

# SAFC Pharma™

## Contract Development & Manufacturing

COMMERCIALIZATION

PHASE 2

PHASE 1

PRE-CLINICAL

Presented to CBDAIF

Date April 29th, 2010

**SAFC** Pharma™  
Inspiring Science

[www.safcpharma.com](http://www.safcpharma.com)

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SIGMA-ALDRICH™

# Sigma-Aldrich Corporation

## Key Facts

- **Headquarters: St. Louis, MO**
- **\$2.1 Billion In Sales (2009)**
- **88,000 Customer Accounts**
- **1,000,000+ Individual Customers**
- **In business > 50 Years**
- **7,700 Employees (3,500 in US)**
- **31 Production Sites (10 Countries)**
- **20 Production Sites in U.S.**
- **7 Worldwide R&D Centers**
- **10+ Congressional Districts Represented**
- **Manufacture over 46,000 of 100,000+ Chemical Products**
- **“Top 10” Fine Chemicals Supplier**
- **220 Patents**
- **846 Product Licenses**



# Sigma-Aldrich Corporation

## The Sigma-Aldrich Family

*Mission Statement:*

*“Enabling Science to improve quality of life”.*

### RESEARCH

2/3 of Sales

#### Research Essentials

Customized account management for economic buyers in research organizations

#### Research Specialties

Traditional broad line of specialty products for laboratory scientists

#### Research Biotech

Innovative, first-to-market research tools for life scientists

### MANUFACTURING

1/3 of Sales

**SAFC**<sup>®</sup>

Inspiring Science™

**Custom development & manufacturing services group for industrial customers**

- SAFC Pharma™
- SAFC Biosciences™
- SAFC Supply Solutions<sup>®</sup>
- SAFC Hitech™

**SAFC** Pharma™  
Inspiring Science

# SAFC - 3 Areas Focused on Pharma Applications

**SAFC** Pharma™  
Inspiring Science

**Clinical & Commercial Contract API  
Manufacturing Services**

**180 API's in 2009**



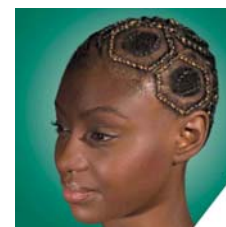
**SAFC** Biosciences™  
Accelerate Success™

- **Critical raw materials for cell culture**  
**Cell-culture medias**  
**Serum and serum-free medias**



**SAFC** Supply Solutions™  
Inspiring Science

- **Customized supply chain services**  
**Kg quantities of key raw materials**  
**10,000 Suppliers**

