



We create chemistry

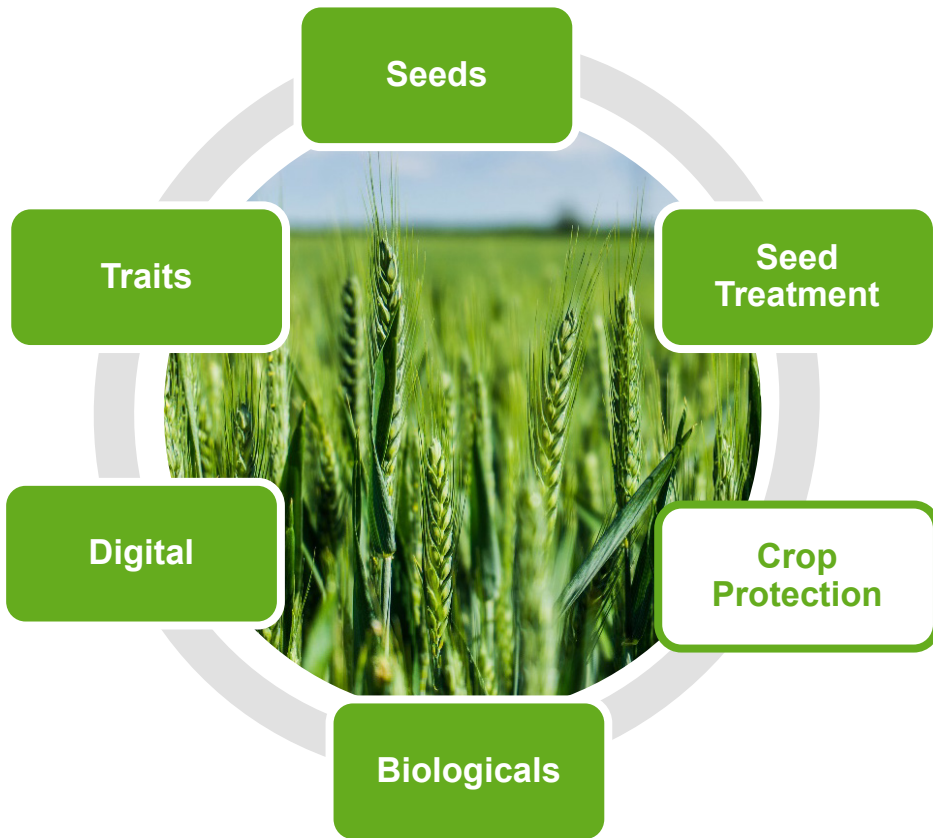
BASF Research Press Conference  
on December 9, 2021

