technology

Purcision is a proven particle engineering technology used to develop new drugs and reformulate and repurpose existing drugs for multiple delivery systems. It is particularly effective for engineering particles for inhaled delivery.

Purcision Engineered Particles



New & Improved Drugs



Inhalation

Orals

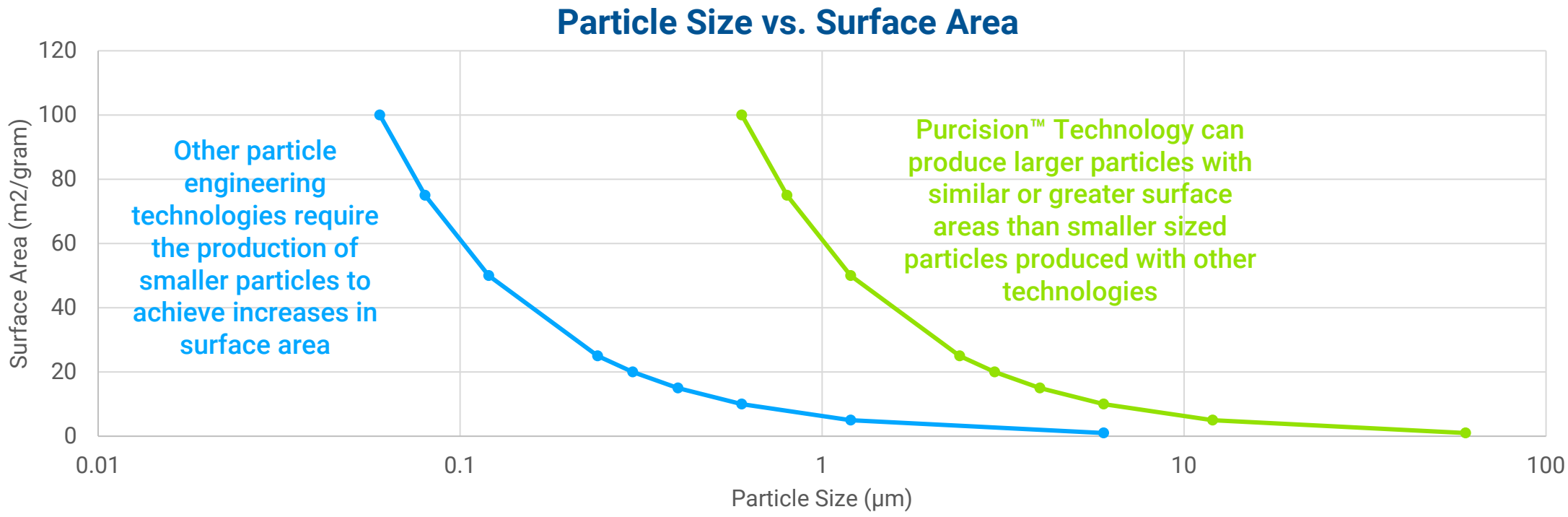
Injectables

Gels/Ointments

Controlled Concentration – Long Duration
Limited Systemic Exposure

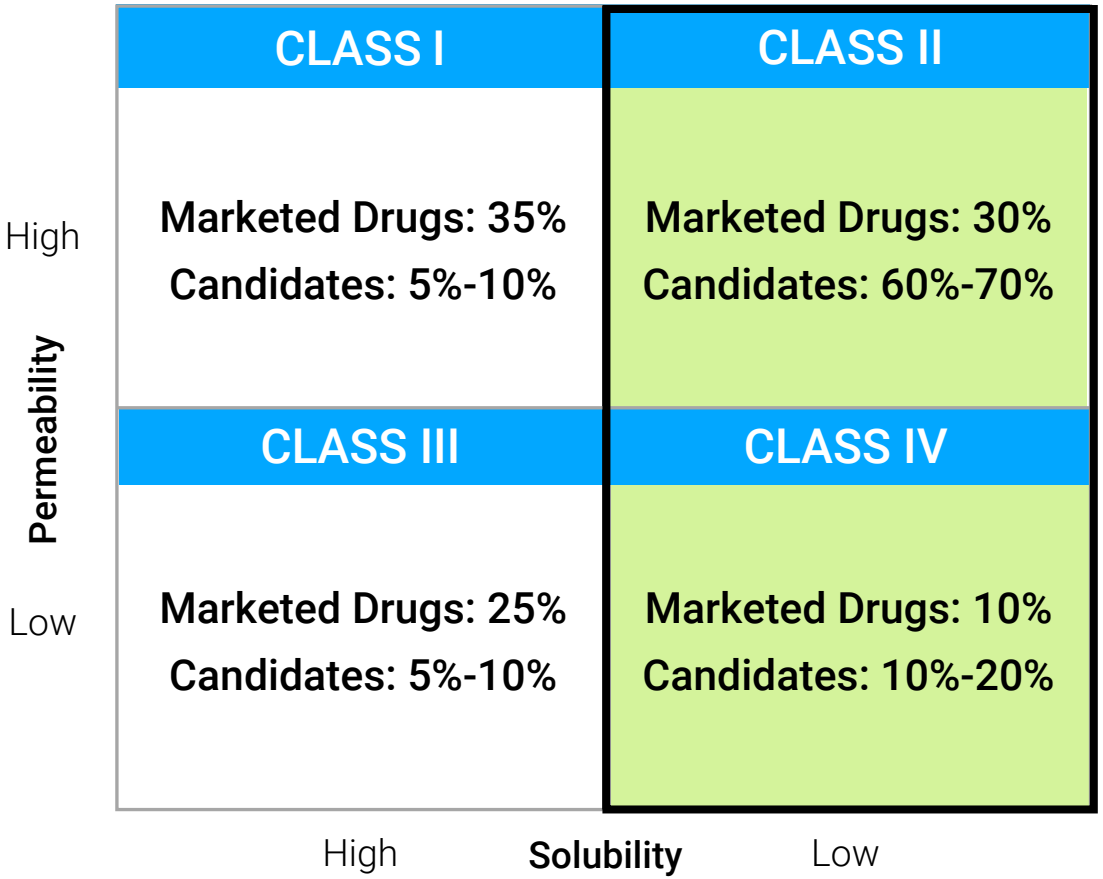
Purcision™ Produces a Unique Particle Size to Surface Area Ratio

- Purcision™ Technology is different from other particle engineering technologies (CESS, RESS, spray drying, milling, et. al.)
- Purcision™ has a unique ability to engineer **large particles with surface area normally associated with much smaller particles**
- **Unique, disproportionate surface area to particle size ratio** is optimal for delivering drug to site of disease (e.g., tumor, lung, et. al.)