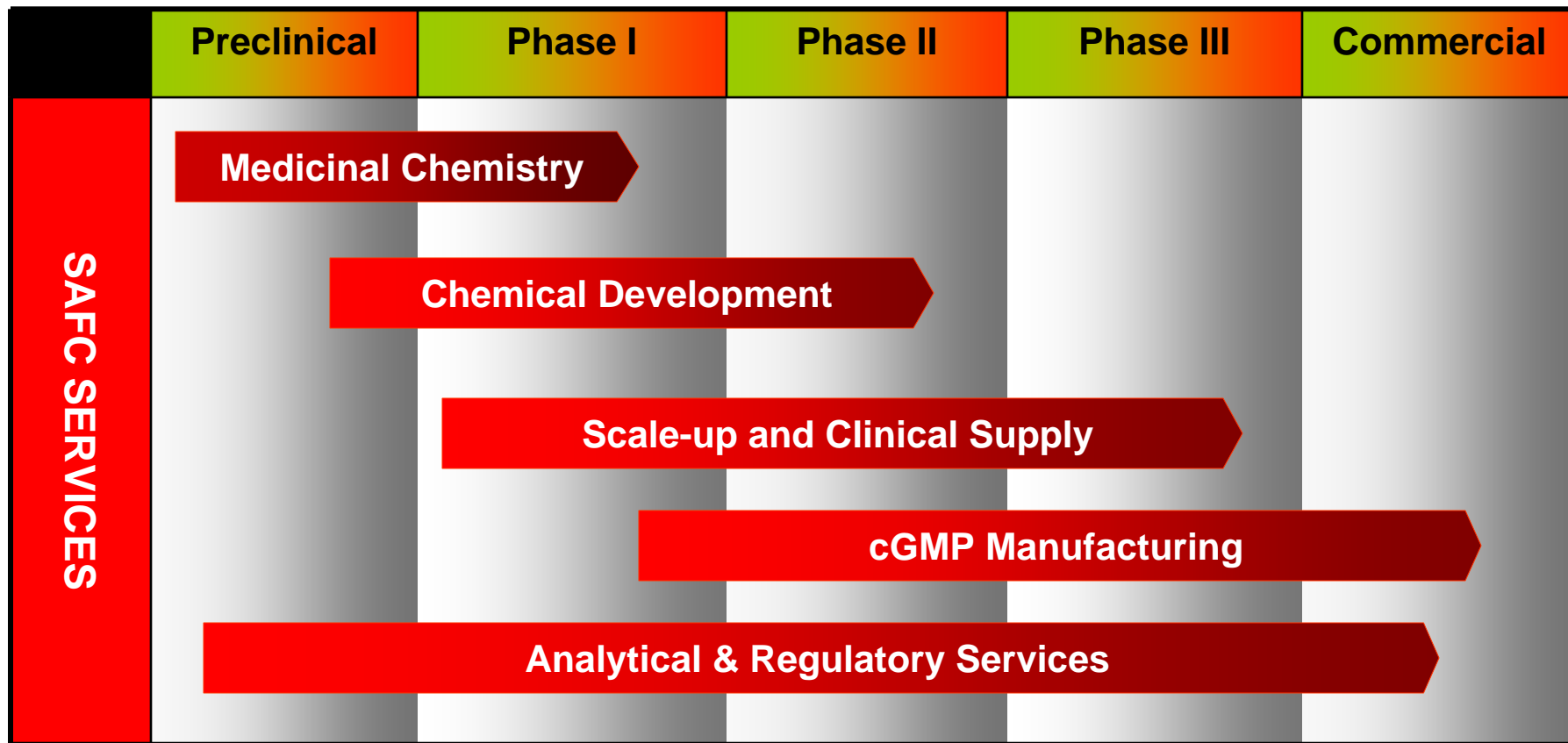


**SAFC** Hitech™  
Enabling Technology

- **Unique chemistry applications for high-  
technology industry**



# SAFC Pharma Services Offering



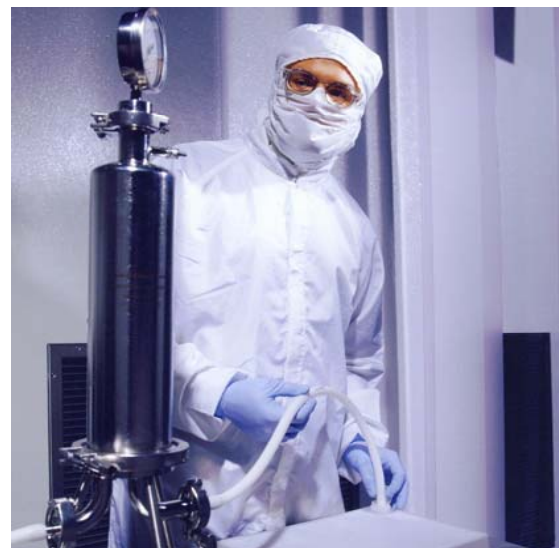
## Pharmaceutical

### Small Molecule API's



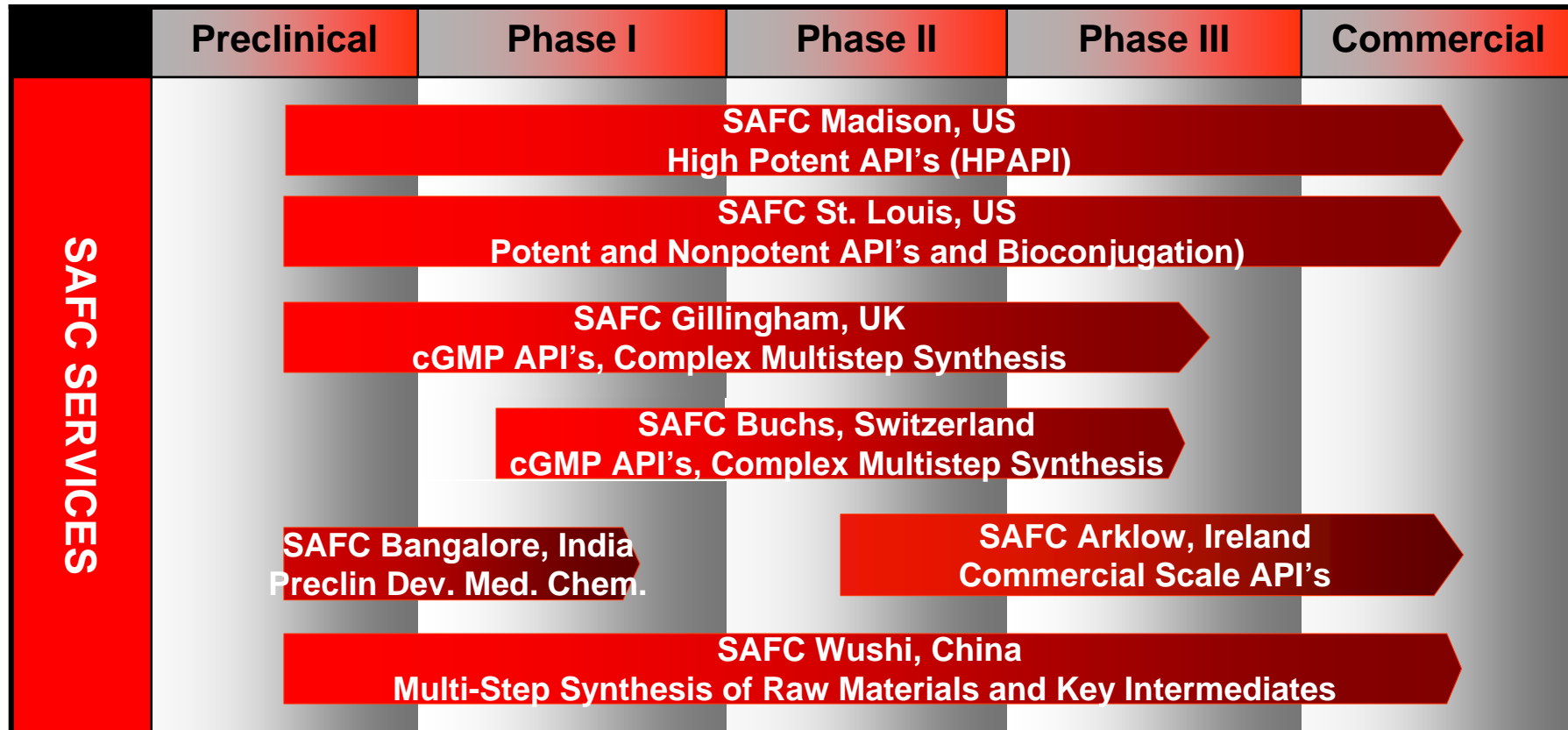
## Biopharmaceutical

### Large Molecule API's



# SAFC Pharma

## Global Small Molecule API Capabilities



# SAFC Pharma Madison

## Project Focus

- **Development and manufacturing of potent substances**
- **APIs only**
  - No Fine Chemicals or catalog products.
- **Highly biologically active materials**
  - Vitamin D analogs & Steroids
- **Small market volume or therapeutic APIs**
  - Acute indication
  - Select formulations (topicals, ophthalmologics)
- **Cytotoxic materials**
  - Traditional chemotherapeutics
  - Anti-cancer materials
- **Commercial volumes**
  - Fit manufacturing capabilities (~ 50 kilogram maximum batch size)
- **Complex chemistries and long synthetic processes**



# SAFC Pharma Madison

## Services Overview

Service Type	Preclinical	Phase I	Phase II	Phase III	Commercial
<b>Chemical Development</b>		<ul style="list-style-type: none"> <li>• Chemical Feasibility</li> <li>• Process Development</li> <li>• Qualification</li> <li>• Scale Up</li> </ul>			
<b>Analytical Development</b>		<ul style="list-style-type: none"> <li>• Analytical Method Development</li> <li>• Impurity ID and Characterization</li> <li>• Method Validation</li> <li>• Stability Testing</li> </ul>			
<b>Manufacturing Services</b>		<ul style="list-style-type: none"> <li>• Small scale (non-GMP) supply</li> <li>• cGMP Kilolab Manufacturing</li> <li>• cGMP Pilot Plant Manufacturing</li> <li>• cGMP Hydrogenation Suite</li> <li>• Campaign summary reporting &amp; documentation</li> </ul>			
<b>Regulatory Affairs</b>		<ul style="list-style-type: none"> <li>• DMF Submissions</li> <li>• CMC Sections</li> <li>• cGMP Compliance</li> <li>• Scientific &amp; Technical Writing</li> </ul>			