## Protecting crops sustainably with fungicides

**Manuel Medinger**  
Global Project Lead Revysol®



# The right balance for better yield



Yield that is valued by society

More biodiversity protection

Higher yield with lower environmental impact

Less CO<sub>2</sub> per ton of protein produced

Help farmers make a living



# Controlling key fungal diseases is essential for better yield



**Crop  
damage & loss**



**Combat diseases  
with high efficacy**

**Resistant  
pathogens**



**Manage resistance  
effectively**

**Off-target  
effects**



**Ensure  
selectivity**

**Regulatory  
changes**



**Anticipate  
regulation**

**Volatile weather  
conditions**



**Foster climate  
resilience**

The multiple facets of crop production require a new approach in R&D



# Transformative approach in crop protection R&D focuses on three elements

## Parallel approach

optimizing performance and regulatory requirements

## Digitalization of R&D

accelerating screening and development

## Addressing crop system needs

offer a combination of solutions



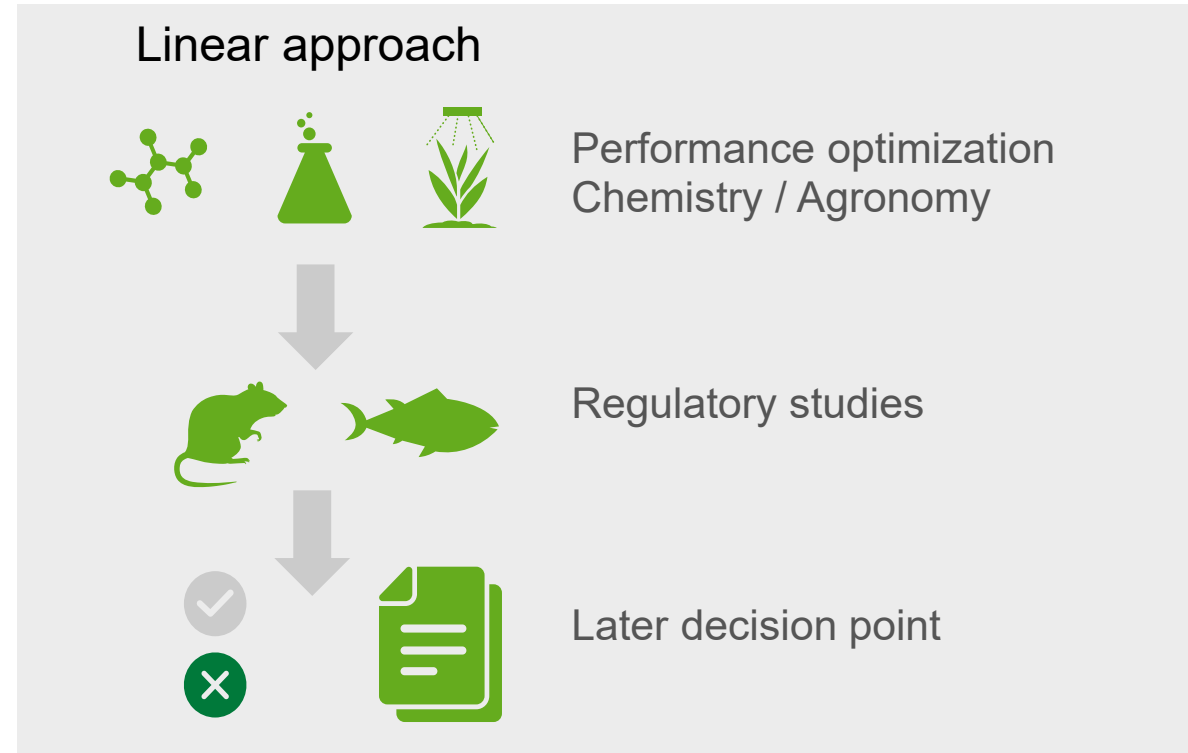
Designed to meet the highest level of performance & regulatory standards





## Historically, industry used a linear approach to maximize performance prior to environmental testing

- Performance and cost optimization first to find most promising candidates
- Regulatory tests to ensure safety for humans and the environment only with finalized candidates
- In case of negative results, candidates had to be stopped late in the process leading to fewer advancing molecules