- Larger, high surface area Purcision™ particles enable **longer retention time at the site of disease** and **effective drug release**
- Solid particles engineered with other technologies <1um require additives to prevent static agglomeration and improved handling



Purcision™ is an Effective Tool for Engineering Poorly Soluble Drugs

Biopharmaceutical Classification System for Drugs



Purcision™
DIRECT TO TARGET DRUGS

CritiTech's Purcision technology is best used to engineer poorly soluble drugs, which consist of 40% of marketed drugs and 70%-90% of drug development candidates.

Purcision Compatibility Criteria:

- **Must be soluble in an organic solvent**
- **Must be insoluble in $scCO_2$**

Source: Nikolakakis and Partheniadis, Self Emulsifying Granules and Pellets: Composition and Formation Mechanisms for Instant or Controlled Release (2017)

Purcision™ Technology Engineers Drug Particles Ideal for Direct Delivery Into the Lungs

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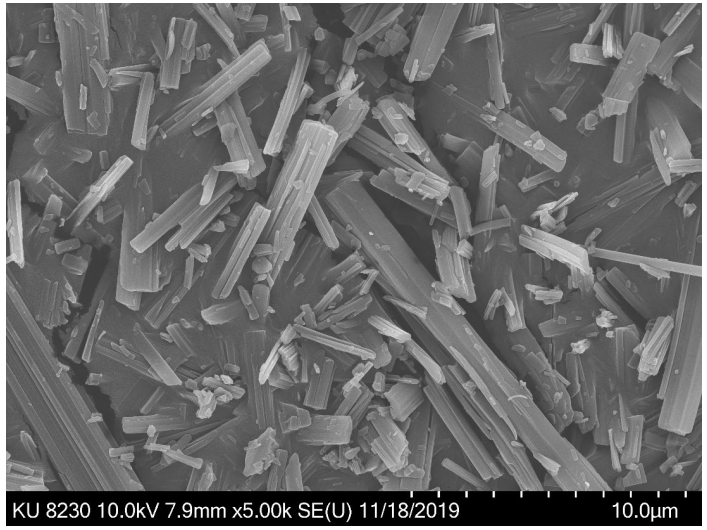
Bulk Drug



