CORNING

Move into industrial production with Corning® Advanced-Flow™ Reactor

Bertrand Gallet
Technical Sales Engineer EMEA

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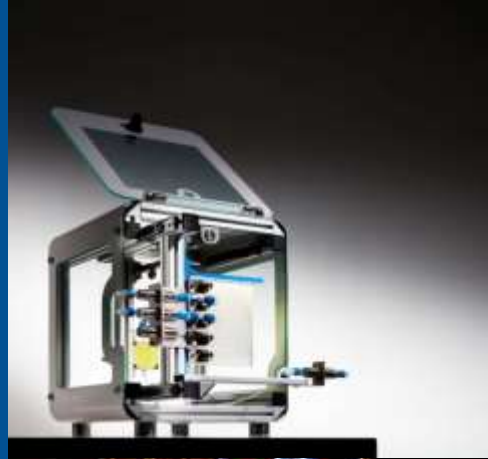
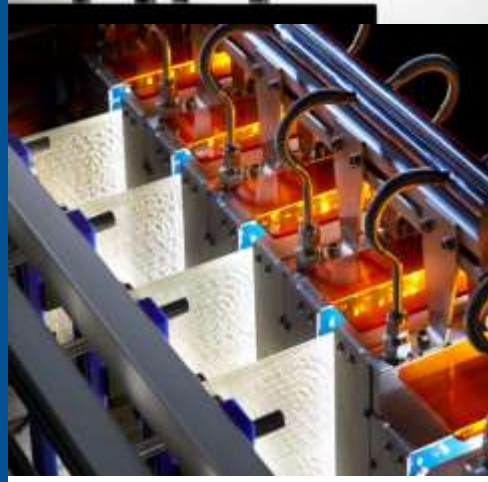
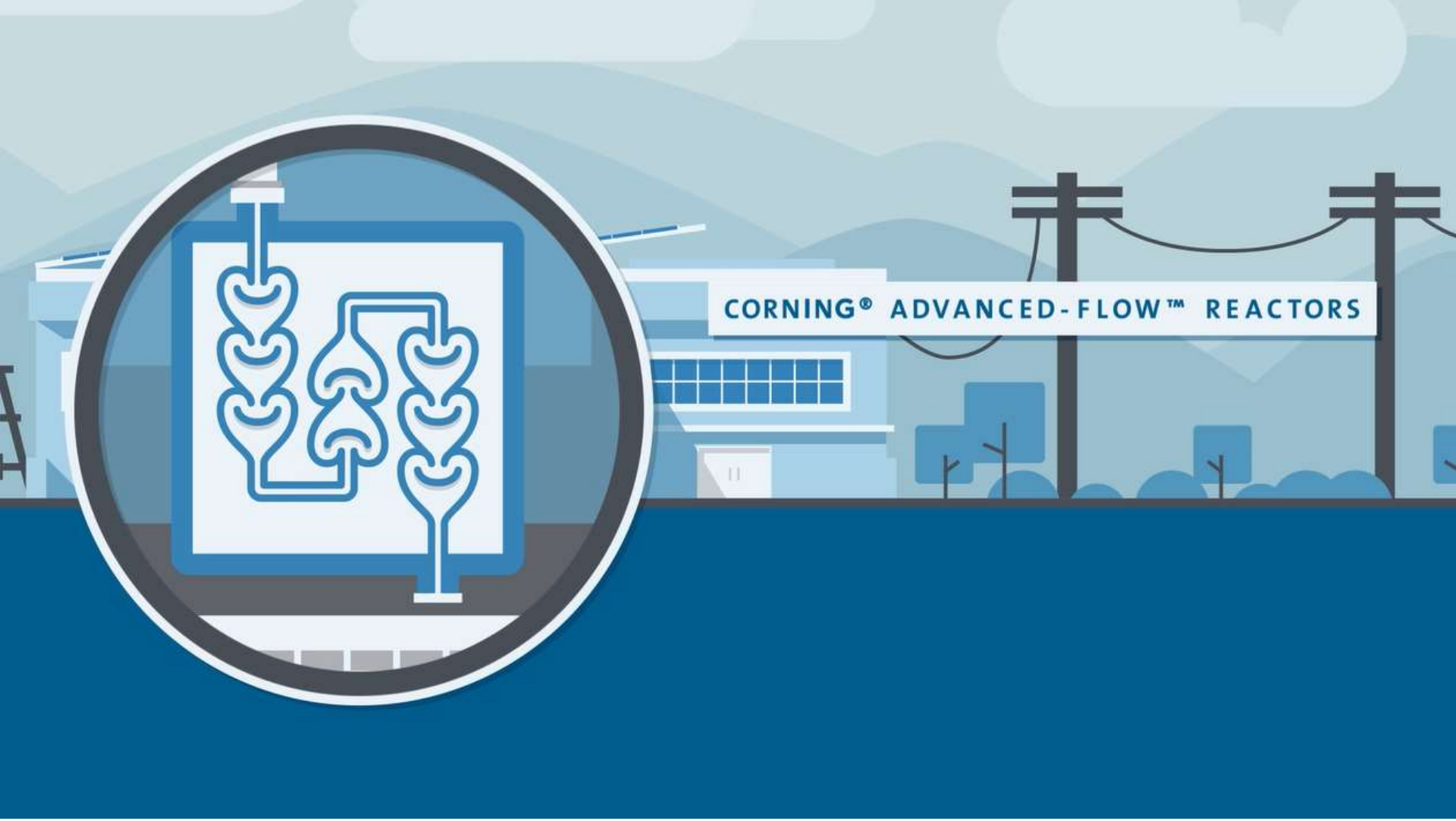
Du rêve de la paillasse à la réalité d'une usine industrielle





