

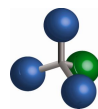


*DSM InnoSyn™  
route scouting services*

**Dr. Oliver May**

Business Manager  
InnoSyn™ route scouting services  
[oliver.may@dsm.com](mailto:oliver.may@dsm.com)  
Phone +31-464760551

**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



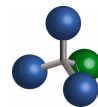
**CONFIDENTIAL**

**Unlimited. DSM**



# Who We Are

**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*

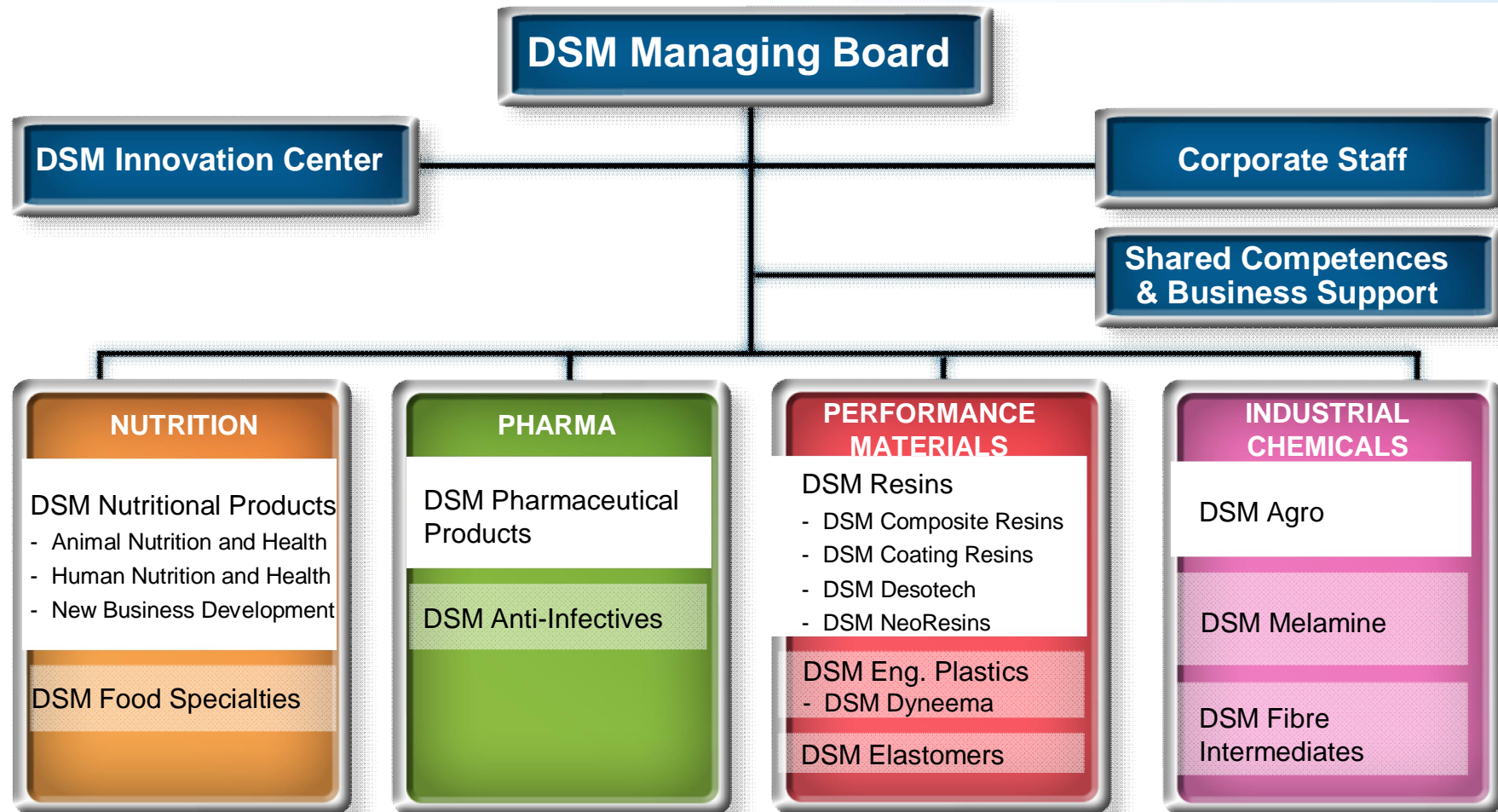


CONFIDENTIAL

Unlimited. **DSM**



# DSM Organizational Chart



DSM Innovation Center



# DSM recognized for sustainability



2009 Dow Jones Sustainability World Index  
#1 in the Global Chemical Industry

“We are continuing to make our operations ever safer and reduce our eco-footprint ever further. We are not compromising our commitment to meeting the ‘triple bottom line’ of People, Planet and Profit. We are sticking to our values, beliefs and principles.”

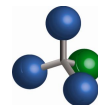
DSM Managing Board, September 4, 2009



World Business Council for  
Sustainable Development

Good Corporate Citizenship  
Endorse obligations in the  
chemical industry’s International  
Responsible Care® Program

**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



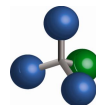
CONFIDENTIAL

Unlimited. **DSM**



# DSM Corporate Financials

	2009 (millions)	2008 (millions)
Key Figures:		
Sales (Continuing Operations)	€ 7,732	€ 9,079
Operating Profit	€ 443	€ 903
Net Profit Excluding Exceptional Items	€ 244	€ 608
Net Profit	€ 337	€ 577
Capital Expenditure	€ 467	€ 739
Per Ordinary Share:		
Net Earnings Excluding Exceptional Items	€ 1.44	€ 3.64
Dividend	€ 1.20	€ 1.20
Workforce (At Year-End)	22,738	23,539

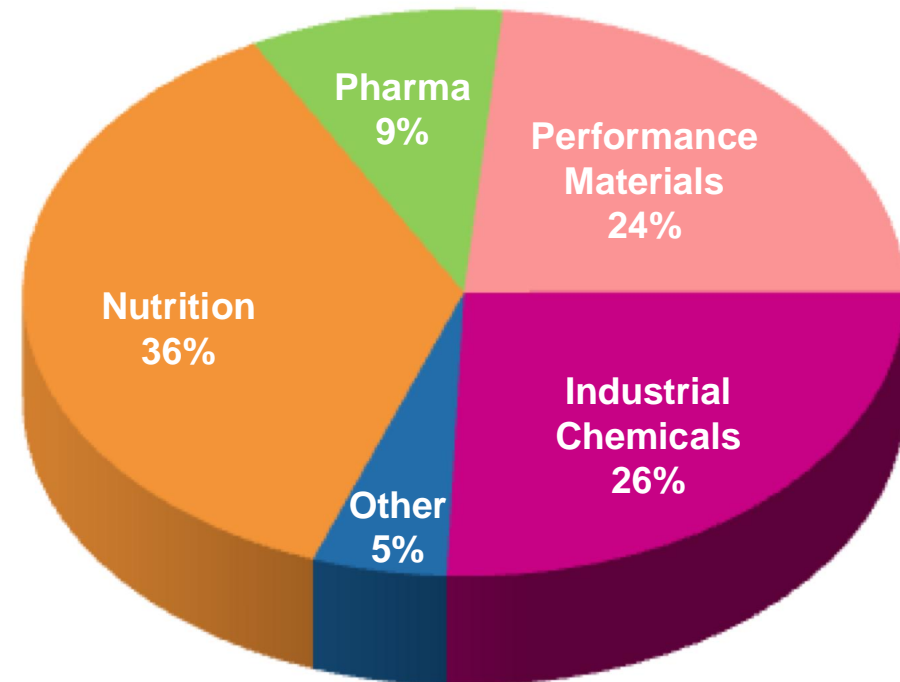




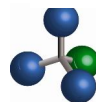
# Corporate DSM Profile

- Global leading multi-specialty chemical company
  - :: Active in 49 countries & 5 continents at over 200 locations
- Overall Sales 2009 = € 7,732 m
- Single A credit rating