- **Bulk API's are higher density solid particles with lower surface areas that limit bioavailability**
- **Excipients are required to achieve desired release rates**

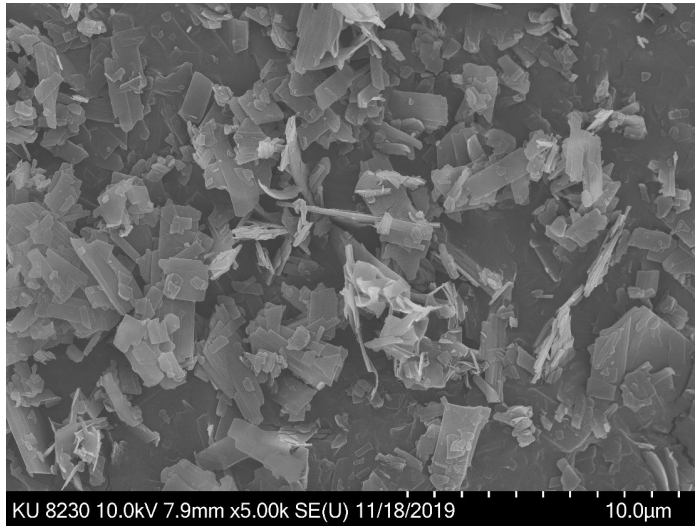
Purcision™

DIRECT TO TARGET DRUGS

Unique Competitive Advantage for Inhaled Drugs

- High Concentration
- Long Duration
- Limited Systemic Exposure
- 100% Pure Drug

Purcision Processed Drug

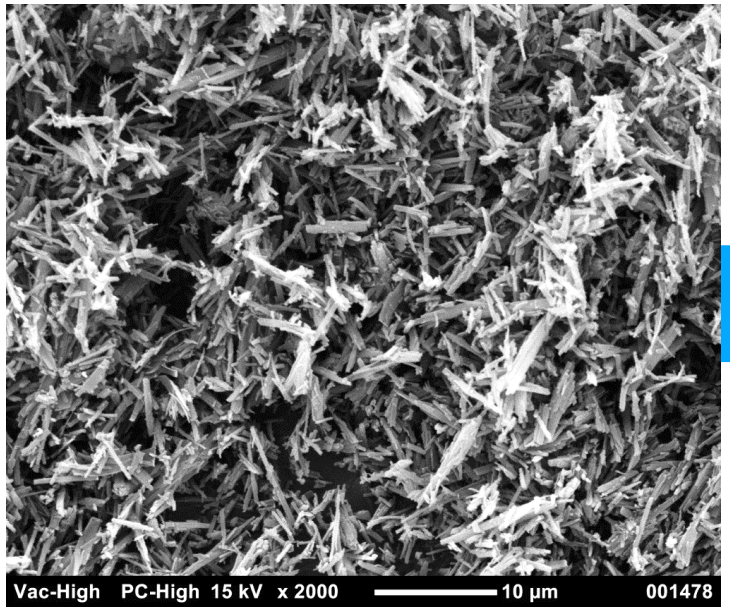


- **Purcision particles are not solid and lower density with higher surface areas that improve bioavailability**
- **Purcision particles enable aerodynamic particle size to be much less than the physical size**
- **No excipients required to achieve desired release rates**

Purcision™ Particles Are Ideal for Direct Delivery Into the Lungs as Dry Powder Formulations

Dry powders engineered using the Purcision technology should be delivered into the lungs at higher concentrations and release drug for a longer periods of time compared to current marketed formulations.

Purcision Inhaled Drugs



Particle Attributes	Benefits
Physical Size	**Particles large enough to reduce removal from lungs by phagocytosis**
Mass Median Aerodynamic Diameter (“MMAD”)	**MMAD values that enable delivery to the deep regions of the lungs**
Density	**Less dense versus raw material which allows the aerodynamic particle size to be less than the physical particle size**
Surface Area	**Surface area increase versus raw material which should enable desired dissolution in the lungs**