# SAFC Pharma St. Louis

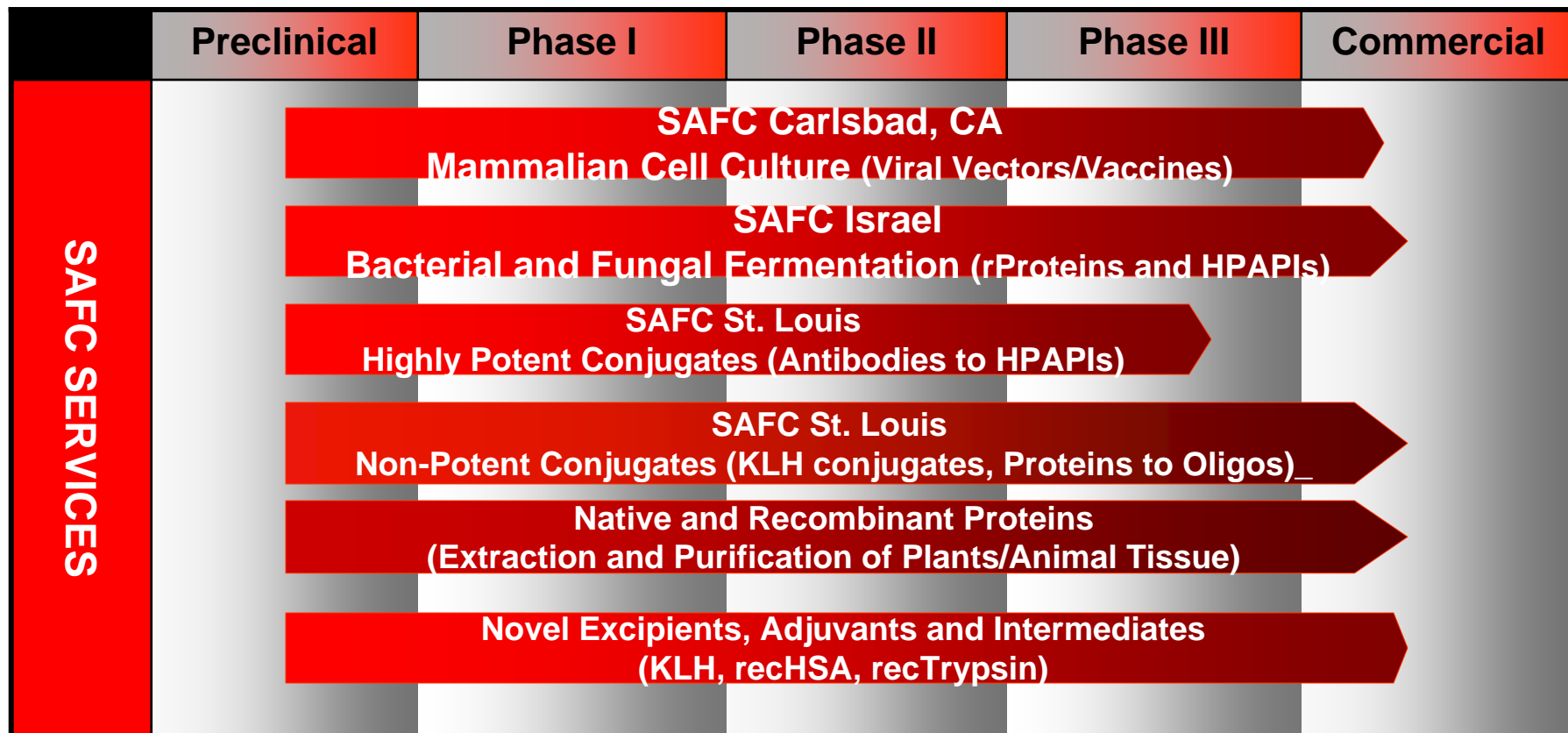
## Potent API Conjugate Technology

- **Combines SAFC's chemical and biologic expertise**
  - Small molecule HPAPI
  - Containment engineering
  - Regulated biologics manufacturing
  - Quality Control
- **HPAPI + targeted delivery molecule**
  - For example with Monoclonal Antibodies
  - Non-biologic conjugations
- **Builds on 30 years of experience**
  - Non-potent conjugates