Agenda

- Corning® Advanced-Flow™ Reactor technology
- Laboratory work with Corning® Low-Flow and Lab Reactor
- Scaling-up strategy, from G1 to G4
- Bringing Photochemistry to Production
- Your next step in flow chemistry



Corning® Advanced-Flow™ Reactor Technology

Founded:
1851

Headquarters:
Corning, New York

Employees:
45,000 worldwide

2016 Core Sales:
$9.7 billion

Fortune 500 Ranking (2017):
298

Corning Incorporated is one of the world's leading innovators in materials science. For more than 165 years, Corning has applied its unparalleled expertise in glass science, ceramics, and optical physics to develop products and processes that have transformed industries and enhanced people's lives.

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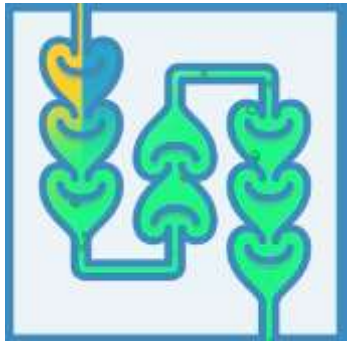
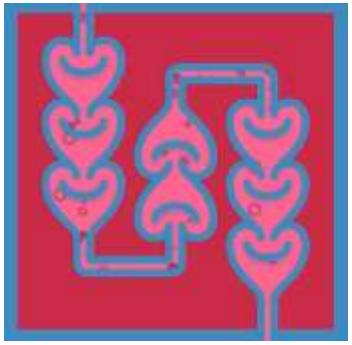
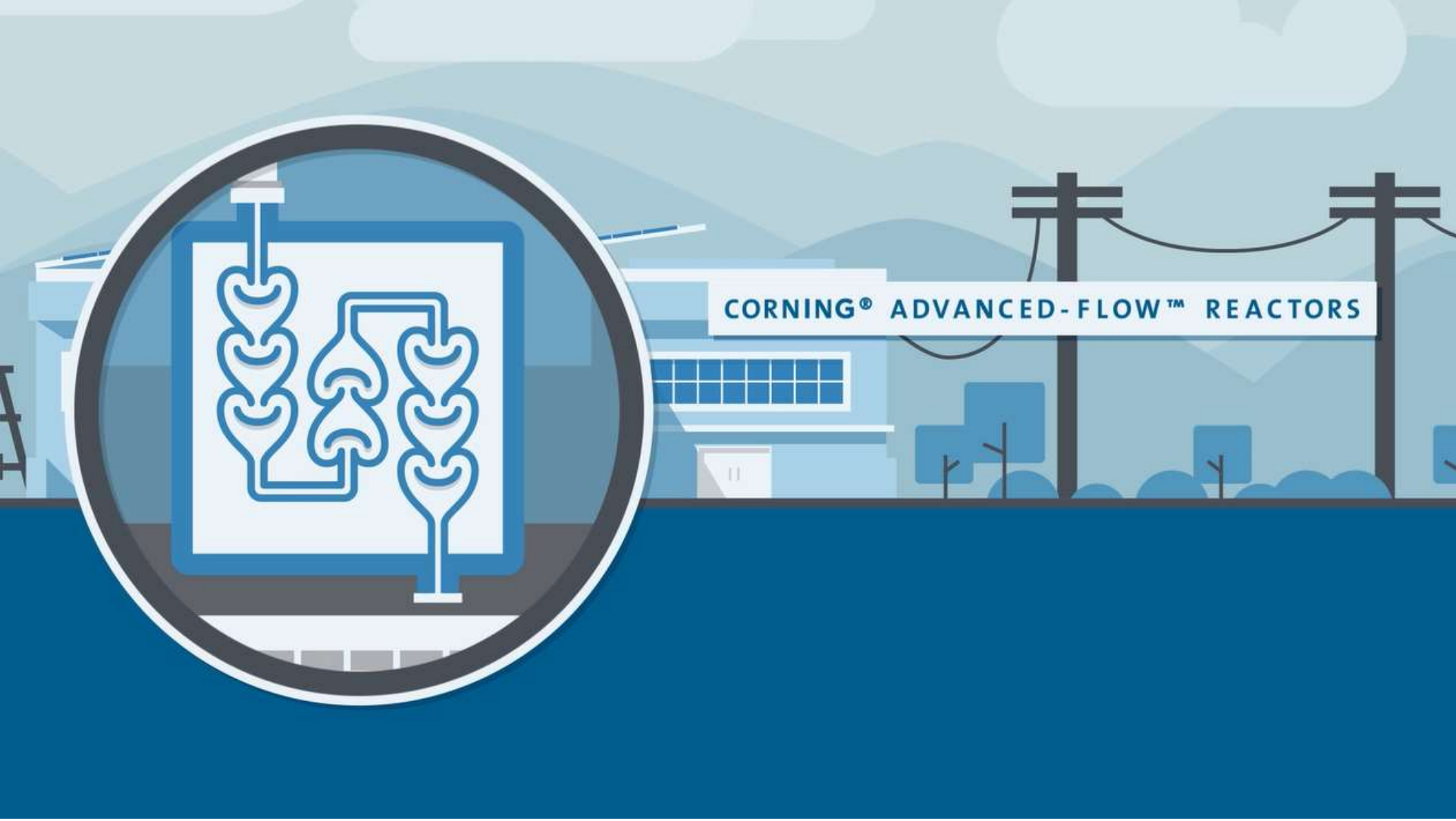
Corning® AFR™: unique concepts and advantages