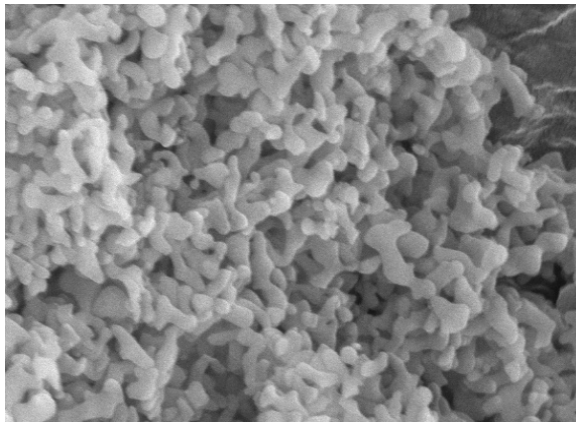
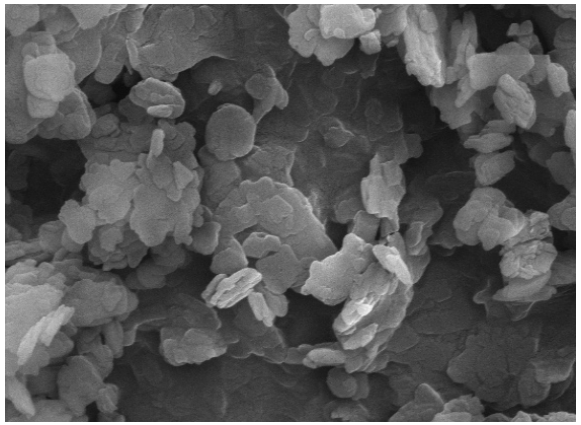
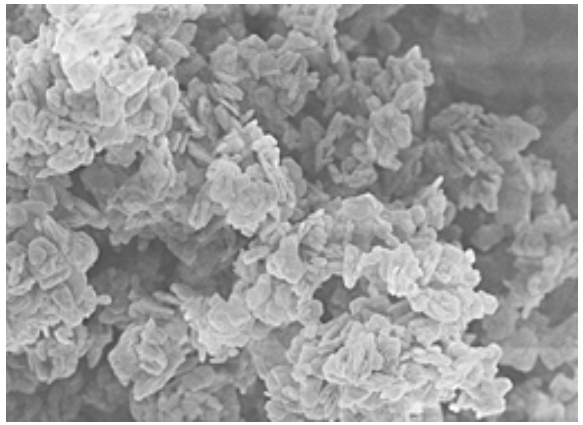
Supercritical Precipitation Engineering

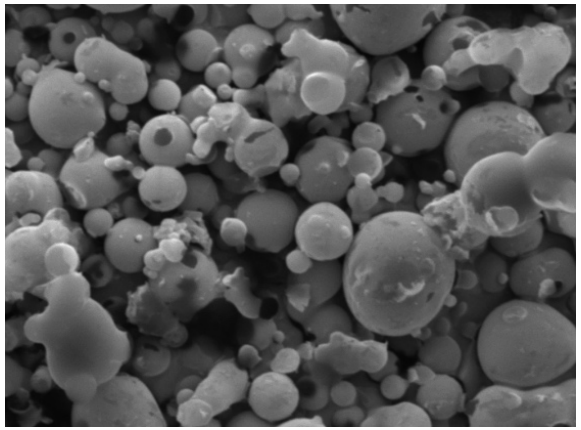
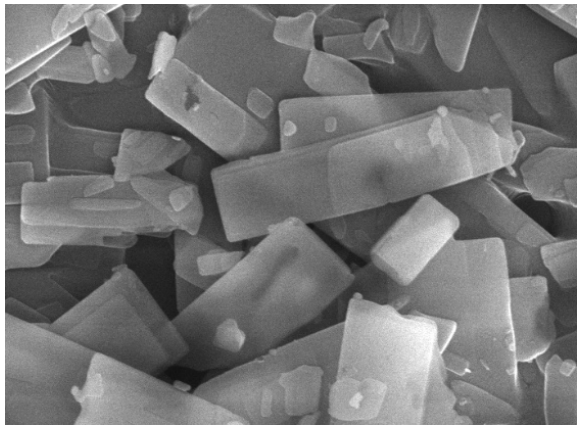
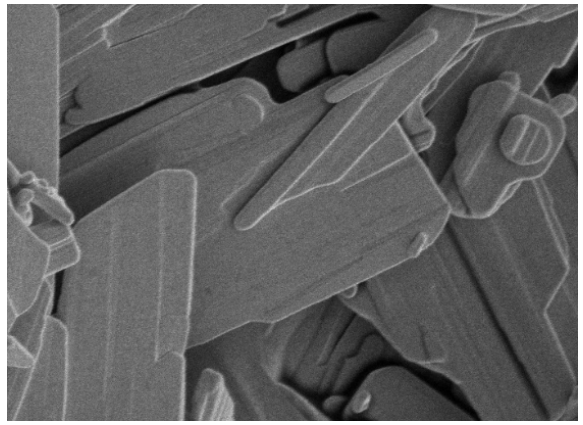
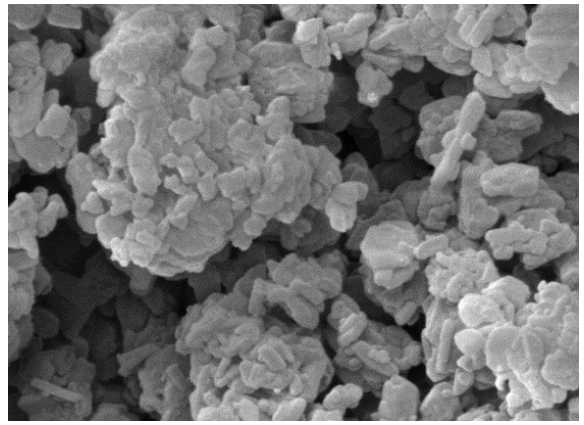
CT PES can modify particle characteristics such as size, shape, and polymorph by adjusting the properties of the feed solution and operating parameters in the SCP systems