2009 Revenue Contribution



**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



CONFIDENTIAL

Unlimited. **DSM**

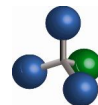
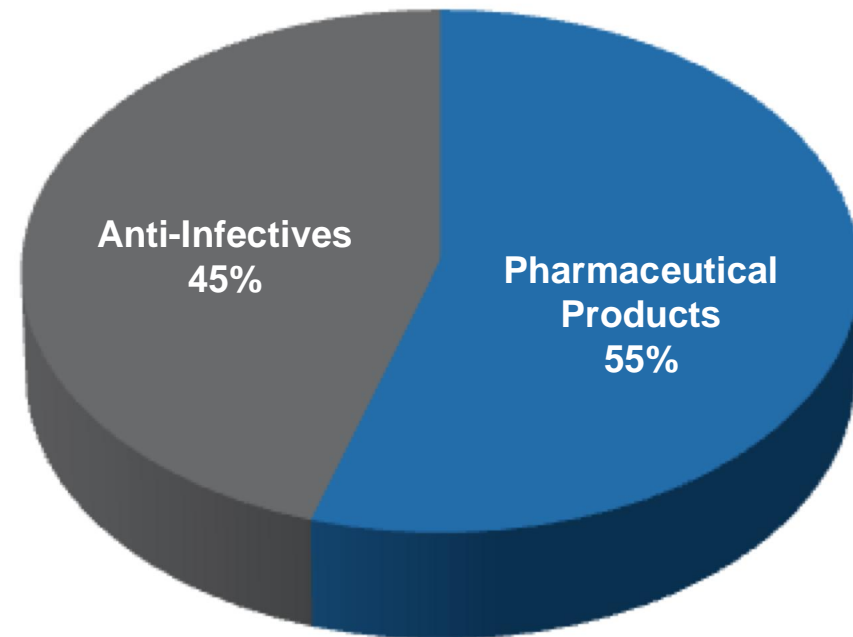




# Pharma Cluster

- DSM is one of the leading global providers to the pharmaceutical industry
  - :: Overall Sales 2009 = € 721 m
  - :: 4,374 Employees
  - :: 26 Sites Worldwide

2009 Revenue  
Contribution



# Where We Fit Within DSM Pharma Activity



One of the leading global providers to the pharmaceutical industry



**DSM Pharmaceutical Products**

## Pharma Chemicals

Chemical custom manufacturing of pharmaceutical APIs and registered Intermediates.

## Biologics

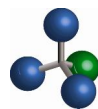
Mammalian cell culture and fermentation custom manufacturing of Biopharmaceutical Ingredients.

## Pharma Dosage Forms

Secondary manufacturing of pharmaceuticals (tablets, creams, injectables etc.) and packaging.

**DSM Innovative Synthesis B.V.**

*A unit of DSM Pharma Chemicals*



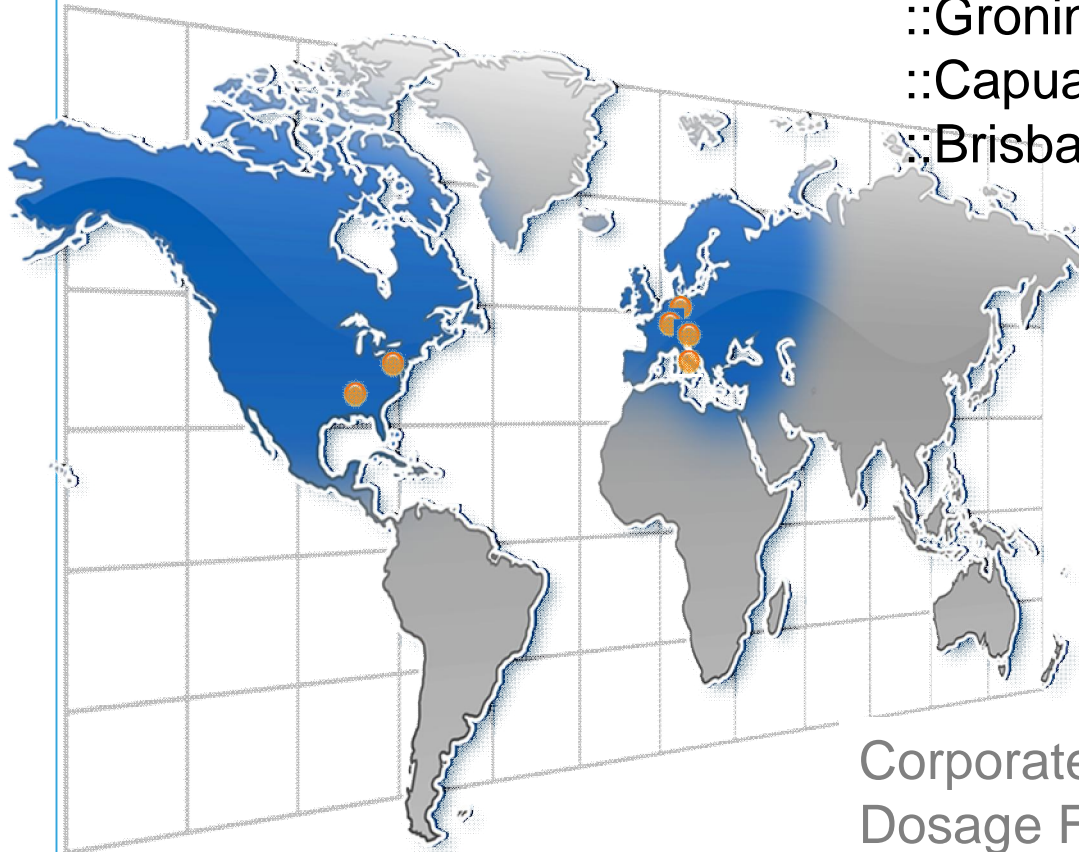
CONFIDENTIAL

Unlimited. **DSM**





# Global Sites



## Biologics:

- ::Groningen, Netherlands
- ::Capua, Italy
- ::Brisbane, Australia

## Pharma Chemicals:

- ::Linz, Austria
- ::Venlo, Netherlands
- ::Regensburg, Germany
- ::Geleen, Netherlands

## Corporate Headquarters & Dosage Form Manufacturing:

- ::Parsippany, NJ
- ::Greenville, NC

**DSM Innovative Synthesis B.V**

*A unit of DSM Pharma Chemicals*





# Integrated Offering

## Manufacturing Services

Capacity: 100 kg - 10 mt  
Staff: 74  
Reactors: 45 m<sup>3</sup>

> 200 °C	> 10 bar
180 to 200 °C	6 to 10 bar
160 to 180 °C	4 to 6 bar

Capacity: 10 mt - 1000 mt  
Staff: 87  
Reactors: 286 m<sup>3</sup>

> 200 °C	> 10 bar
180 to 200 °C	6 to 10 bar
160 to 180 °C	4 to 6 bar
0 to 10 °C	1 to 3
-10 to 0 °C	
-20 to -10 °C	
< -20 °C	