High Mixing	High Heat Exchange	Materials	Seamless Scale-Up	Complete units
				
HEART patented shape **Ideally for immiscible and multiphase systems**	**Combined heat exchange and reactive path in a sandwich structure** **Independent thermal control**	**Glass and Ceramic** **Superior corrosion resistance**	**Reactors designed for seamless scale-up** **Direct from Lab to Production**	**Complete turn-key solutions** **Engineered and customized units**

Corning® Advanced-Flow™ Reactor Value Proposition

Revolutionary Improvement vs. Batch



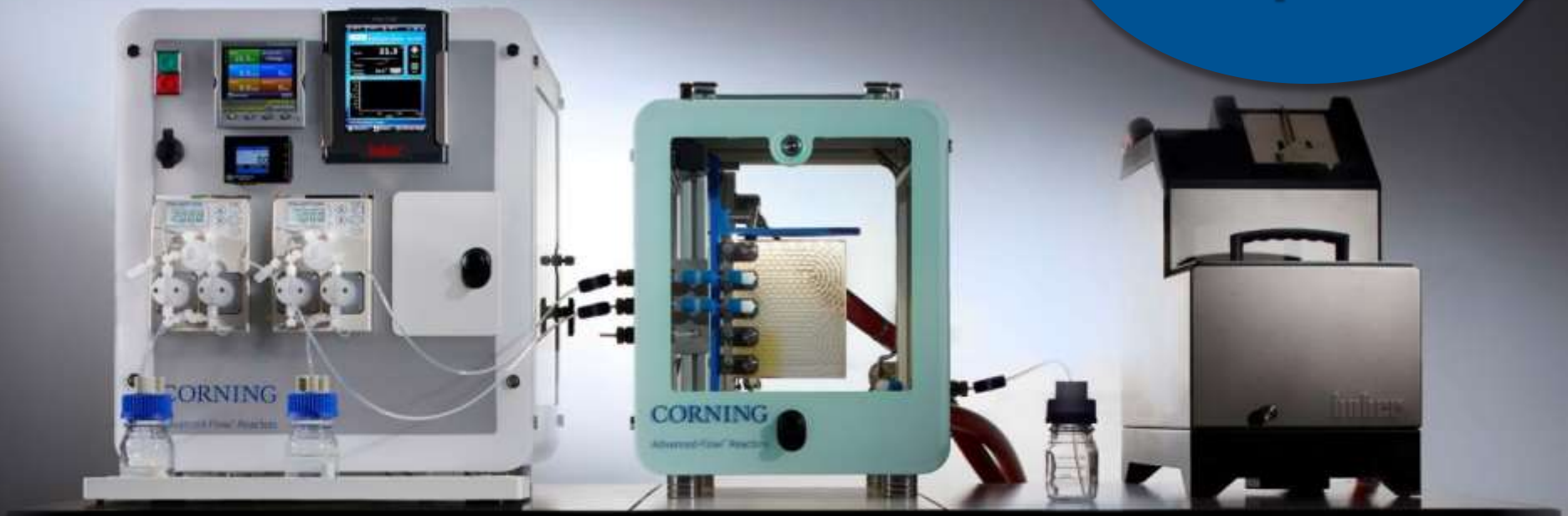
Laboratory work with Corning® Low-Flow and Lab Reactor

What is AFR® Lab Reactor ?

A complete **Plug and Play Lab System**
(reactor + auxiliaries)

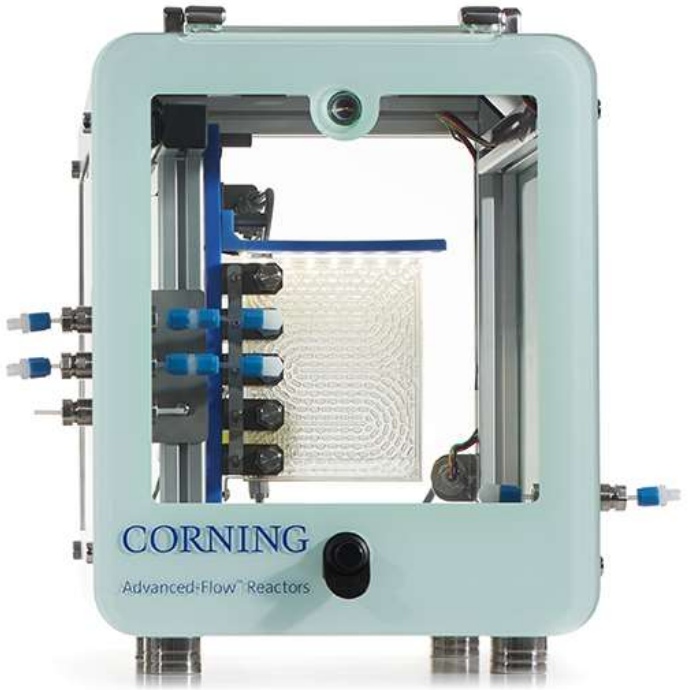
Ready to start & easy to use

Being **seamless scalable with AFR® products**



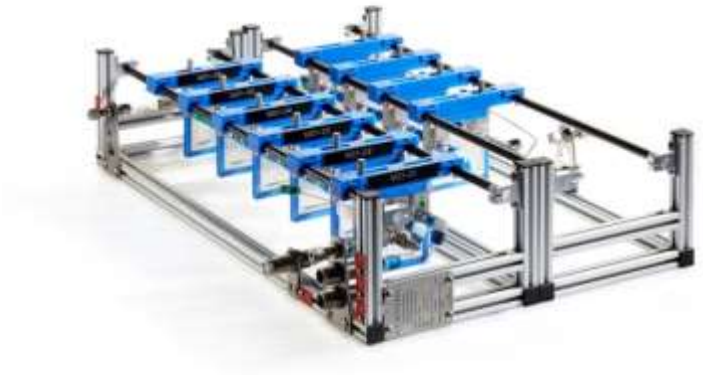
Lab Reactor reaction module: Key features