- Solvent selection
- API concentration
- Temperature
- Pressure
- Solution/feed flow rate
- scCO2 flow rate
- Ultrasonic energy
- Nozzle configuration

Purcision™ Size and Shape

Purcision technology can be tuned to produce various particle sizes and shapes of API (8 different drugs)

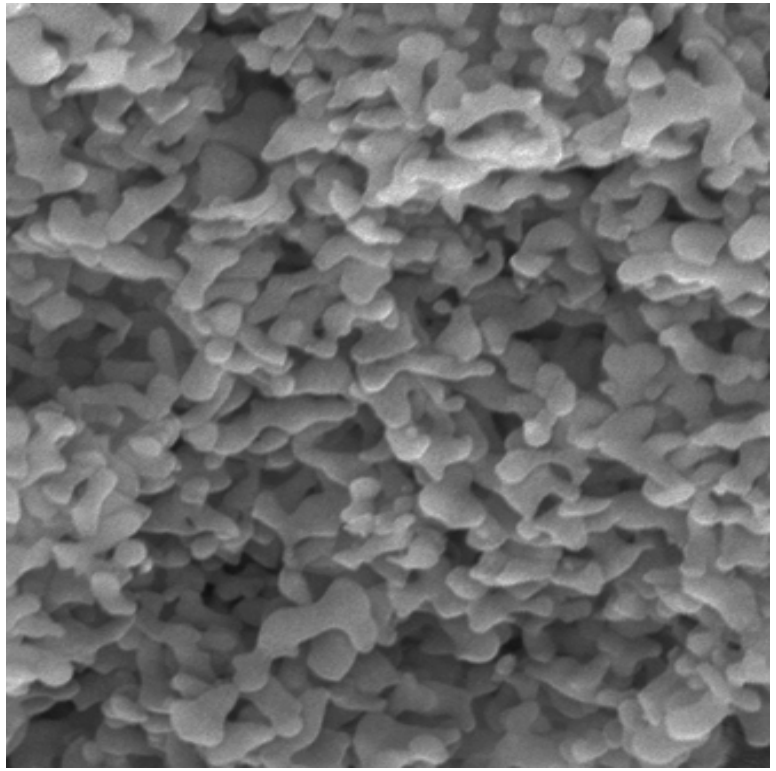




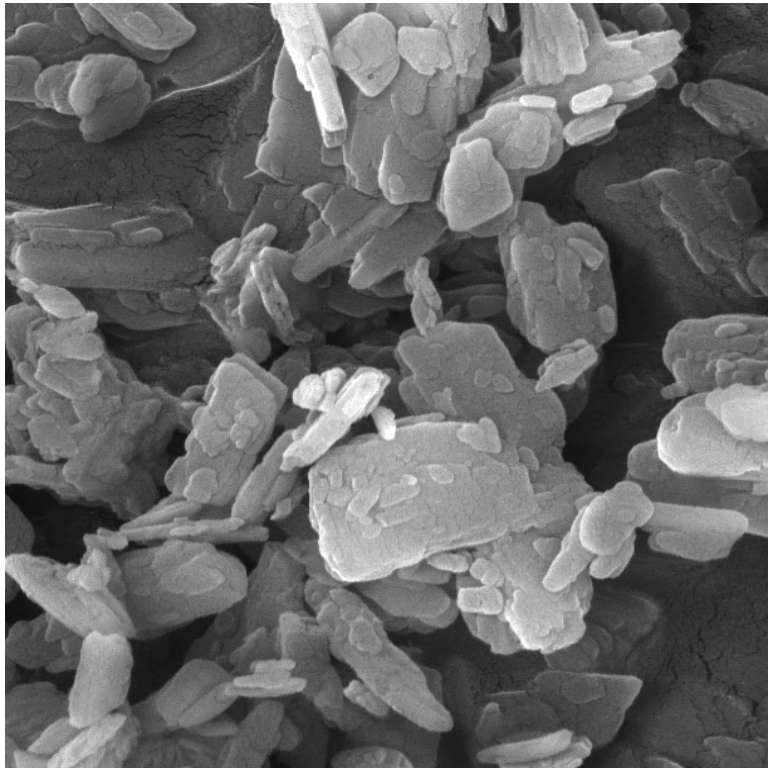
Purcision™ Morphology

The Purcision technology can be tuned to produce different forms of an API (same drug – different processing conditions)