**CGMP**

Material	Count
glass lined	174
stainless steel	11

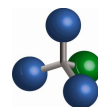
> 12 m <sup>3</sup>	8
10 to 12 m <sup>3</sup>	14
8 to 10 m <sup>3</sup>	
6 to 8 m <sup>3</sup>	1
4 to 6 m <sup>3</sup>	4
2 to 4 m <sup>3</sup>	
1 to 2 m <sup>3</sup>	
0,1 to 1 m <sup>3</sup>	

ø 10 m<sup>3</sup>

## Differentiating Technologies

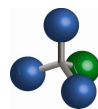
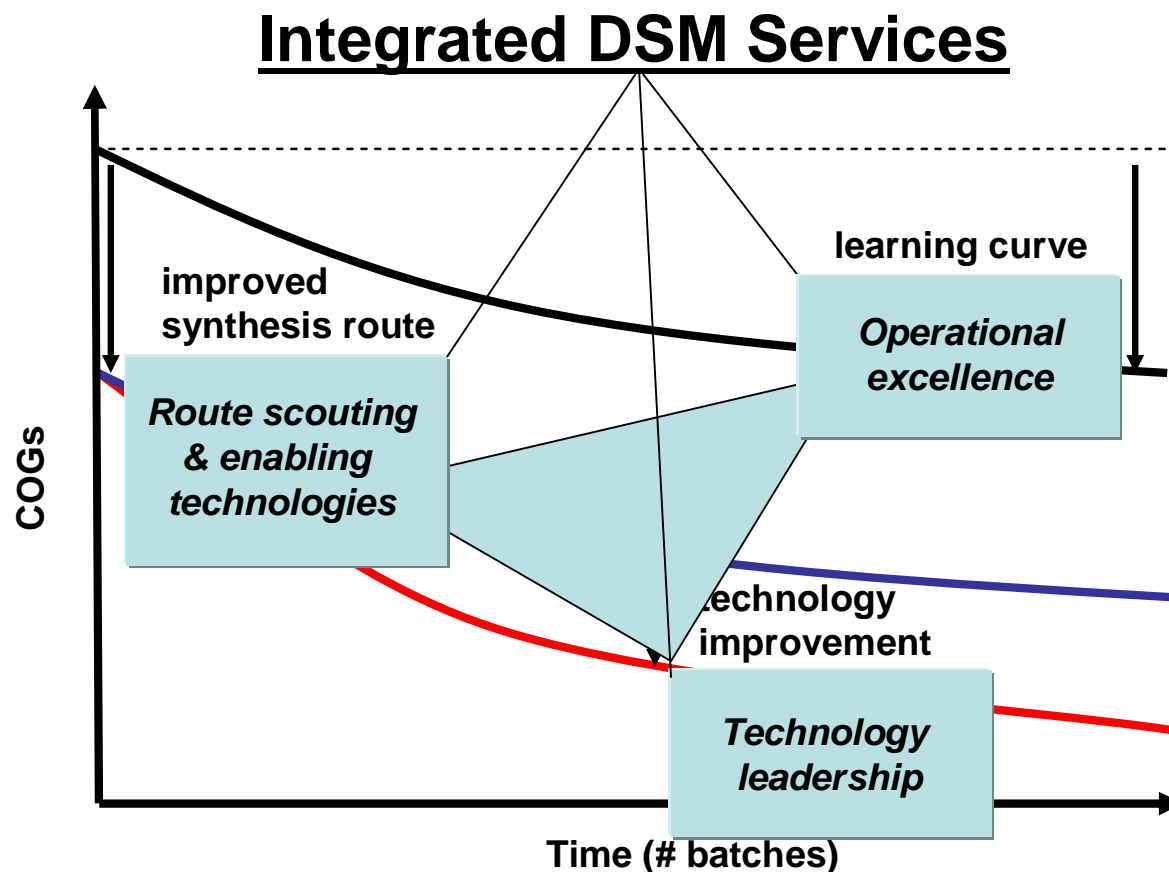
**Integration of all competences!**

Integrated offering provides highest value for most customers





# Value from integrated offering





# Integrated Offering

## Manufacturing Services

Capacity: 100 kg - 10 mt  
Staff: 74  
Reactors: 45 m<sup>3</sup>

> 200 °C	> 10 bar
180 to 200 °C	6 to 10 bar
160 to 180 °C	4 to 6 bar

Capacity: 10 mt - 1000 mt  
Staff: 87  
Reactors: 286 m<sup>3</sup>

> 200 °C	> 10 bar
180 to 200 °C	6 to 10 bar
160 to 180 °C	4 to 6 bar
0 to 10 °C	1 to 2
-10 to 0 °C	
-20 to -10 °C	
< -20 °C	

**R**

glass line

**Reactors**

glass lined    stainless steel

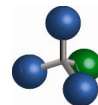
> 12 m <sup>3</sup>	8
10 to 12 m <sup>3</sup>	14
8 to 10 m <sup>3</sup>	
6 to 8 m <sup>3</sup>	1
4 to 6 m <sup>3</sup>	4
2 to 4 m <sup>3</sup>	
1 to 2 m <sup>3</sup>	
0,1 to 1 m <sup>3</sup>	

ø 10 m<sup>3</sup>

## Differentiating Technologies

Integration of all competences!

Integrated offering provides highest value not for all customers







# Why not for all?

### Manufacturing Services

Capacity: 100 kg - 10 mt  
Staff: 74  
Reactors: 45 m<sup>3</sup>

Capacity: 10 mt - 1000 mt  
Staff: 87  
Reactors: 286 m<sup>3</sup>

Reactors

> 200 °C	8
180 to 200 °C	1
160 to 180 °C	1
0 to 10 °C	1
-10 to 0 °C	1
-20 to 0 °C	1
> 10 bar	6
6 to 10 bar	1
< 1 bar	1