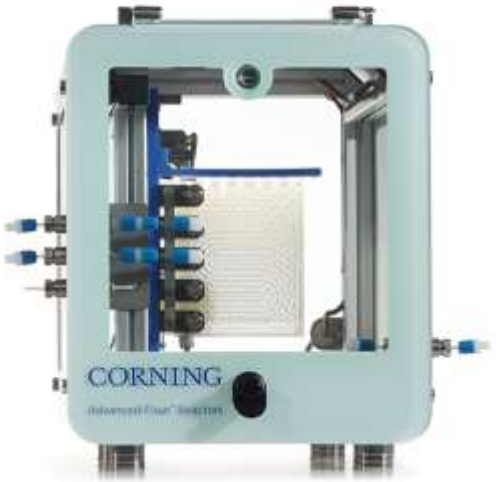
- **Up to 2 G1 LF glass fluidic modules**
- Outstanding mixing and heat exchange with **patented HEART design**
- **Low internal volume** : 2,5 ml per fluidic module
- **Seamless scale-up with other AFR® products**
- **Back pressure regulator** for pressure control integrated
- T° measurement
- Full metal free system



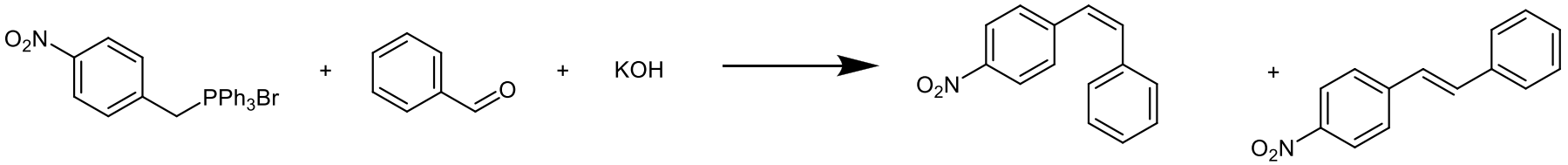
Why to use it at Lab scale?

- Numerous parameters to test
- Small volume of reagents
- Quick results required
- Extremely broad chemical conditions
- Broad range of temperature
- Scalable conditions
- Corrosive conditions
- Exotermic Reactions





Screening of reaction time and temperature



- Wittig reaction
- Quick screening of reaction conditions
- High mass transfer allow to work with multi-phasic conditions

	8 ml/min	4 ml/min	2 ml/min	1 ml/min	0.5 ml/min
20 °C					
30 °C					
40 °C					
50 °C					
60 °C					
70 °C					
80 °C					
	20.3 s	40.5 s	81 s	162 s	324 s

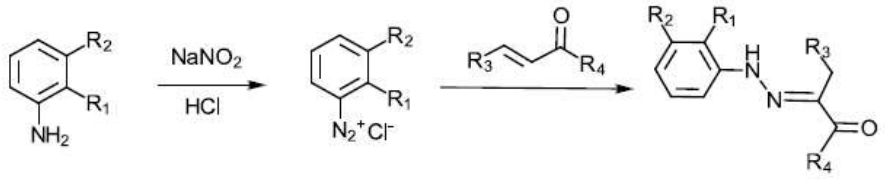
Customer case

Medichem

Context

Diazotization

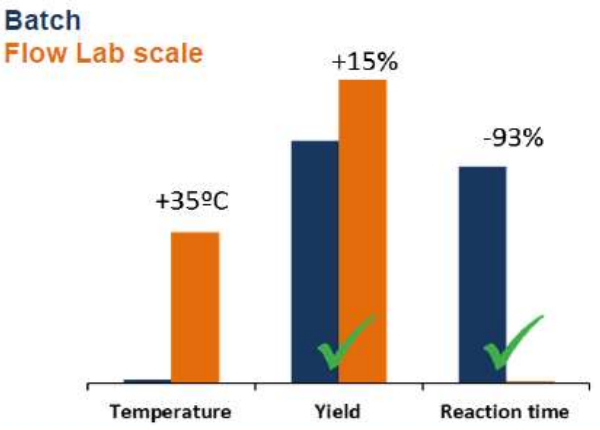
Risk of precipitation of a shock sensitive intermediate



Step 1

Preliminary tests in flow at lab scale (g/min) using Low Flow reactor

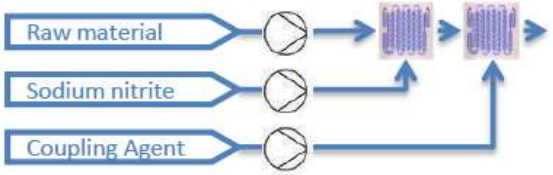
Improved yield, precipitation is avoided

