

Corporate Presentation

Transforming Discovery Research into Innovative Medicines through Value-Based Partnership



***CreaGen, Inc.
299 Washington Street
Woburn, MA 01801***



Resources

- Established in 2003
- Corporate Headquarters: 299 Washington Street, Woburn, MA
- Scientists: Experienced Ph.D chemists with more than 15 years in the pharmaceutical industry
- Existing laboratories: 25,000 sq feet newly expanded facility with ~ 10,000 sq feet chemistry laboratory
- Equipment: Waters LC-MS, Varian NMR (300 MHz), Waters auto purification system, Agilent analytical and Preparative HPLCs, Yamazen and Biotage Combi-flash systems, TCAMs for parallel synthesis, Microwave synthesizer, Genevac evaporators.
- Library accessibility: online journal subscription, SciFinder subscription
Laboratory recording: Perkin Elmer ELN Software

Team

- **Raj (SB) Rajur, PhD, Founder & CEO**
30 Years of academic, industrial and management experience: ArQule, Millipore, Boston College, Northeastern University, Massachusetts General Hospital and Harvard Medical School
- **Hwa-OK Kim, PhD, Sr. Director of Chemistry**
30 Years of industrial and management experience: Aurigene Discovery Technologies, Molecumetics, Marion Merrell Dow and New Mexico State University
- **Norton P. Peet, PhD, Chair, SAB**
30 Years of industrial and management experience: Aurigene Discovery Technologies, ArQule, Aventis, Marion Merrell Dow, University of Nebraska and MIT
- **Robert Perni, PhD, Member, SAB**
35 Years of industrial and management experience: Sirtris Pharmaceuticals, Vertex Pharmaceuticals, Sterling Winthrop and Dartmouth College
- **Mark Tebbe, PhD, Member, SAB**
30 Years of industrial and management experience: Atlas Ventures, Quench Bio, Forma Therapeutics, Eli Lilly, University of Notre Dame

Team

- **David Barnes-Seeman, PhD, Director of R&D and External Alliances**

- At Harvard: Ph.D. with EJ Corey, postdoc with Stuart Schreiber
- 15 years at Novartis
- Extensive track record in successfully using SBDD, managing external CRO chemistry, and leading cross-functional discovery and preclinical development teams
- Expertise in Metabolic Disease, Neurodegeneration, Neuropsych, Immunology, Infectious Disease, Oncology, ImmunoOnc, Musculoskeletal
- Expertise in small molecules, bifunctional degraders, bioconjugates, and peptides

- **Donald Pang, PhD**

- An Imperial College graduate and former leader from Holton's taxol team
- Led multiple successful early discovery and GMP development teams (Amgen, Cubist, entrepreneurial/start-up teams)
- Extensive track record in early-stage discovery, process chemistry, and managing external CRO chemistry

- **A team of equivalently talented Ph.D. chemists**

Including two who did postdoctoral research at Harvard with Andy Myers

Expertise

Medicinal Chemistry:

- Oncology, Antiviral and Anti-infective, Cardiovascular, CNS, and metabolic diseases
- Small Molecules, High Throughput parallel library synthesis and purification
- Natural products, carbohydrates and unnatural amino acids
- Conjugation Chemistry
- Modalities:
 - Nucleosides and Oligonucleotides
 - Peptides and Peptide Nucleic Acids (PNA), Cyclic peptides
 - Novel Bicyclo[1.1.1]pentane (BCP) scaffolds and libraries
 - Macrocycles and Macrocyclic libraries
 - Antibody Drug Conjugates (ADC)
 - PROTACs and Molecular Glues

Analytical Chemistry:

- High Throughput purification and analysis

Why Collaborate with CreaGen

- CreaGen is a US based company located in Massachusetts
- CreaGen has an established track record with biotech and pharmaceuticals
- Interdisciplinary strengths at CreaGen ensure that customers receive the best value for their investments
- CreaGen can provide integrated services through its partners

CreaGen's Competitive Advantage:

- Flexibility, competitive pricing and fast turnaround time
- Dedicated project teams and segregation of projects
- Special request capabilities
- Automated parallel synthesis and separations
- Customized data input and output
- Multiple sample delivery formats: dry, in solution, standardized amounts/concentrations, multiple copies, etc.

Services

CreaGen performs services that are

- project-based
- FTE-based
- collaboration-based

- Medicinal chemistry and lead optimization
- Building blocks/scaffolds/key intermediates
- Customer tailored focused libraries
- High throughput purification and QC solutions

Our Partners

AstraZeneca  abbvie **AMGEN**[®]  MedImmune



FLEXPharma



magenta
THERAPEUTICS



Debiopharm Group[™]
WE DEVELOP FOR PATIENTS


MICROBIOTIX
Inc.

