Innovative Pharmaceutical Solutions for Discovery Chemistry, Biology and cGMP Manufacturing
Overview

• Serving biotech and pharma community since 1998

• Proven track record of advancing small molecules from initial hits to IND

• Two sites in the major biotech hub of US (San Francisco area):
  • Santa Clara – chemistry and biology discovery services
  • Santa Rosa – FDA inspected kilo lab facility; cGMP

• Cutting edge technology and operations

• 60 scientists (50% Ph.D.)

• Completely US-based

• No competing drug discovery efforts
## Services Platform

### Nanosyn Discovery Services

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<th>Target to Hit:</th>
<th>Hit to lead:</th>
<th>Lead optimization:</th>
<th>IND Support:</th>
<th>API manufacturing</th>
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| • Target to Hit assay development  
• HTS validation  
• Fragment Screening  
• “Smart” HTS utilizing fragment screening technology | • Proprietary active series development  
• Structure activity relationship  
• Selectivity testing | • Structure – activity relationship for two lead series  
• Back-up series  
• Cell-based activity testing | • Work with network of CROs to support identified leads through IND submission  
• Systems in place to follow FDA guidance and audit trail | • Process and Analytical development  
• cGMP kilo lab; Phase I through commercial  
• DEA regulated APIs  
• Commercial product |

### Nanosyn Development Services

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<th>Pre-Clinical Development</th>
<th>Clinical Studies Phase I-III</th>
<th>Drug manufacturing</th>
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<td><strong>API manufacturing</strong></td>
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Nanosyn Unique Capabilities

Proprietary focused libraries platform
- Enables highly efficient support of high speed hit expansion, hit to lead, lead optimization, as well as computational drug discovery, fragment drug discovery, structural biology driven, etc. programs
- Utilized by over 100 clients’ programs
- Highlighted in major industry conferences; recognized as the “best in industry”

World leader in microfluidics mobility shift technology
- Platform was built with over $100M investment
- Largest collection of networked microfluidics HTS instruments in the industry
- Largest portfolio of biochemical assays run on microfluidics instruments

Programs support early discovery through API cGMP manufacturing
- cGMP kilo lab; over 30 years experience as an FDA registered facility; excellent regulatory history
- DEA bulk manufacturing license
- Commercial product – Nanosyn is the supplier of the major component of a medical device for a Big Pharma company
Nanosyn Solutions from Start to Finish

Discovery chemistry
• Medicinal chemistry
• Synthetic chemistry
• Hit-to-Lead
• Fragment based lead discovery
• Focused libraries
• Custom synthesis
• Scale up

Discovery biology
• Assay development
• High-precision HTS/profiling
• Validation studies
• Target production
• Cell-based assays
• Molecular biology

Process chemistry and cGMP manufacturing
• Process R&D
• Analytical method development
• Kilo-scale production
• Phase I to commercialization

Nanosyn Headquarters
Santa Clara, CA

Nanosyn cGMP Site
Santa Rosa, CA
Innovative Pharmaceutical Solutions for Discovery Chemistry, Biology and cGMP Manufacturing

NANOSYN Chemistry
A Solid Core Offering in Medicinal and Synthetic Chemistry

Capabilities

- State-of-the-art facilities; 40,000 square feet; 39 chemical hoods
- One of the highest ratio of instrumentation per FTE in the industry
- Rapid access to starting materials (in house chemical stock > 80,000 reagents)
- Controlled substances RD and analytical licenses (Schedule II-V)

Services

- Medicinal chemistry (hit to lead, lead optimization)
- Synthetic chemistry
- Fragment-based lead discovery
- High value Focused libraries
- Custom synthesis of reference compounds, metabolites, substrates, etc.
- Rapid scale-up (up to 10 kg)
- HPLC Purification
“Chemistry on Demand” – Proprietary focused libraries platform

- Industrialized processes – proprietary automated processes for synthesis/characterization flow
- Infrastructure allows for purification, drying, analysis, data processing, and custom formatting of up to 3,000 compounds per week for multiple projects
- “Quality build” approach; automated data analyses and reports generation; 100% deliverables undergo QC

Cutting edge technologies

- CLND compound quantitation; single crystal X-ray for crystal packing analysis
- Microchemistry approach; solid phase synthesis techniques
Innovative Pharmaceutical Solutions for Discovery Chemistry, Biology and cGMP Manufacturing

NANOSYN cGMP Manufacturing
Nanosyn’s manufacturing capabilities began as a joint venture in 2009 with the France-based PCAS group.

The Company has six GMP suites, two class 10,000 clean rooms, and a state-of-the-art R&D facility.

The facility has been FDA-registered since 1979 and the Company has a DEA bulk manufacturing license.

Commercial product with one of the top 25 pharmaceutical companies.

In 2015 Nanosyn acquired the remaining stake from the PCAS group and now owns 100% of the manufacturing business.
Based upon the heat output the Adiabatic temperature rise is ca. 95°C.