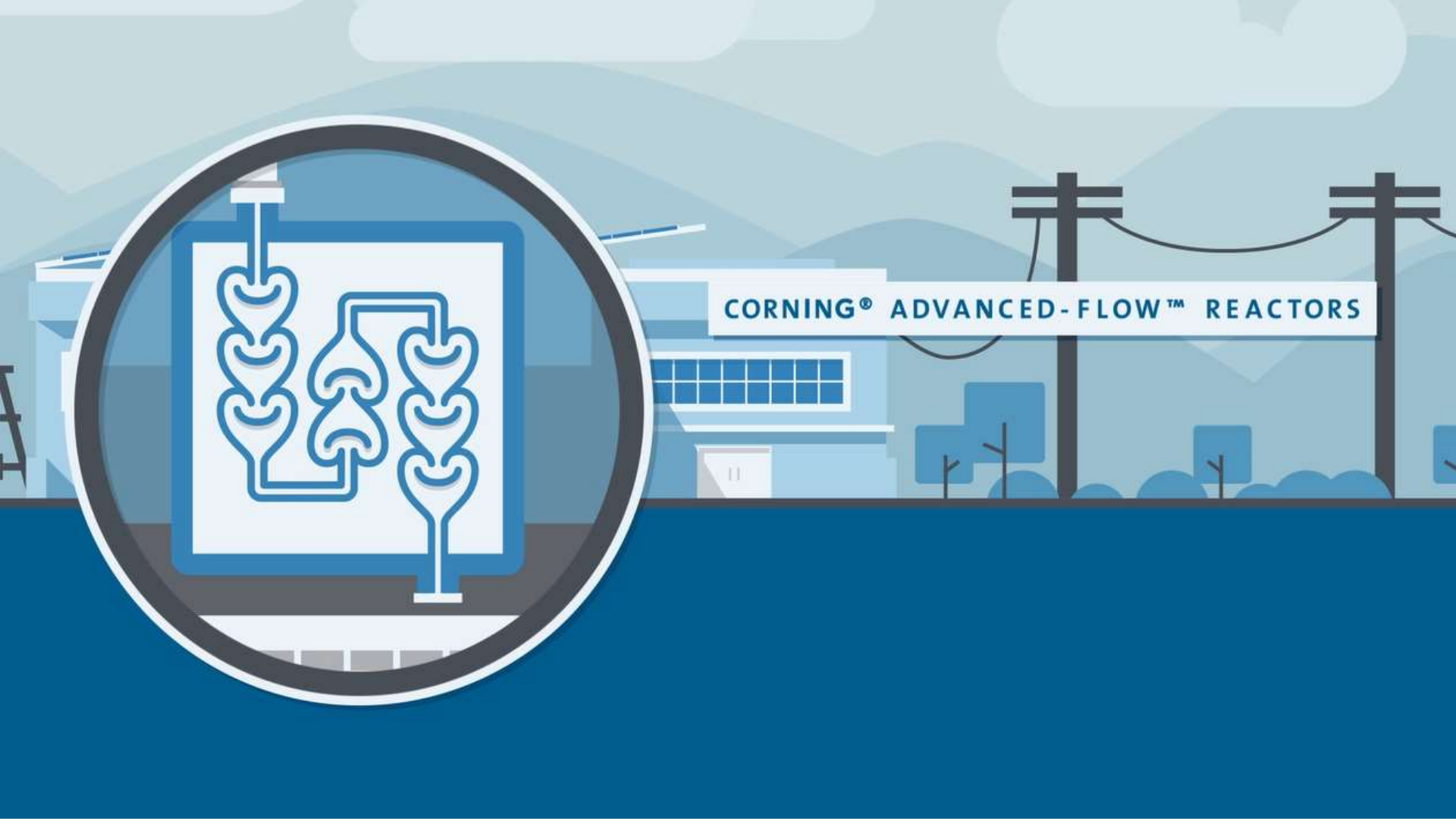


Step 2

Scale-up to kilo lab: scale-up factor 18

Planned by end of this year

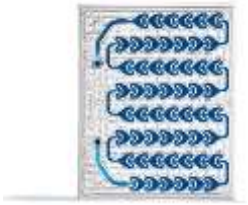




Scaling-up strategy, from G1 to G4

AFR Seamless scale-up principle

G1 Platform



G4 Production

Reactor Residence time = Reactor Internal Volume ÷ Mixture Volumetric Flow Rate

G1 Case :
Reactor Volume = **6 FM** x 8 ml/FM = 48 ml

Mixture flow = 150 ml/min
= **9 l/h**
= **64.8 M^3/y**

Residence time = 48 ÷ 150 = 0.32 min = **19.2 s**

G4 Case :
Mixture flow = 6000 ml/min
= 360 l/h = **2160 M^3/y**

Residence time = **19.2 s** = 0.32 min

Internal Volume = 0,32 x 6000 = 1920 ml
# of FMs in reactor = 1920 ÷ 250 = **8 FM**

Customer case

G4 reactor system for Active Pharmaceutical Ingredient (API) production

- Development done with a G1 SiC reactor
- Seamless scale-up to a G4 size reactor
- Installation of a G4 reactor with related dosing lines
- ATEX and FDA compliance requirement
- Timeline from first talk to chemistry running in G4: less than 2 years.