biota[™]
TECHNOLOGY



 **Dyne**
THERAPEUTICS


KalVista
Pharmaceuticals

 **DANA-FARBER**
CANCER INSTITUTE



Joslin Diabetes Center

Asahi **KASEI**

 National Center
for Advancing
Translational Sciences

 **NIH** **NIAID**



 **OCTAGON**
THERAPEUTICS

MaxThera
Beating Antibiotic Resistance By Design

 **Calibr**
at Scripps Research

TERRA 

 **UrSure**

 **CREAGEN** INC

Case studies: SBDD & CRO FTE mgt by CreaGen employees

Neprilysin: Preclinical Candidate Delivery (DBS)

Project requirements:

- Lead team and mostly outsourced chemistry to deliver back-up candidates that mitigated PK and BBB penetration issues

Accomplishments:

- Used Maestro to design & deliver two candidates
- Managed 6 FTEs in India to effectively contribute to candidate delivery
- Led cross-functional discovery team to deliver two candidates into preclinical development
- Led cross-functional preclinical development team to deliver IND-package

HCV polymerase NS5B: Preclinical Candidate Delivery (DBS)

Project requirements:

- Lead team and outsourced chemistry to deliver preclinical candidates

Accomplishments:

- Used Maestro to design & deliver one candidate
- Managed 6 FTEs in India to effectively contribute to candidate delivery
- Led cross-functional discovery team to deliver two candidates into preclinical development
- Led cross-functional preclinical development team through non-GLP tox

Case studies: SBDD & CRO FTE mgt by CreaGen employees

Protein Tyrosine Phosphatase 1B: Preclinical Candidate Delivery (DBS)

Project requirements:

- Soon before presumed no-go decision, was asked to lead team in a final push

Accomplishments:

- Used Sybyl to design 100 pM singly charged inhibitor with superb PK properties
- Led cross-functional discovery team to deliver four candidates into preclinical development
- Led cross-functional preclinical development team & cross-disease-area teams to reach decision points

Factor X1a: Preclinical Candidate Delivery (DBS)

Project requirements:

- Lead lab & CRO to overcome potency, selectivity, & PK issues to deliver a preclinical candidate

Accomplishments:

- Used Maestro to design multiple classes with rigidification in a linker region
- Taught associates SBDD and guided them, resulting in a co-first-author publication for one:
 - Lorthios, E.; Roache, J; Barnes-Seeman, D et al. *J. Med. Chem.* **2020**, *63*, 8088-8113.
- Delivered the only candidate from the project into preclinical development
- Managed 6 FTEs in India to effectively contribute to candidate delivery

ACC: Preclinical Candidate Delivery (DBS)

Project requirements:

- Lead lab to overcome potency & PK issues to deliver a preclinical candidate

Accomplishments:

- Used Sybyl to design, then synthesized our 1st in vivo tool compound + a preclinical candidate

Case studies: SBDD & CRO FTE mgt by CreaGen employees

Cubist Pharmaceuticals: early discovery engine

Project requirements:

- Increase effectiveness of early discovery at Cubist

Accomplishments:

- Identified lack of SBDD as a key company limitation at the time & brought SBDD to Cubist by championing and leading two projects into structurally-enabled lead optimization
- Transformed Cubist from exclusively peptide antibacterial based research into an organization with small molecule SBDD capabilities: Managed ~ 6-10 FTEs at two CROs

Alfalfa Pharmaceuticals: VP R&D (DP)

Project requirements:

- Build out chemistry lab, hire & mentor PhD/MS/BS chemists, and manage CRO collaborations

Accomplishments:

- Use of bicyclo[1.1.1]pentane (BCP) motif as bioisotere in anti-infective research. Managed 12-15 FTEs at 3 CROs

Propel Sciences, LLC: Co-Founder, CSO (DP)

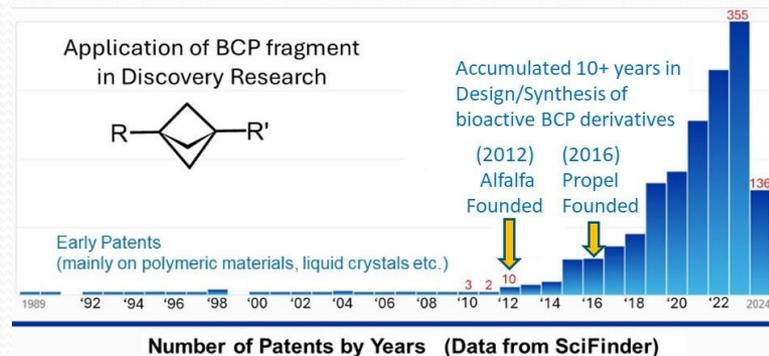
- Application of BCP and other rigid bicyclic homologs in discovery of novel therapeutic agents (explored 9 projects)

Successful GMP campaigns (DP)

At Amgen: Managed 3 FTEs in a US CRO to successfully deliver a 1.8 kg GMP batch

At Cubist: Improved a three-step process for a Neulasta precursor from 60% to 94% purity

content and successfully transferred to and managed 2 FTEs at a US CRO to deliver a 2 kg GMP batch



Case studies: Synthesis and Lead Optimization Representative Examples

CS I: Institute (Antiviral): Lead Optimization

Project requirements:

- Final 6-month push on the hardest nucleoside targets that had failed prior attempts

Accomplishments:

- Multiple first-ever in nucleoside chemistry bond constructions

CS II: Multinational Pharma (Oncology) : Lead Optimization

Project requirements:

- Design and optimize leads, synthesize novel analogs of the leads for weekly screening
- Provide all medicinal chemistry expertise to client in designing new analogs and libraries. Explore new synthetic routes.