Small amount of accumulation

Heating period immediately following end of dosing

• Process Identification
• Process Development
  • Salt Screening
  • Reference Standards
• Analytical Method Development and Validation
  • Scale-up Services
  • Multi-Step Syntheses
  • Technology Transfer
• Custom Polymer Synthesis
• Custom Engineering Solutions

Chemical Development; non-GMP and cGMP API Synthesis
A unique feature of the manufacturing site is that it allows for flexible, personal and cost effective services (kilo lab), and has cGMP capability designed for clinical trials and small scale commercial APIs.

- Regulatory and CMC section support
- Experienced team with decades of successful track records in the industry; capable of solving the most challenging chemical development issues
- DEA analytical and bulk manufacturing DEA license Schedule II-V
- Commercial product – Nanosyn is the supplier of the major component of a medical device for a Big Pharma company
Quality Assurance

• Quality system designed for clinical trial & commercial APIs

• The facility has been FDA registered since 1979 and was last inspected by the FDA in 2015; no 483 observations

• Overseen by a quality assurance director, an analytical development manager, and a quality control manager all with over 15 years of experience
Innovative Pharmaceutical Solutions for Discovery Chemistry, Biology and cGMP Manufacturing

NANOSYN Biology
Biochemical Screening and Profiling
- HTS, Fragment screening
- Dose response studies
- Selectivity Profiling

Biochemical Assay development
- Target Protein expression
- Substrate Identification
- Assay validation

Biochemical MoA Studies
- Kinetic studies (Ki, Kinact, residence time)
- Dialysis and rapid dilution studies
- Substrate competition studies

Cell-based Screening and Profiling
- Medium to High throughput screening
- Dose response studies
- Drug combination studies
- Selectivity cyto-toxicity Profiling

Cell based assay development
- Cell viability and proliferation assays
- Apoptosis/necrosis assays
- In-Cell ELISA and biochemical assays
- In-Cell Active site occupancy assays

Development of new Cell models
- Generation of target-specific cell models
- Reporter cell lines
Discovery Biology Services – Unique Capabilities

Nanosyn - the World Leader in Microfluidic Technology

- The platform is based on a $100M investment
- Largest collection of networked, climate controlled microfluidic HTS instruments in the world
- Proprietary library of peptide substrates – largest in the world; enables development of new assays within 10 business days or faster
- Largest portfolio of biochemical assays run on microfluidics instruments
- Unique ability to perform Mechanism of Action kinetic studies (ongoing collaboration with several top 25 pharma companies during last five years)
- Broad kinase, epigenetic and protein homeostasis experience; high throughput screening capabilities (over 100,000 compounds per day)
Biochemical Screening and Profiling - >500 Assays

- DUBs
- PDEs
- Kinome
- PMTs
- HATs
- HDACs
- KDMs
Added Value to Clients’ Research Programs

Epigenetic Research Initiative

- Collaboration with Mayo Clinic
- Cell-based screening against Nanosyn’s epigenetic compound library
- Disease Pathway Identification via cross-interrogation of cell data and biochemical selectivity profiles of the active probes
- Pathway analysis via probe combination studies
- Supply of active molecular probes for the follow up cell-based and animal studies

Nanosyn is a co-author in a key publication in Nature Biotechnology
“Targeting the Untargeted Kinome: The GSK Published Kinase Inhibitor Set”

- Thorough characterization of the Published Kinase Inhibitor Set
- Open resource platform for academic and commercial researchers in the pre-clinical phase of drug discovery through partnership with teams around the world
- Combined effort between Nanosyn, GlaxoSmithKline, the National Institutes of Health, the European Molecular Biology Laboratory–European Bioinformatics Institute, and the Structural Genomic Consortium
Biology Technological Capabilities

- Microfluidics
- Data center
- Fluorescence (all types)
  - Luminescence
- Compound handling
- Cell culture
- Cell based assay robotics
Why Come to Nanosyn?

- **Quality:**
  The quality and integrity of the science and technical processes on which we partner with clients is paramount.

- **Communication:**
  Efficient, effective communication is fundamental to the success of all client projects.

- **Service partnership:**
  Clients are in full control of all IP.

- **Time is of the essence:**
  On-time delivery of results and materials is second only to ensuring their quality.

- **Innovation:**
  It is fundamental to our clients’ success that we continuously add the most recent science and technology to our knowledge base and lab instrumentation.
Nanosyn Approach to Collaboration

Since 1998 Nanosyn has successfully engaged in numerous relationships with partners ranging from virtual Biotech/Academia to major Biotech/Pharma

- Nanosyn Contract Services
  - Customers can access discrete capabilities on a fee for service basis or by FTE

- Nanosyn Partnership
  - Collaborators can outsource complex activities or entire programs
  - Start with either Nanosyn intellectual property or partner’s ideas

With extensive capabilities in place, our objective is to be a trusted, reliable partner in drug discovery.
Thank you!

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