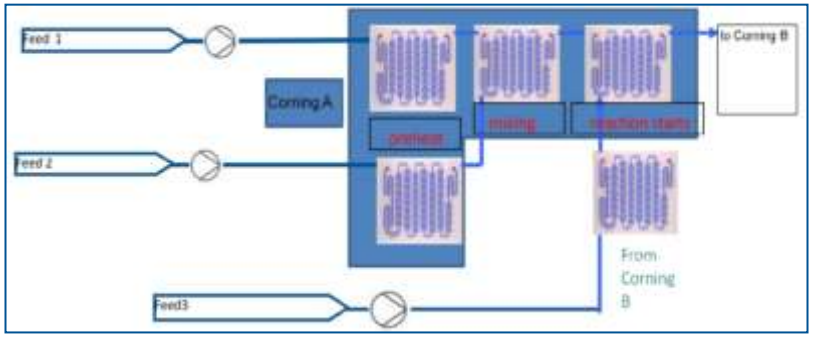
ANGELINI

**Pictures are a courtesy of Angelini (Italy)*

Customer case

Process development in Low Flow and G1

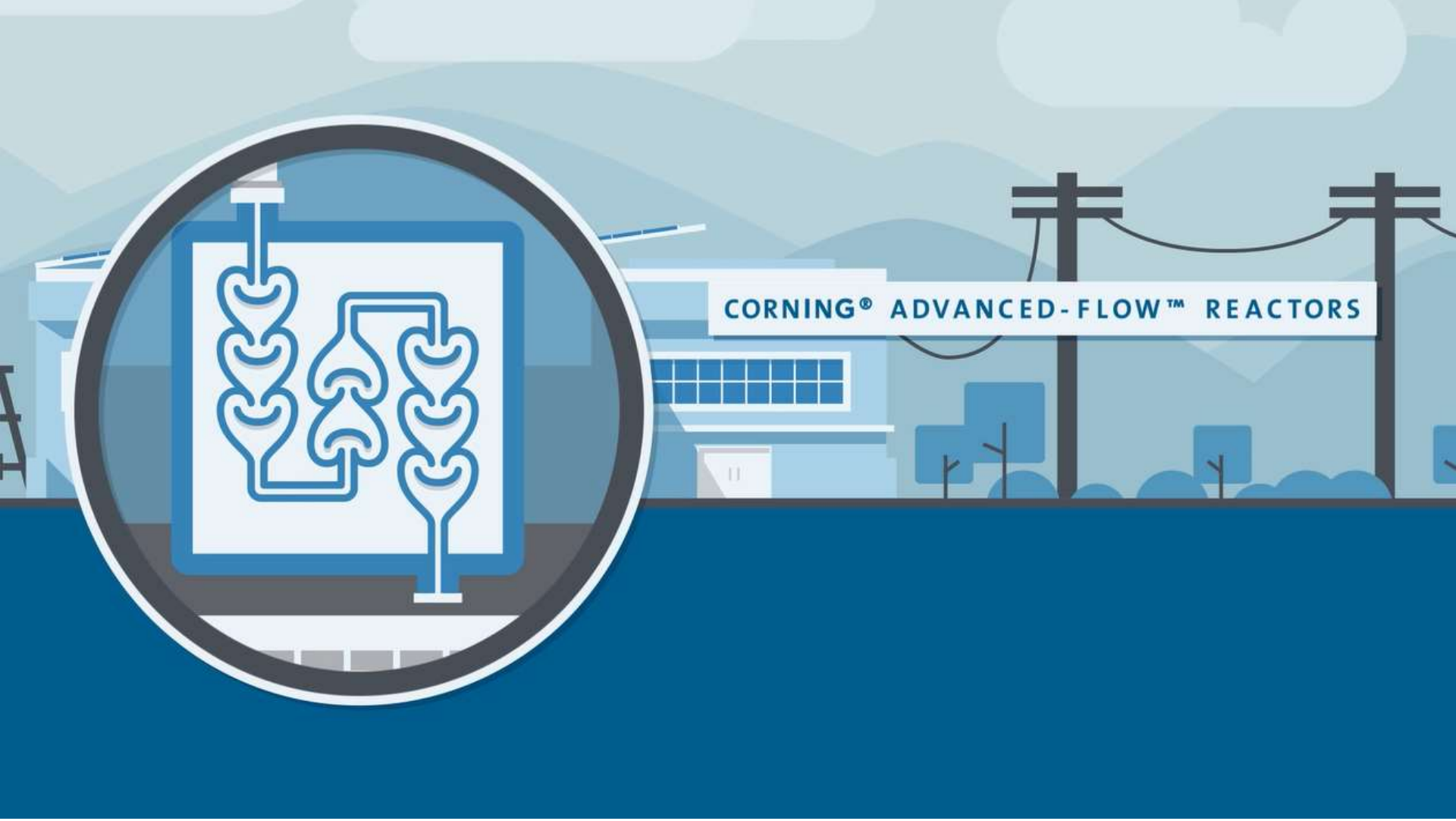
- Flow rate about 15 l/h
- Accurate pumping is critical: non pulsating, positive displacement pumps.
- Capable of handling the reagent and some amount of particulate solids.



Production unit with G1

- Flexible tool
- Resistance toward corrosion
- Required already compliance with FDA guideline

Data and pictures are a courtesy of Teva



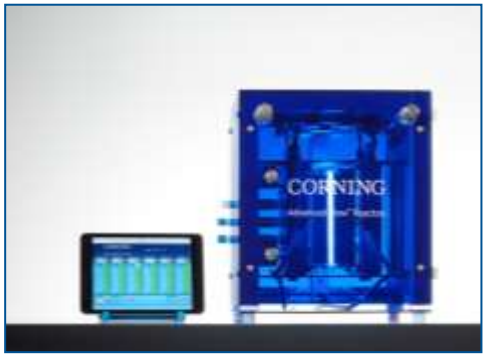
Bringing Photochemistry to Production

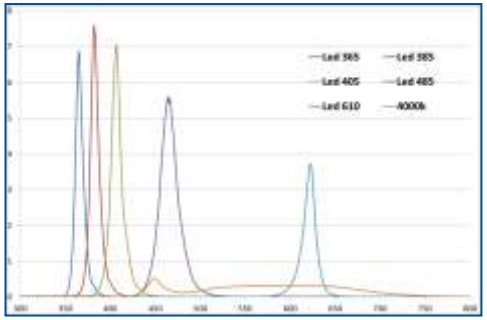
Photochemistry

- Unique combinaison of Corning Advanced-Flow Reactors with highly engineered LED lightning modules