174 m<sup>3</sup>

11

stainless steel

### Differentiating Technologies

Org. chem

Homcat

Biocat

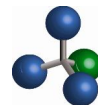
Microreactor

**Integration of all competences!**

**Customer in-house manufacturing strategy**

**Poor fit of DSM asset (e.g. high tox; low volume)**

**Changes in Pharma**

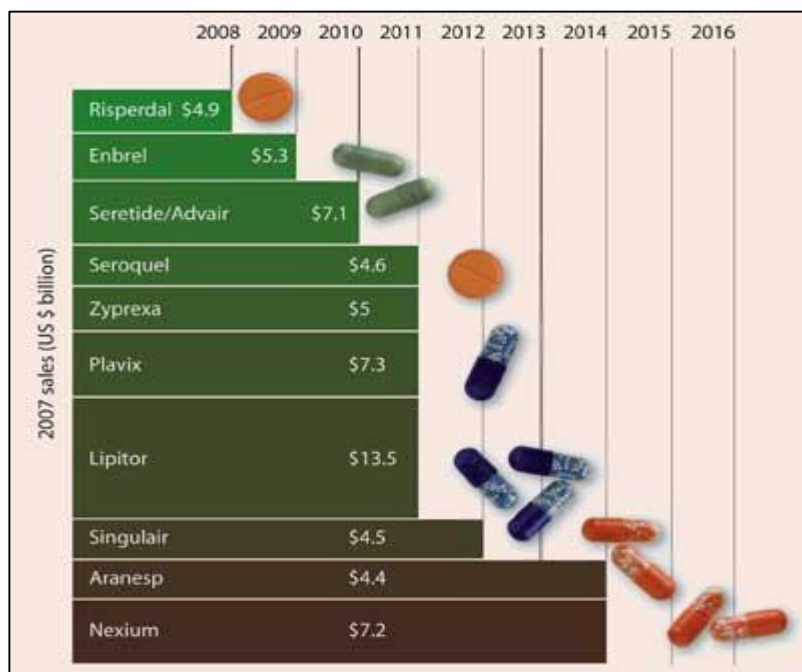




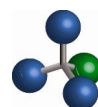
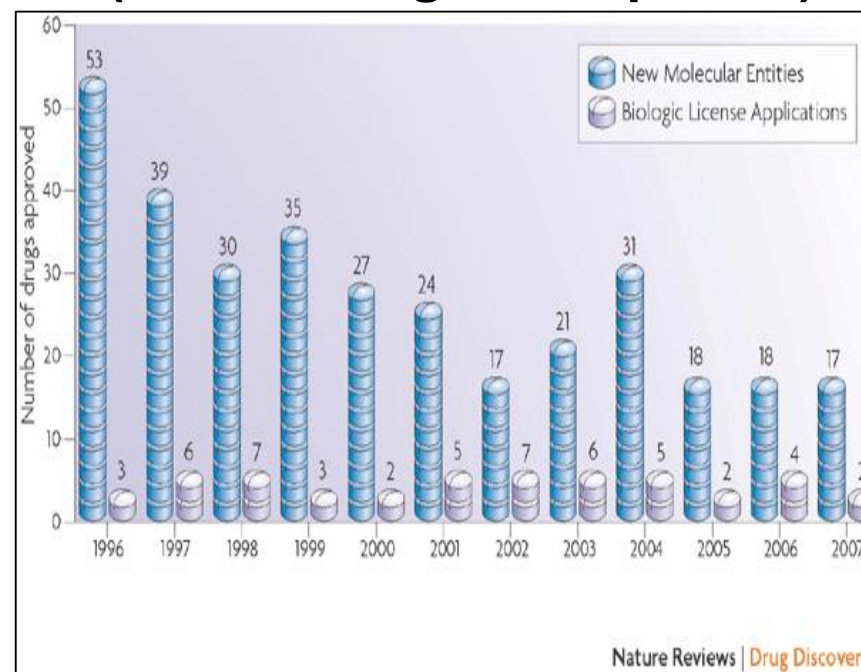
# Challenges in Pharma



## Patent cliff (generics competition)



## Stagnating Pipeline (& increasing develop. cost)



# Challenges for Pharma



## Increasing cost pressure from Health Care Systems



BARACK OBAMA AND JOE BIDEN'S  
AND ENSURE AFFORDABLE, ACCES  
**Health care costs are skyrocketing.** Health insu  
times faster than wages in the past 8 years, and i  
Many insurance plans cover only a limited numb  
unlimited financial liability. Over half of all pers  
affordable health care is compounded by serious  
Americans die from medical errors in hospitals e  
administrative and overhead costs, an...

<http://www.barackobama.com/pdf/issues/HealthCarePlan.pdf>

### Germany's health-care debate

**Dr Rösler's difficult prescription**

**The hard case of reforming German health care**

Apr 29th 2010 | BERLIN | From *The Economist* print edition

A doctor on call for reform



ENJOY a "prevention holiday" on Germany's most beautiful island, urges the Aquamaris Strandresidenz, a spa-hotel on Rügen in the Baltic: your health insurance will pick up part of the bill. If prevention fails, a "cure" somewhere just as nice might be covered. Germans, normally quick to complain, find little fault with their health care. It covers everyone, unlike America's. It does not ration life-saving treatments, unlike Britain's. Patients can see any doctor they please. Treatment costs little beyond their statutory payments to the system. Yet Germany's 130-year-old health-insurance system needs fixing. It is expensive and will get more so as the population ages and technology advances. On measures like recovery from heart attacks or breast cancer, Germany is no better than its peers. Statutory health-insurance, which covers 90% of Germans, is financed from payroll contributions by workers and employers. If nothing is done, rising health costs will make labour dearer and jobs scarcer. Painful choices loom.





# Challenges for Pharma

How to reduce the development cost for innovative drugs

→ Licensing in, **reduce cost at all levels**

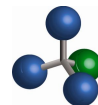
How to fight generics (low cost competition)?

→ Life cycle extension, **reduce cost at all levels**

How to maintain profit margin under the cost pressure from payers and generic drug manufacturers?  
How to manage supply chain and manufacturing organizations?

→ Focus on first best in-class drug, **reduce cost at all levels**

**Pharma was never more challenged by cost than today...**

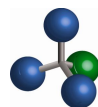


# Today's Manufacturing Practice



- Large inefficient batch equipment
- Low utilization 30 - 40 % on average
- Capital and labor intensive
- High inventories and excessive warehouse space
- High transportation costs
- High operating costs
- Low product variety
- Excessive amounts of product non-conformances
- Re-work times due to stage and final product testing

**Many processes have high cost saving potential...**



# Challenge for Process R&D



## Early Development

Fast supply of APIs for clinical tests, accepting higher manufacturing costs due to suboptimal technologies and routes w/o compromising product quality.



*There (hopefully) comes a time where **manufacturing routes do matter!***

## Late Development

Supply of APIs based on inherently safe, robust, economically and environmentally viable processes.



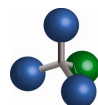
*There (for sure) comes a time where **manufacturing cost do matter!***