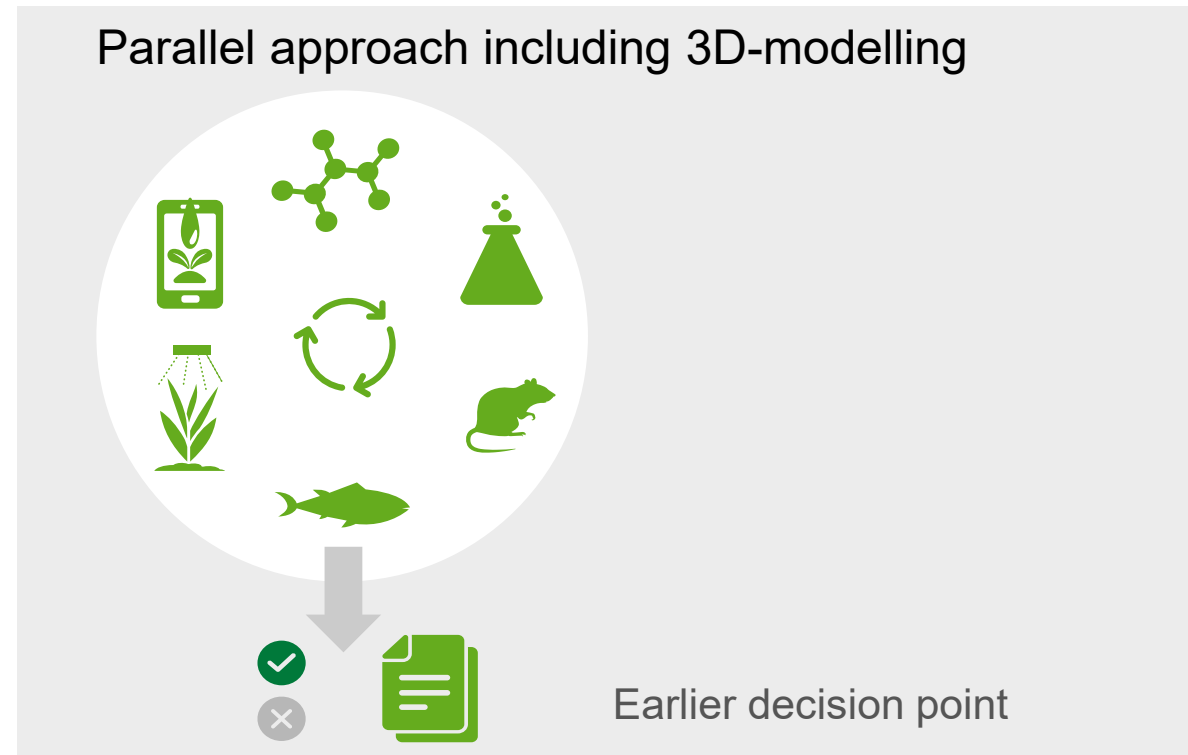


BASF adapted research process to a parallel approach



# New research process better meets sustainability requirements in an early stage

- Identify potential off-target effects early on
- Develop in-vitro tox predictors to minimize animal testing
- Optimize regulatory requirements and performance in parallel
- Support chemical optimization with 3D modelling



Newly implemented research process increases effectiveness to align environmental requirements with field performance



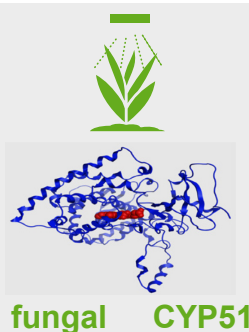
# Disease control and off-target effects were decoupled with the help of molecular modelling

## Structure design supported by 3D-Modelling

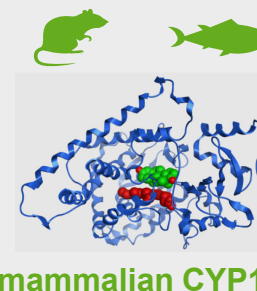
### Desired inhibition

Molecular target of triazole fungicides fungal CYP51<sup>1</sup>

→ target assay developed



maximizes  
selectivity



### Undesired inhibition

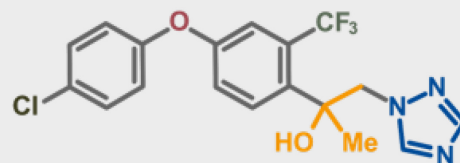
Aromatase (CYP19<sup>2</sup>) affected by triazoles

→ in vitro / in vivo correlation successful

enables

## Design & synthesis of novel triazole with

Increased target (CYP51) inhibition



Reduced off-target (CYP19) inhibition

This new methodology in the R&D approach led to the discovery of Revysol<sup>®</sup>