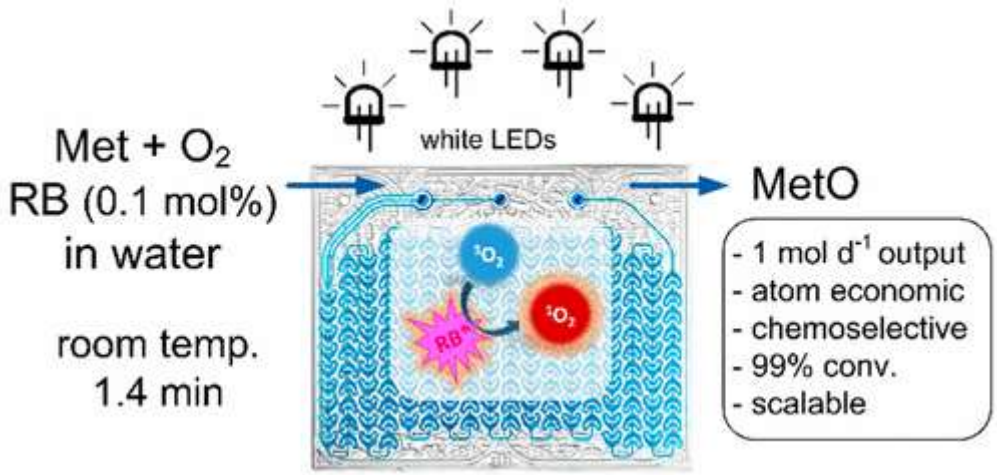
- Start-up kit: the Lab Photo Reactor
  - 6 different wavelength
  - Wireless intensity control
  - Small internal volume

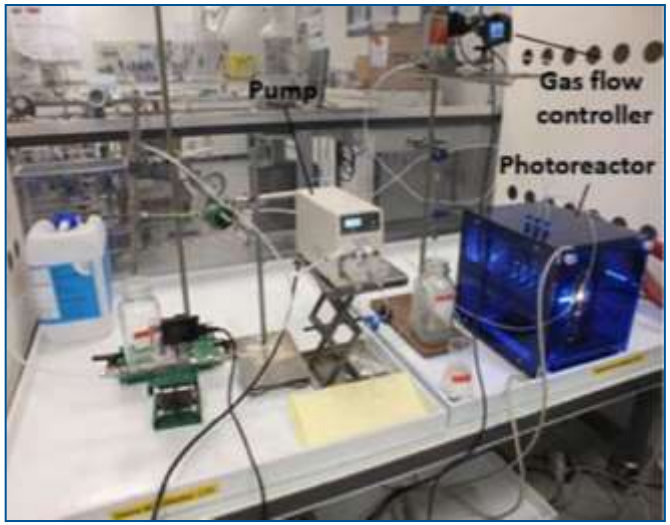
- Production in G1 Reactor and possibility to move to even larger scale

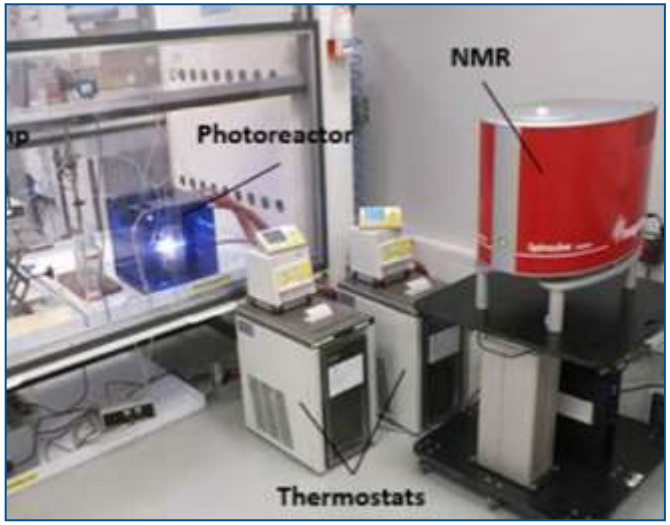




Exemple: Methionine oxidation







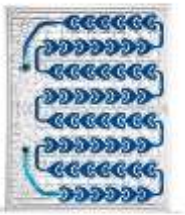
- Sustainable process engineering
- No waste generation
- Safe operating conditions

Org. Process Res. Dev., 2017, 21 (9), pp 1435–1438

Characterization with Actinometer

$$2Fe^{III}(C_2O_4)_3^{3-} \xrightarrow{hv} 2Fe^{II}(C_2O_4)_2^{2-} + 2\,CO_2 + C_2O_4^{2-}$$