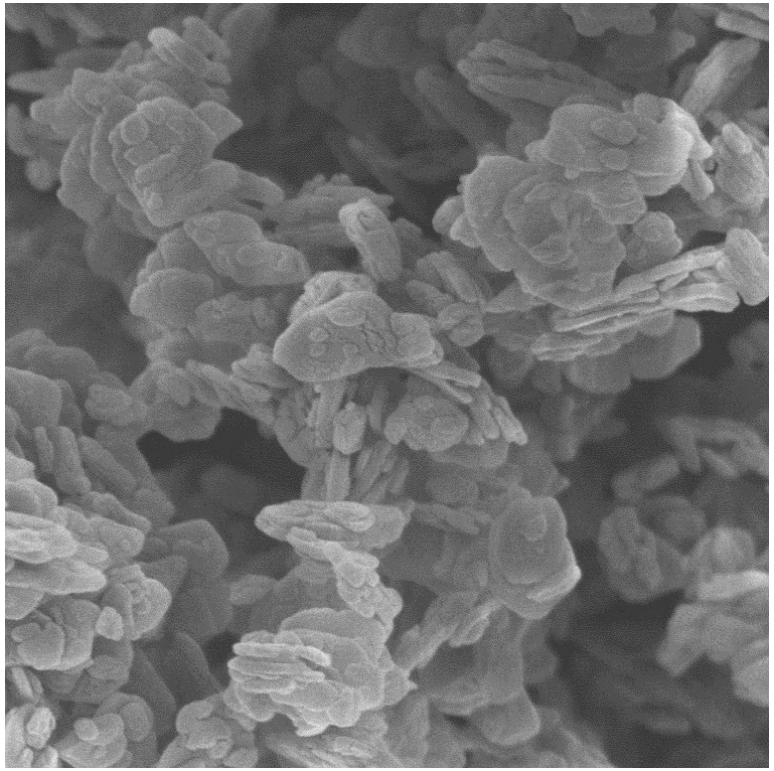
Amorphous



Co-crystal

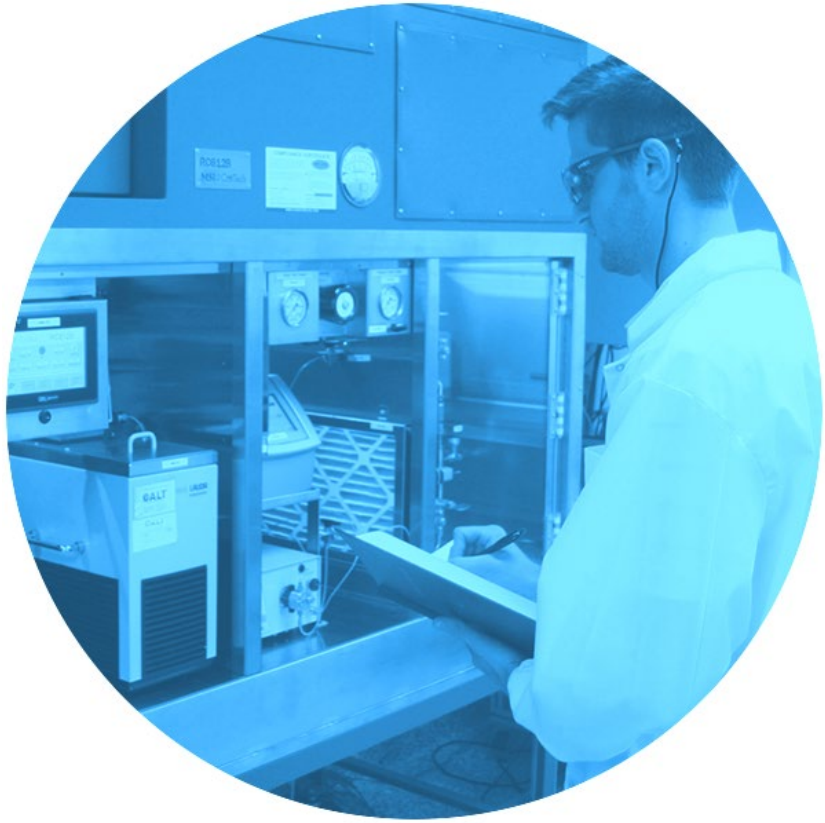


Crystalline



Purcision™ Addresses Numerous Drug Development Problems

- **Improves dissolution, pharmacokinetics and stability** of poorly-soluble drugs
- Enables multiple routes of delivery but is **excellent for local, targeted administration**
- **Low bulk-density, high surface area particles** result in **increased drug load and residency time** – especially useful for delivery into the lungs or nasal cavity
- **Pure drug** – no excipients required – especially useful when the amount of drug dosed is limited by available space (e.g. intratumoral injection) or by route of delivery (e.g. inhalation)
- Much **better control over physical particle attributes** compared to conventional micronization technologies



Potential Benefits of Purcision™ Inhaled Drugs

- Higher drug concentration and longer duration of action in the lungs compared to systemic standard of care treatments
- Improved safety – lower and adjustable systemic exposure
- More efficient dosing – lower dose can achieve effective concentration of drug in the lung
- Low COGS
- Purcision powders do not require “cold-chain”
- Fast and easy administration using a dry powder inhaler
- Improved shelf-life, temperature tolerance, and transportability compared to IV formulations
- Reformulates existing drugs and provides patent protection on improved formulations

Purcision™ Manufacturing

- **Commercial-scale** and **fully-validated cGMP equipment**
- Used to manufacture drugs for numerous clinical trials
- Low cost - high yields typically > 90% (much more efficient compared to spray drying)
- Minimal induction of electrostatic charges
- Milligrams to 100’s of kilograms
- **Excellent reproducibility** from POC to commercial production
- Virtually **eliminates residual solvents** – no secondary drying necessary

Purcision™ Equipment

POC and Development Units – RC612 and RC612B

- Supercritical fluid carbon dioxide: small batch production
- Milligram to gram quantities of 200mg to 50g

cGMP Manufacturing Units – cFPC-411 (Cytotoxic) and FPC-716 (Non-cytotoxic)

- Supercritical fluid carbon dioxide: continuous manufacturing
- Produced cGMP materials for multiple Phase II trials