## Off patent

Cost, cost, cost

**DSM Innovative Synthesis B.V.**

*A unit of DSM Pharma Chemicals*



CONFIDENTIAL

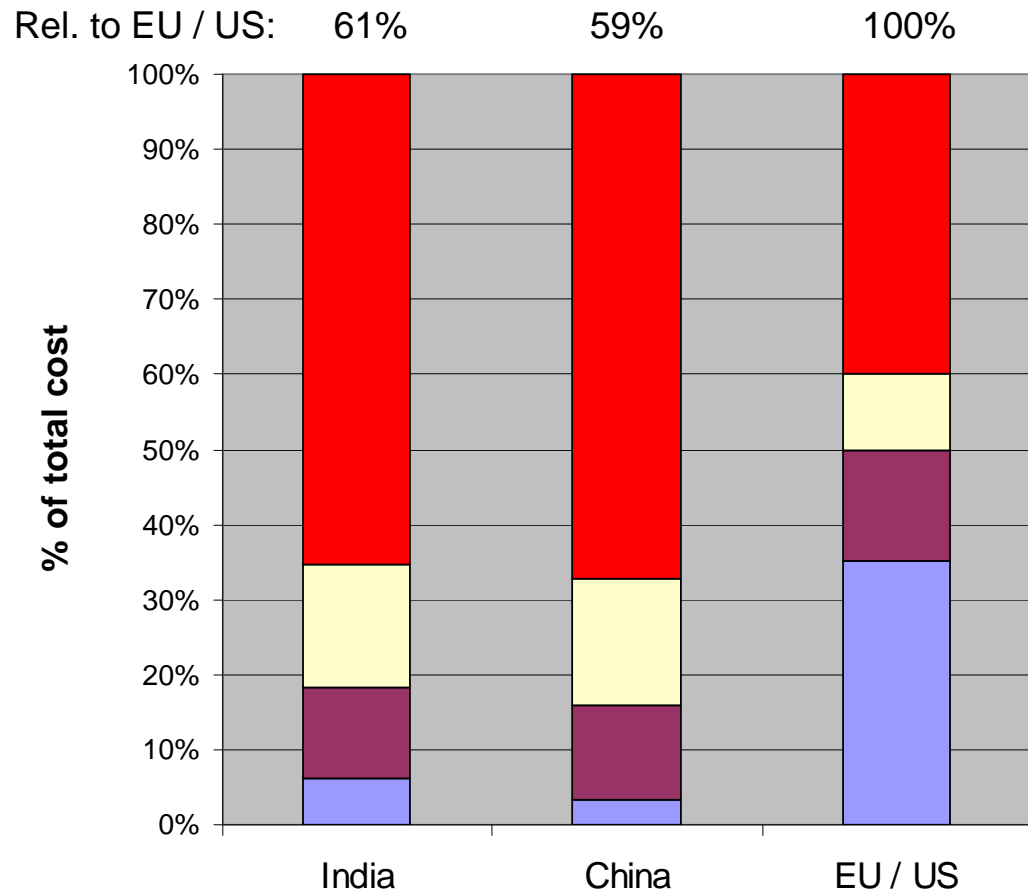
Unlimited. **DSM**





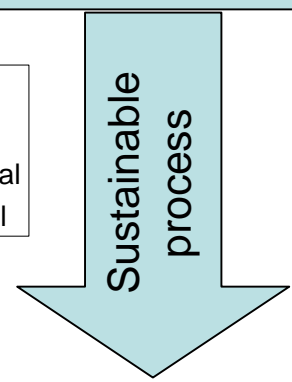
# Manufacturing Cost

**API Cost 3%-8% of Branded Pharma Sales Revenue\***



**Important target:**  
Reduction of raw material cost  
Reduction of synthesis steps

- Material
- Depreciation
- Indirect Personal
- Direct Personal



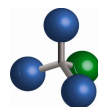
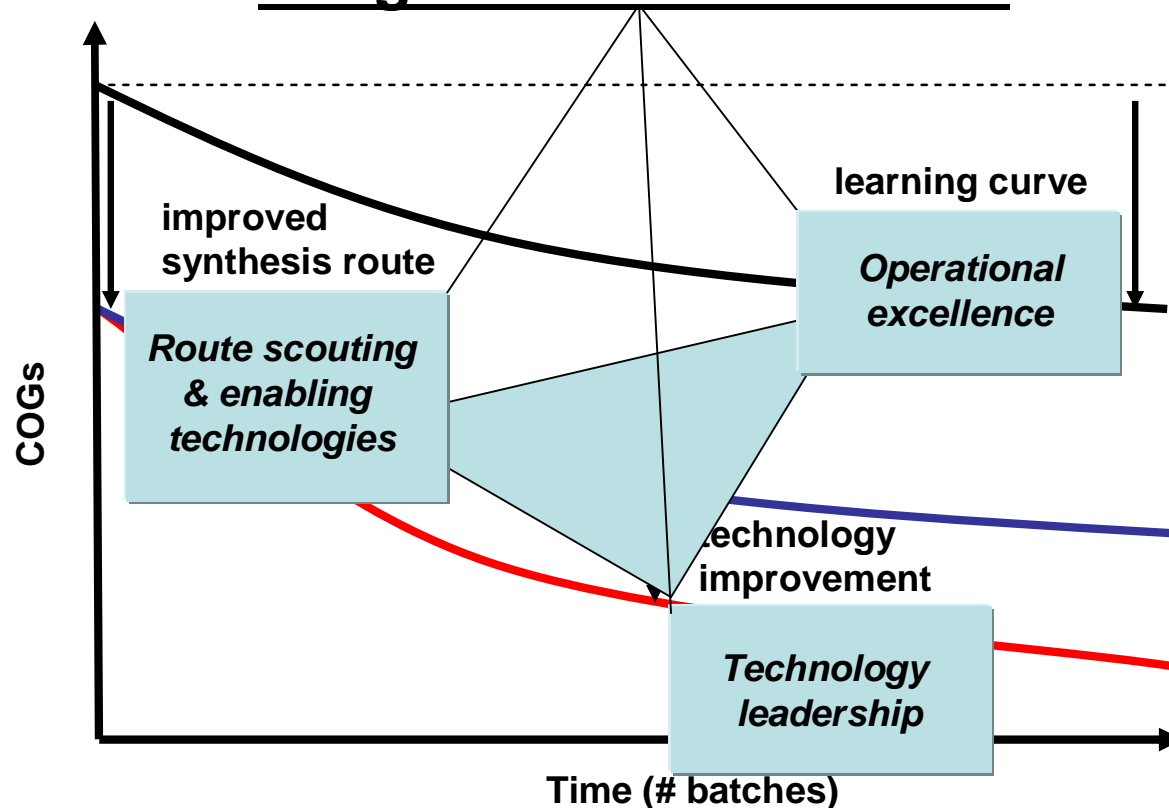
**Via  
Route Scouting**

\* Source: Drug Discovery Today, November 2006



# Value from integrated offering

## Integrated DSM Services



# Value we provide



## InnoSyn™ route scouting services

**Consulting**  
Ideation for synthesis routes for your API

**Route scouting**  
Identification of the (best) alternative routes

**(Bio)catalyst screening**  
Identification of the most promising catalysts

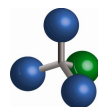
**Pre-feasibility**  
Proof-of-principle based on parameter optimization (incl. micro-reactor technology)

**Full feasibility**  
Tech package, sample preparation and licensing options

**Mini-plant services**  
Kg supply, support in transfer and implementation

- We provide the most sustainable synthesis route  
-> **cost reduction / competitiveness**
- as proven scalable tech package  
-> **seamless scale-up**
- with control of IP  
-> **blocking lowest cost routes**
- to be implemented at most appropriate manufacturing partner  
-> **flexibility (business model)**

**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



CONFIDENTIAL

Unlimited. **DSM**

# Additional Service Offering



## InnoSyn™ route scouting services

### Consulting

Ideation for synthesis routes for your API

### Route scouting

Identification of the (best) alternative routes

### (Bio)catalyst screening

Identification of the most promising catalysts

### Pre-feasibility

Proof-of-principle based on parameter optimization (incl. micro-reactor technology)

### Full feasibility

Tech package, sample preparation and licensing options

### Mini-plant services

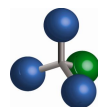
Kg supply, support in transfer and implementation