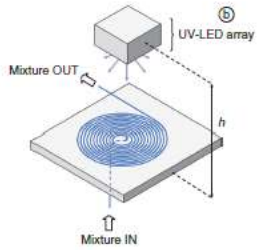
G1



V= 8 ml

G3

V= 60 ml

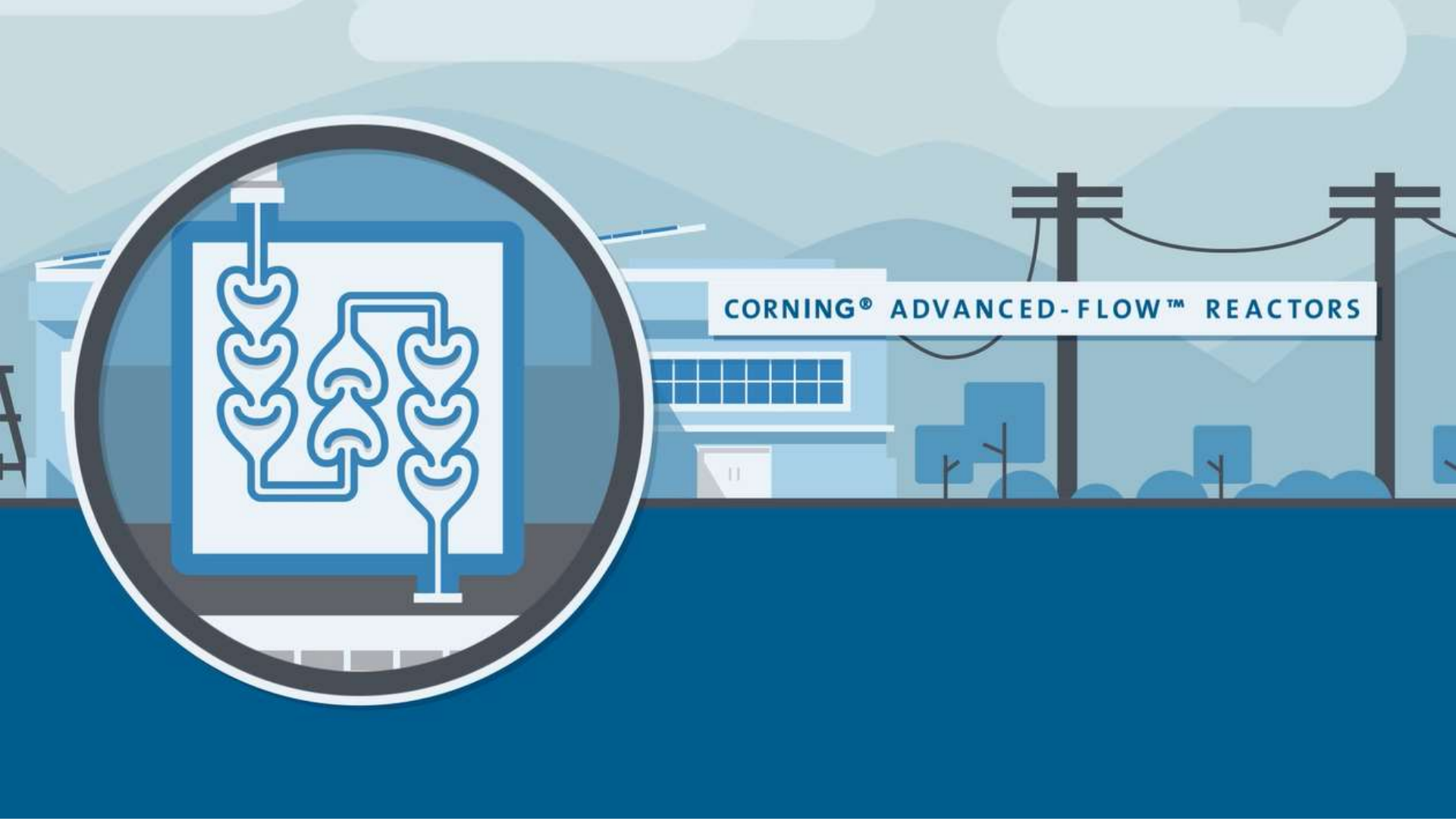


V= 0,54 ml

Scale up

	Light Intensity (Einstein/L*s)	
1 FM 420nm	$3.69*10^{-3}$	
1 FM 405nm	$3.14*10^{-3}$	Gen1
1 FM 365nm	$1.98*10^{-3}$	
1FM 405nm	$4.05*10^{-3}$	
1 FM 365nm	$2.49*10^{-3}$	Gen2
1 FM G3 420nm	$4.78*10^{-3}$	
Microreactor 365nm*	$0,71*10^{-3}$	

**Prat et al, International J. Chem. Reac. Eng. 2014; 12(1): 257-289*



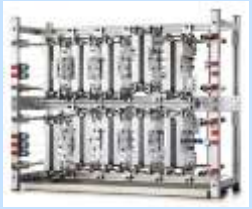
Your next step in flow chemistry

From Lab to Industrial Production

Application Process Development & Small Production

Industrial Production

Lab scale stepping into flow chemistry, Application process development



G1 SiC

80 t/y

G1

G1 Photo

G1 Glass

250 t/y

G2

G2 SiC

1000 t/y

G3

G3 Glass

2000 t/y

G4

3500 t/y

GP4

SiC

Concluding Remarks

- **Corning Advanced-Flow Reactors provide**
  - High Mass transfer
  - High Volumetric Heat transfer
  - Seamless Scale-up

- **Corning Advanced-Flow Reactors deliver**
  - High performance reactors
  - Turn key solution with all auxiliaries needed
  - Customised solution to fit individual needs

- **Corning Advanced-Flow Reactors support**
  - Customers all over the world
  - With a strong R&D team
  - To allow you to go fast to production

CORNING

THE FUTURE FLOWS THROUGH
CORNING® ADVANCED-FLOW™ REACTORS

Advanced-Flow™ Reactor Technologies

www.corning.com/reactors