- Production capacity of ~75 g/hr./system (drug dependent)

CT PES can process cytotoxic and non-cytotoxic with the Purcision™ Technology

Summary of Drug Development and Manufacturing Experience

- Clinical-stage, pharmaceutical drug developer and manufacturer located in Lawrence, KS
- Experience with >200 compounds across >10 drug classes
- Developed & manufactured several drug products that have completed or in the process of completing numerous Phase I/II clinical trials
- Extensive patent portfolio: >100 patents (e.g. composition of matter, formulation, method of administration, manufacturing processes and equipment, et. al.) used to support partners' drug development programs
- Technical leadership team with >150 years of drug development and manufacturing experience

Pharmaceutical Drug Development, Manufacturing & Program Management Capabilities

CritiTech has experience executing drug development programs and managing cross-functional drug development teams from discovery through clinical trial manufacturing.

Early-Stage Development → Formulation & Preclinical → Phase I → Phase II → Phase III → FDA Review

Phyton Biotech
US BIOTEST
iPHARMA
LOVELACE BIOMEDICAL
TEXAS
NanOlogy
KCAS
CardinalHealth™
PTL Particle Technology Labs
eurofins
Latham BIOPHARM GROUP
THE UNIVERSITY OF IOWA PHARMACEUTICALS
KU THE UNIVERSITY OF KANSAS
Catalent
MRIGlobal
DavosPharma
charles river
Æon Respire, Inc.
Sterigenics A Sotera Health company

Drug Development & Manufacturing Facilities

R&D Laboratories

Analytical Testing Laboratories

Separate cGMP Facilities

- Dedicated non-cytotoxic and potent
- Dedicated cytotoxic and potent

Non-cGMP and cGMP Manufacturing

- Purcision™ Technology
- Spray Drying
- Fill/Finish (blending, capsule filing, vial filling)
- Schedule drugs II-V
- Potent Drugs
- Grams to 100's of kilograms
- POC to commercial manufacturing







Material Characterization & Analytical Capabilities

CritiTech provides a suite of material characterization and analytical services to support our clients drug development projects from proof-of-concept through cGMP production. Our testing data and documentation is reviewed by experienced technical and quality staff to ensure it can be used to support regulatory filings.