## Differentiating Technologies



**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



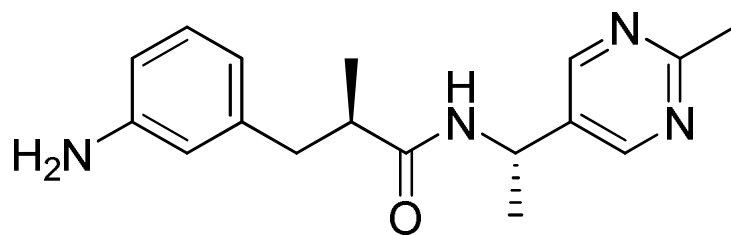
CONFIDENTIAL

Unlimited. **DSM**

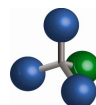
# Example for Integration



## Customer target

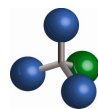
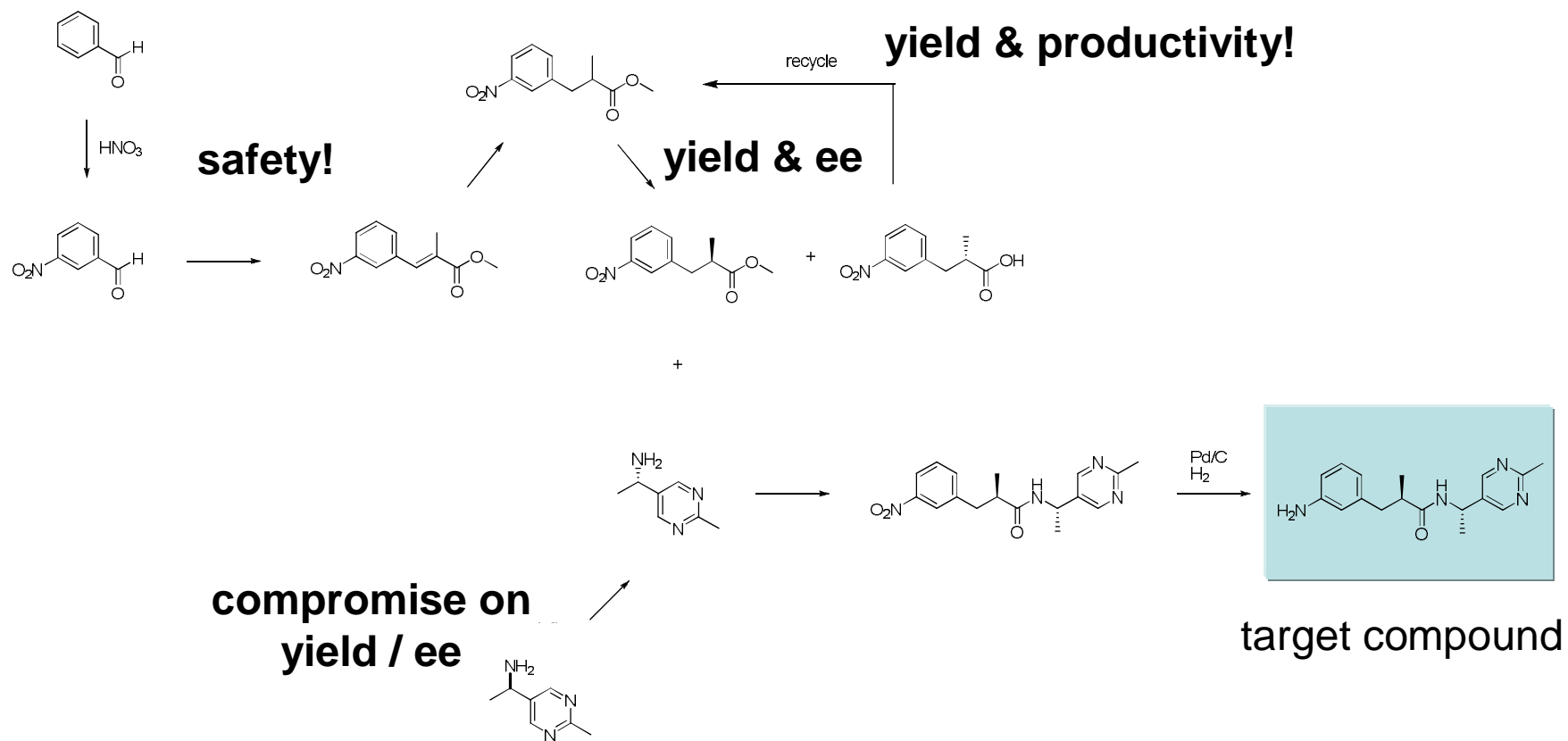


## Differentiating Technologies

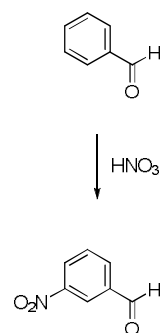




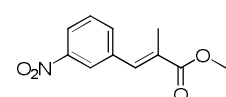
# 1<sup>st</sup> Manufacturing Route



# 2<sup>nd</sup> Manufacturing Route

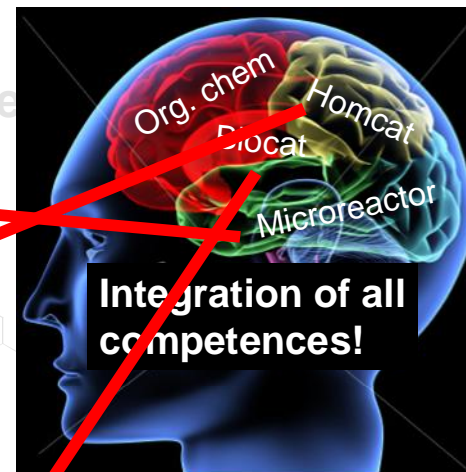


safety!

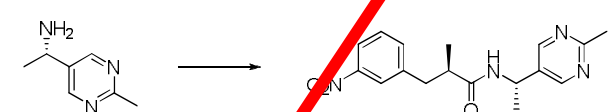


recycle

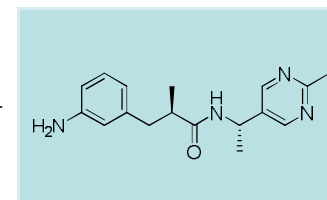
yield & ee



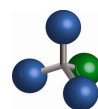
compromise on yield / ee



Pd/C  
H<sub>2</sub>



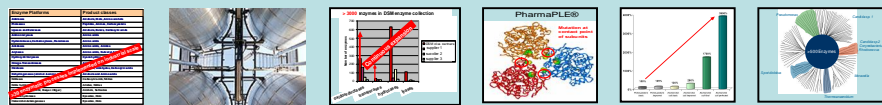
target compound



# Technology Leadership



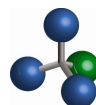
## Unmet track record and capabilities



- Broadest collection of off the shelf enzymes (>3000)
- Excellent expression and enzyme design capabilities
- Secure supply of enzyme at any scale (with FTO!)
- Unmet track record (also regulatory) in large scale implementation (>30 processes industrialized)
- Critical mass for all important expertises
- Open innovation approach provides access to huge network



## Differentiating Technologies



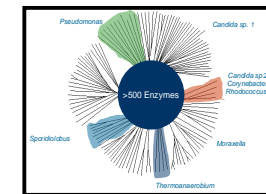
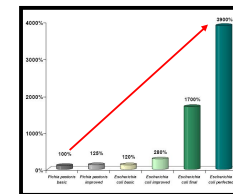
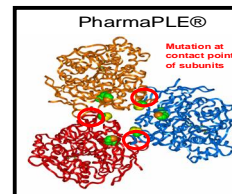
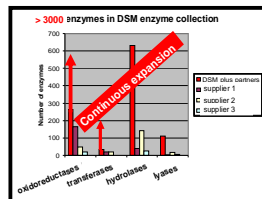
# World leader in Industrial Biocatalysis