Accomplishments:

- 3-Year collaboration FTE based contract
- Provided more than 600 compounds and many novel scaffolds during the tenure of the program. True extension of customer's chemistry program

CS III: Multinational Pharma : Antibody Drug Conjugates (ADC)

Project requirements:

- Design and synthesize novel linkers. Conjugate novel small molecules and drug candidates to linkers. Introduce reactive functionalities on the linker to conjugate to antibodies.
- Provide conjugation chemistry expertise to client. Synthesize libraries of small molecules. Explore new synthetic routes.

Accomplishments:

- 3-Year FTE based collaboration
- Provided several conjugates to client for screening. Developed several novel hydrophilic molecules to conjugate to antibodies to minimize aggregation. True extension of customer's ADC program

CS IV: Biotech. (Antivirals):

Project Requirements:

- Synthesize Novel analogs of Tenofovir, Filociclovir, Cidofovir, and Dolutegravir.
- Conjugation of Tenofovir analogs for developing a point of care test to monitor and promote adherence to PrEP for HIV prevention.

Accomplishments:

- Two-year collaborations: Developed efficient routes for linkers and modified antiviral drugs.

CS V: Biotech. (Diabetes):

Project Requirements:

- Synthesize various Plasma Kallikrein Reference compounds
- Provide multi-gram quantities of compounds for in vivo studies with aggressive timeline

Accomplishments:

- Two-year collaborations: Developed efficient route with fewer synthetic steps to synthesize the reference compounds.

CS VI: Biotech. (Anti-infective): Lead Optimization

Project requirements:

- Supported the client's chemistry team for all aspects of synthesis, route scouting and library synthesis
- Provide all medicinal chemistry expertise to client in designing new analogs
- Develop SAR

Accomplishments:

- Six-year collaboration: supported client's Federal grants and contracts

Case study: Representative Academic/Government Examples

Government Contracts:

a) NCATS: DEL project

- Synthesis of 96 boronic acid conjugated DNA encoded libraries
- Completed the synthesis and purification of 96 unique library compounds within budget and delivered the compound on time

b) NIAID: 7-Year contract for preclinical Antiviral and HIV Program.

Project requirements and accomplishments:

- Design and Synthesis of antiviral and anti-infectives
- Ongoing program

c) NCATS: Synthesis of commercial preclinical candidate

Project requirements and accomplishments:

- Synthesis of 10 grams of ERK inhibitor
- Completed the synthesis within budget and delivered the compound on time.

d) DOD: 5- year IDIQ contract for Antiinfective programs.

Project requirements and accomplishments:

- Completed two task orders to synthesize 22 novel small molecules
- Completed the synthesis and delivered the products on time within the allocated budget

CreaGen New services

Hybrid Model:

- FTEs from Woburn facility supplemented with additional FTEs from established CRO partners in India
- Managed by CreaGen Project manager in Woburn
- Integrated Drug Discovery (IDD) services provided through the Indian CRO partner
- FTE management, data analysis, timely delivery, and regular progress updates are conducted through US facility

Managed Outsourcing Model:

- All FTEs at established CRO partners in India are managed by CreaGen Project manager at Woburn
- CreaGen can help recruit offshore CROs with relevant expertise
- Seamlessly take over the clients existing FTE programs and provide the same comprehensive services
- FTEs can be involved in IDD programs or just synthesis
- FTE management, data analysis, timely delivery, and regular progress updates are conducted through US facility

Compound Management:

- Provide compound management services to virtual and small to midsize biotech and pharmaceutical companies through US-site

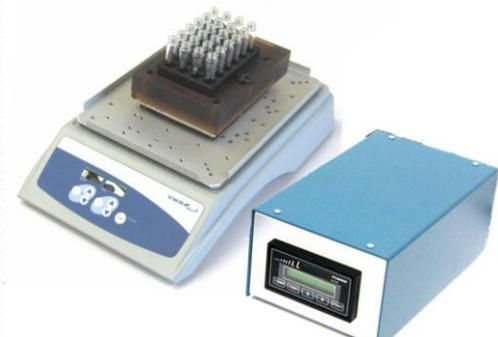


CreaGen Infrastructure & Equipment



CreaGen parallel synthesis workstations

- 1, 2 and 4 position heater/shakers
- Heating up to 150°C
- Variable speed
- Timed shutoff
- Integration with automation



Synthesis workstations: cont'd



Lyophilizer



SmartFlash AI 580S



High speed evaporator
GeneVac (EZ₂)

Purification Systems



Mass directed purification



Biotag Isolera

CreaGen analytical workstations



Varian, 300 MHz NMR



TQ- LCMS

Summary

- Competitive pricing
- Excellent communication
- Quality services
- On-time delivery
- Customer satisfaction