<sup>1</sup>CYP51 (Lanosterol 14 alpha-demethylase): enzyme in fungal membrane

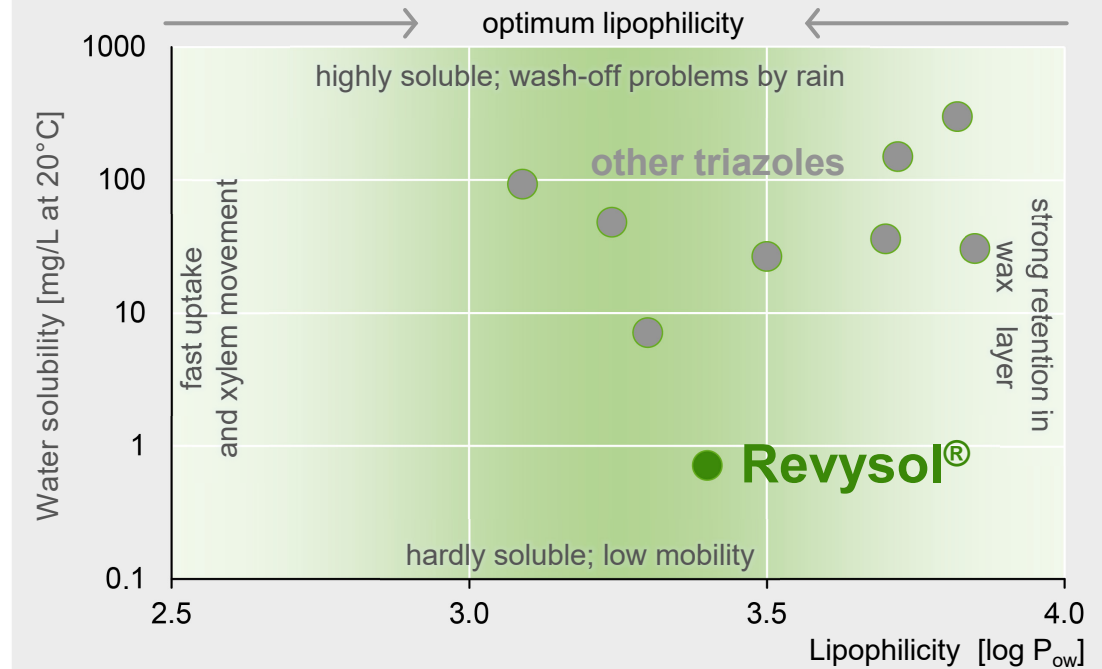
<sup>2</sup>CYP19 (estrogen synthase): enzyme in the biosynthesis of mammalian estrogens



# Understanding the molecular properties was key to optimizing delivery and performance through formulation

- Higher solubility of active ingredients
  - ▶ enables easy uptake by the plant
  - ▶ is susceptible to washout in rain events
- Revysol® active ingredient has a lower solubility than other azoles
- Special formulation of Revysol® enhances uptake despite low solubility

Physical properties of triazoles

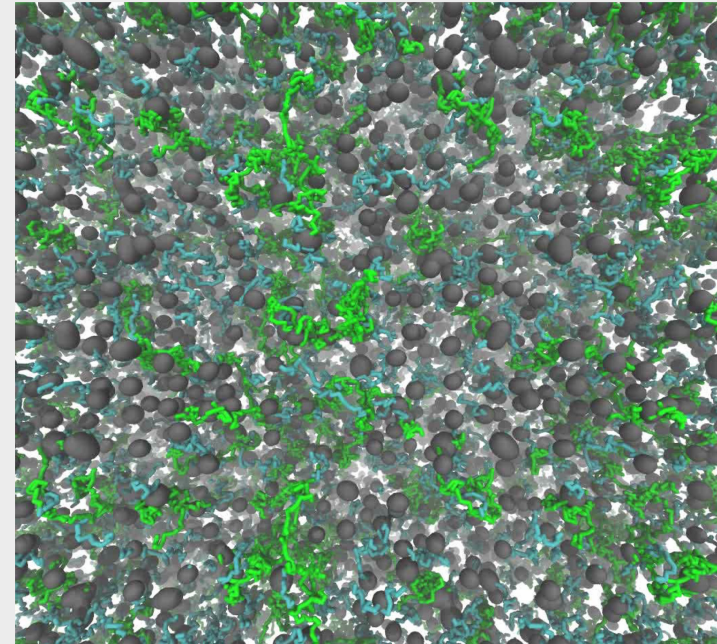


A targeted approach was necessary to reach the fungicidal target in the plant

# Formulation innovation needed to enable outstanding stability and uptake

- Standard formulation practices could not dissolve Revysol® sustainably and durably
- Computer-aided simulation with different emulsifiers used to predict optimal behavior of Revysol® in water
- Over 100 different formulations tested for uptake and translocation