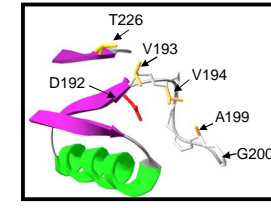
Enzyme Platforms	Product classes
Aspartases	Amino acids, Amino acids
Proteases	Peptides, Amino, Carboxylic acids
Lipases and Esterases	Alcohols, Esters, Carboxylic acids
Amino acid Lyases	Amino acids
Hydrolases	Amino acids, Carboxylic acids, Saccharides
Amidases	Amino acids, Amino acids
Acylases	Amino acids, Alcohols
Hydrolytic Lipases	Carboxylic acids
Omega 3 desaturases	Carboxylic acids
Oxidases	Aldehydes, Carboxylic acids
Carbohydrate Glycosyltransferases	Carbohydrates and derivatives
Nitriles	Carboxylic acids, Nitriles
Nitrile hydratase	Amino acids, Nitriles
Vinyl monomer hydrolase	Amino acids, Nitriles
Epoxide hydrolase	Epoxides, Diols
Hydroxyl dehydrogenase	Epoxides, Diols

*>30 enzymatic processes implemented on industrial scale*

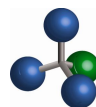
Used in tons scale production  
Used in 100 and 1000 metric tons



- Broadest collection of off the shelf enzymes (>3000)
- Excellent expression and enzyme design capabilities
- Secure supply of enzyme at any scale (with FTO!)
- Unmet track record (also regulatory) in large scale implementation (>30 processes industrialized)
- Critical mass for all important expertises
- Open innovation approach provides access to huge network



**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



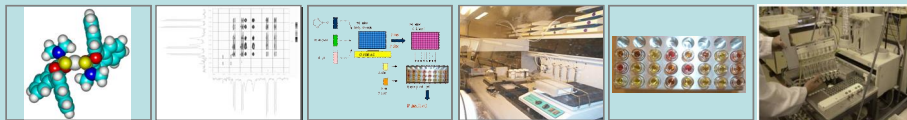
CONFIDENTIAL

Unlimited. **DSM**

# Technology Leadership



## Unmet track record and capabilities



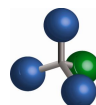
- Screening for the right catalyst from our HomCat Platforms
- Custom made Monophos™ catalysts (instant HomCat) for asymmetric reduction
- Proprietary methods for aromatic chemistries including couplings and amine synthesis
- Rapid reaction optimisation in parallel microreactors
- HomCat process development and full scale implementation
- Rapid identification of cost effective catalytic systems



## Differentiating Technologies



**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*

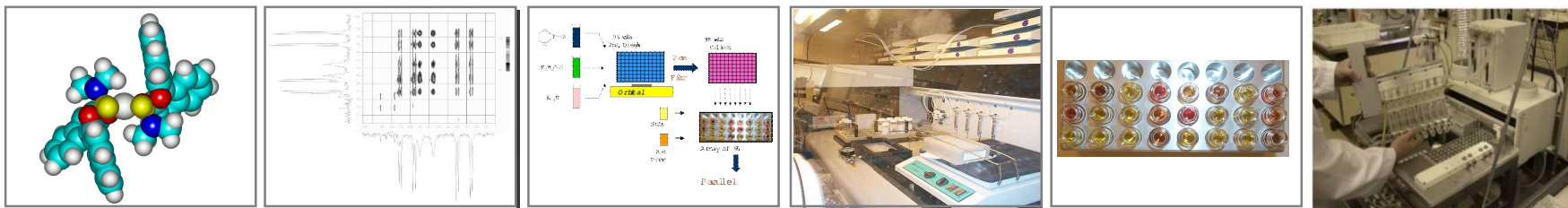


CONFIDENTIAL

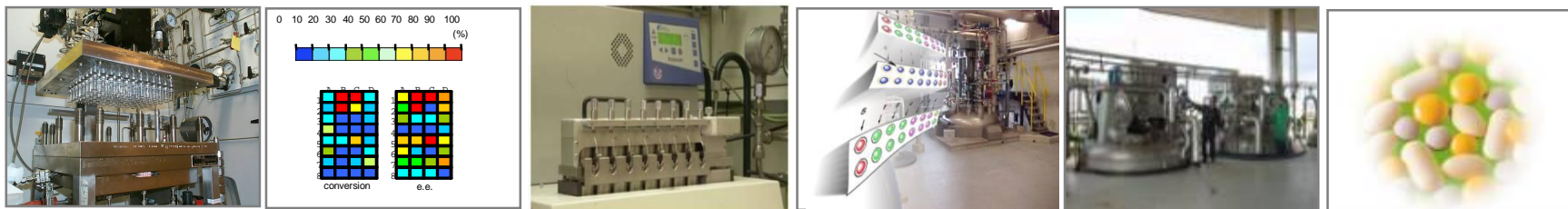
Unlimited. **DSM**



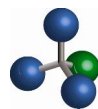
# HomCat Platform Screening & Development



- Screening for the right catalyst from our HomCat Platforms
- Custom made Monophos™ catalysts (instant HomCat) for asymmetric reduction
- Proprietary methods for aromatic chemistries including couplings and amine synthesis
- Rapid reaction optimisation in parallel microreactors
- HomCat process development and full scale implementation
- Rapid identification of cost effective catalytic systems



**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



CONFIDENTIAL

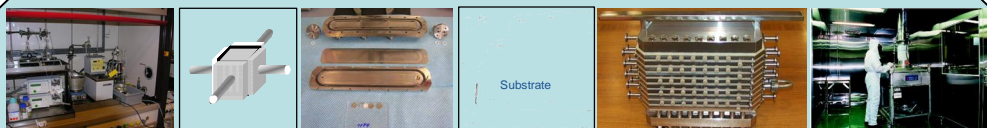
Unlimited. **DSM**



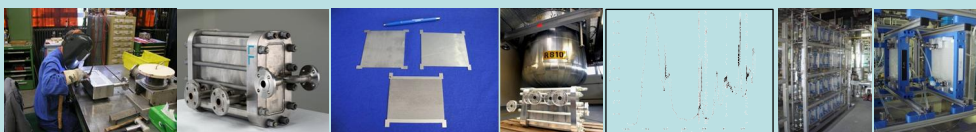
# Technology Leadership



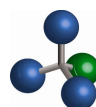
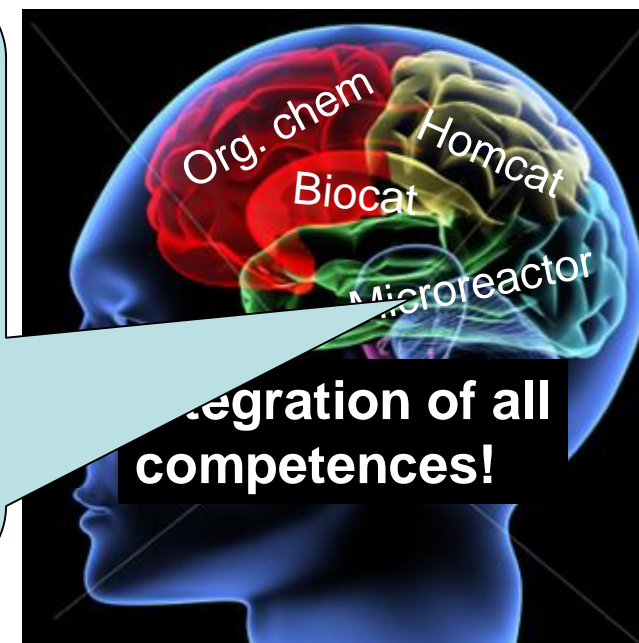
## Unmet track record and capabilities