# SAFC Pharma

## Biopharmaceutical Capabilities



# SAFC Pharma

## Viral Vectors/Vaccines – Carlsbad, CA



### Offices/Labs

Offices  
Process/Product Development  
Quality Control  
Laboratory Services

### Manufacturing

cGMP Manufacturing



# SAFC Pharma

## Carlsbad Site Overview

- **Leading CMO for viral intermediates and final drug product**
- **Manufacturing facility designed for viral drug products - containment BL-2+**
- **Completed more than 60 audits since 2001**
- **Vaccines/Gene Therapy Focus**



# SAFC Pharma

## Carlsbad - Service Offerings

- **Process/Assay Development Services**
- **Intermediates and final products**
  - **Master and Working Viral Banks/Cell Banks**
  - **Special expertise with disposable manufacturing systems**
  - **Successfully manufactured over 400 cGMP lots**
  - **Manufactured product for North America, Europe, and Asia**
- **Mammalian cell cultures to grow cells and produce high-titer product**
- **Sterile Formulation, Fill, & Finish**
  - **Dedicated ISO6/class 1000 Fill Suites**
  - **EU and FDA compliant**
  - **Current capacity of up to 10,000 vials per day**
  - **Various container/closure systems**



# SAFC Pharma St. Louis Transgenics

- One of the industry's only cGMP transgenic facilities
- One of the world's largest transgenic facilities (*up to 5,000 KG of biomass/week*)
- Completely segregated plant and animal operations:
  - Prevents cross contamination
  - Facilitates transition from animal sourced to plant sourced biologics
- Builds on 50 years experience in extraction/purification development and scale-up



# SAFC Pharma St. Louis

## cGMP Manufacturing Capability for Biologicals

### Upstream Extraction



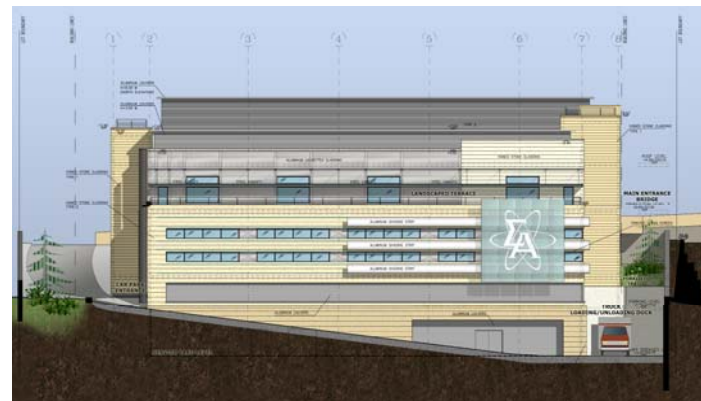
### Downstream Purification



# SAFC Pharma Israel

## Bacterial and Fungal Fermentation

- **Process development and commercial manufacturing focused on HPAPIs and recProteins:**
  - Secondary metabolites (antibiotic like molecules)
  - Cytotoxins
  - Large molecule proteins
  - Cell wall fragments (Lipid A)
- Dactinomycin manufactured at site since 1980's
- Biosafety Level 2
- Builds on over 30 years experience in fermentation derived products
- Complements Madison, SAFC's multi-step organic synthesis facility



# SAFC Pharma

## Quality Organization

- **SAFC Quality and Regulatory Staff**
  - >200 Quality and Regulatory Professionals within SAFC
  - >400 Quality and Regulatory Professionals within SIAL
- **Experience SAFC Adds**
  - **Manufacturing (small and large molecule)**
    - Manufacture 49 Commercial APIs
    - Manufacture 150 Clinical Phase APIs
  - **Regulatory**
    - Supported 4 Biologic clients with Type C FDA Meetings
    - Over 200 active DMFs filed globally
    - Experienced in BRS Program APHIS permits for plant transgenics transport across state and international borders
    - USDA Inspected and Approved for handling of plant transgenics
    - EU Audited for QP (Qualified Persons) for transgenics
    - Since 2000 we have hosted >40 Regulatory Inspections Globally all with positive outcomes
      - 26 of the 38 were FDA Inspections (22 GMP and 4 PAI)

# SAFC Pharma

## Project Management Philosophy

- **Project Manager Functions**
  - **Primary Point of Contact**
  - **Works with Manufacturing Team Leader, Analytical, Manufacturing & Regulatory Affairs**
  - **Coordinates Activities**
  - **Provides Weekly Summary Reports**
- **Gantt Chart Tracking**
- **Contract Management/Business Development**
- **PMP Certification**
- **EVMS Experienced**



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*Thank You*