- Analytical Method Development
- Formulation Development and Analysis
- Analytical Validation Studies
- Particle Size Analysis
  - Laser Diffraction – Liquid and Dry Powder Dispersion
  - Laser Obscuration
- Aerodynamic Particle Size Analysis
  - NGI
- Sorptometry – Surface Area Determination
  - BET
- Residual Solvent Determination
  - Gas Chromatography
  - HPLC
  - UV/Vis Spectroscopy
- Identification
  - FTIR
- Moisture Determination
  - Karl Fischer Titration
  - Loss on drying
- X-Ray Powder Diffraction
- Imaging
  - Optical microscopy with digital image analysis
  - Scanning Electron Microscopy (EDX)
  - Transmission Electron Microscopy (EDX)
- Quantification and Purity
  - HPLC (ELSD, UV, & PDA)
  - UV/Vis Spectroscopy
  - GC (FID & ECD)
- Bulk and Tapped Density of Powders
- Physical Chemical Properties
  - LogP, LogD, pKa, and pH dependent solubility
- Dissolution
  - USP Apparatus 1 and 2
- Potentiometric Titration
- Optical Activity
  - Polarimetry
- Calorimetry
  - DSC
- ICH Stability
  - Analytical Testing in-house
  - Storage Outsourced

Example of Clinical-Stage Drug Development & Manufacturing Experience

CritiTech has developed and manufactured oncology drug products with its Purcision™ Technology that are licensed to a partner, NanOlogy. CritiTech is a part owner of NanOlogy.

NanOlogy

Local Injection

Intraperitoneal
Intracystic
Intratumoral
Intravesicular

Inhalation

Topical

Advantages

No Drug-Related SAE's	High, Sustained, Local Concentration	Continuous Tumor Kill	Stimulation of Immune System

Example of Clinical-Stage Drug Development & Manufacturing Experience

CritiTech has developed and manufactured oncology drug products that have completed or are in the process of completing numerous Phase I/II clinical trials.

Product	Indication	Route of Delivery	Preclinical	Phase I	Phase II	Phase III
NanoPac® (Injectable Suspension)	Locally Advanced Pancreatic Adenocarcinoma	Intratumoral				
	Mucinous Cystic Pancreatic Neoplasms	Intracystic				
	Peritoneal Malignancies/Ovarian Cancer	Intraperitoneal				
	Prostate Cancer	Intratumoral				
	Non-Small Cell Lung Cancer	Direct Injection				
NanoPac® (Topical)	Cutaneous Metastasis	Topical				
NanoPac® (Inhalation)	Non-Small Cell Lung Cancer	Inhalation				
NanoDoce® (Injectable Suspension)	High-Risk Non-Muscle Invasive Bladder Cancer	Resection Bed Injection Intravesical Instillation				
	Muscle Invasive Bladder Cancer	Resection Bed Injection Intravesical Instillation				
	Renal Cell Carcinoma	Intratumoral				

Why Choose CritiTech as your Drug Development Partner?

- Experts in solubility and bioavailability enhancement
- Deep particle engineering expertise
- Proven track record – developed and manufactured multiple drugs for numerous clinical trials
- Clients include three “Top 15” pharmaceutical companies
- Technical leadership team with >100 years of industry experience
- Highly-skilled, professional, and collaborative technical staff
- Rapid project turnaround times
- Best-in-class customer service and high-quality deliverables

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Customer Feedback

"...we appreciate all the professionalism that you and your company have brought to the project..."

"...will certainly look for an opportunity to work with you in the future, your skills and work ethic are exemplary and unique..."

"...very impressed with the technical work..."

"...the material you spray-dried for us is better than what we have received from anyone else..."

"...thank you for the wonderful work that you have done on this project and we look forward to continuing to work with your company..."

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CritiTech®
Particle Engineering Solutions

Let’s connect

For inquiries please contact:

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President
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mmcclorey@crititech.com