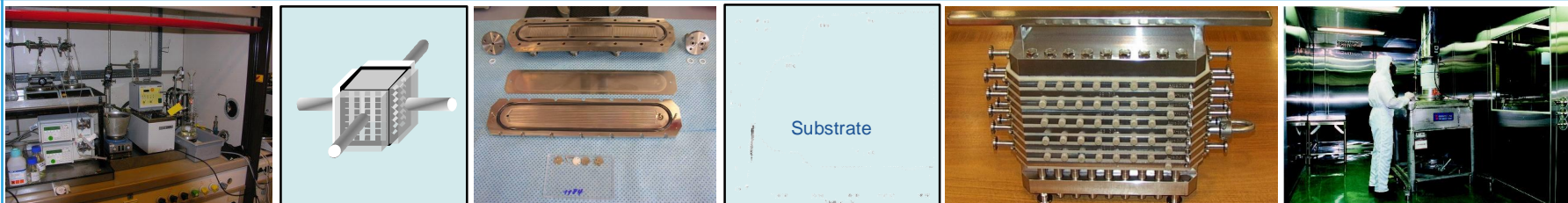
- Flow process development from lab to pilot to full-scale plant
- ...in a variety of reactor concepts
- Integration of reaction and work-up
- Rapid reaction optimisation and numbering up
- ...using various hazardous reagents
- ...under cGMP conditions



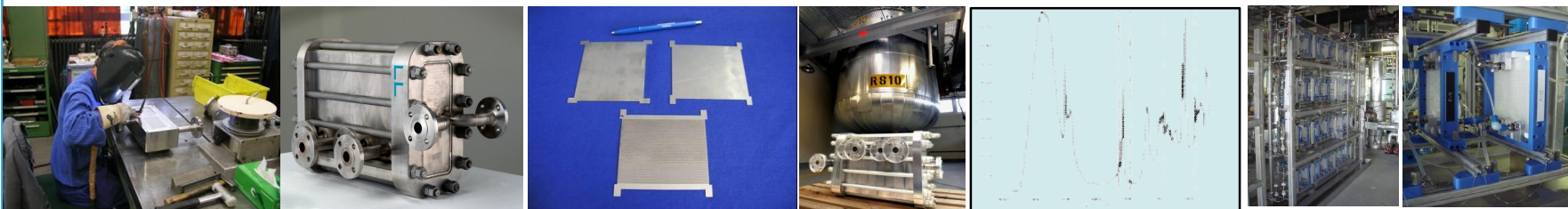
## Differentiating Technologies



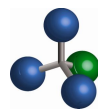
# Development and numbering up of continuous reactions in microreactors



- Flow process development from lab to pilot to full-scale plant
- ...in a variety of reactor concepts
- Integration of reaction and work-up
- Rapid reaction optimisation and numbering up
- ...using various hazardous reagents
- ...under cGMP conditions



**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



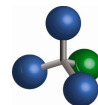
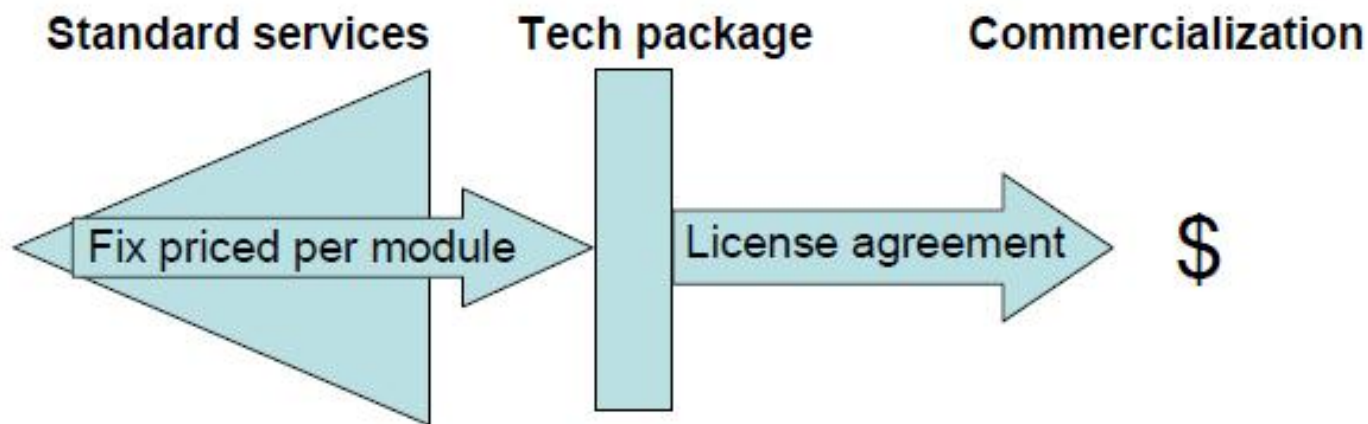
CONFIDENTIAL

Unlimited. **DSM**



# Business Model

- “Fix” priced standard service packages
- Access to enabling DSM background IP (incl. potential third party IP) via license agreement for transfer of fully developed tech package





# Summary

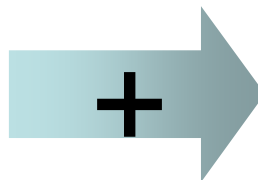


DSM Pharmaceutical Products



## Pharma Chemicals

Chemical custom manufacturing of pharmaceutical APIs and registered Intermediates.



## InnoSyn™ route scouting services

InnoSyn™ route scouting services

Differentiating T...

Consulting  
Idea for synthesis routes for your API

Route scouting  
Identification of the (best) alternative routes

(Bio)catalyst screening  
Identification of the most promising catalysts

Pre-feasibility  
Proof-of-principle based on parameter optimization (incl. micro-reactor)

Full feasibility  
Tech preparation, scale-up, transfer and implementation

DSM Route Scouter

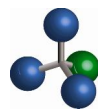
FDA APPROVAL

Biocat  
Homocat  
Microreactor

Integration of all competences!

Response to changing customer demand

**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



CONFIDENTIAL

Unlimited. **DSM**

# Contacts



## Business Manager

Dr. Oliver May  
+31 46 4760551

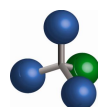
[info.innosyn@dsm.com](mailto:info.innosyn@dsm.com)

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



**See next presentation  
and visit us at DSM booth 5G12, hall 5**

**DSM Innovative Synthesis B.V.**  
*A unit of DSM Pharma Chemicals*



CONFIDENTIAL

Unlimited. **DSM**