## Modeling process to optimize stability in water



Revysol® molecules (**grey**) and the tested emulsifiers (**green**) to keep Revysol® dissolved. The simulation and predictive modeling process resulted in the use of specific emulsifiers that coat the surface of the Revysol® molecules and avoid crystallization.

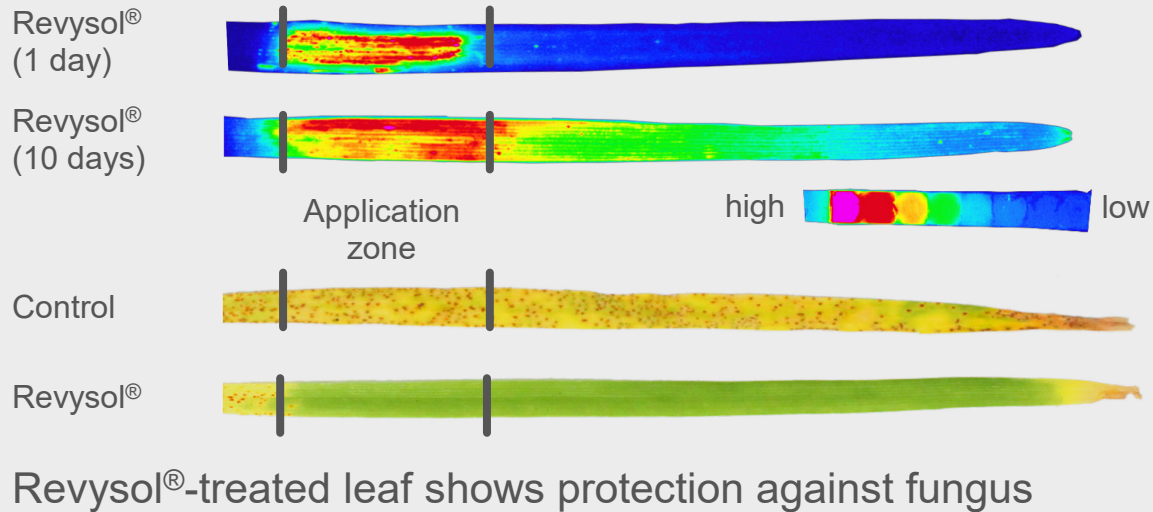
Through computer modeling, a customized emulsifying system was found to turn the low solubility into long-lasting protection



# Tailor-made formulation protects Revysol® from weather effects, reducing application per hectare

## Wheat leaves treated with Revysol®

Radio labelled Revysol® shows uptake & distribution in leaf



## Electronic microscopy of Revysol® in the leaf



Revysol® is well protected from UV degradation and wash-off due to the formation of an inner-leaf reservoir

BASF's formulation experts increased sustainability by optimizing the behavior of the molecule in the plant

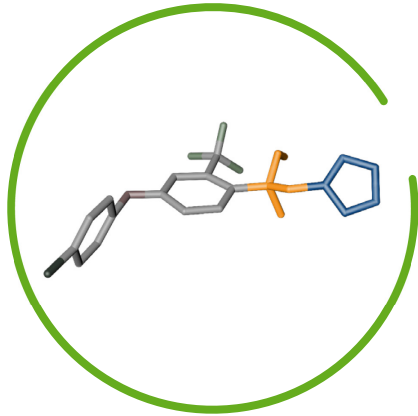
# Transformative approach in R&D enables sustainable, new-generation solutions like Revysol®



Higher yield  
on less land



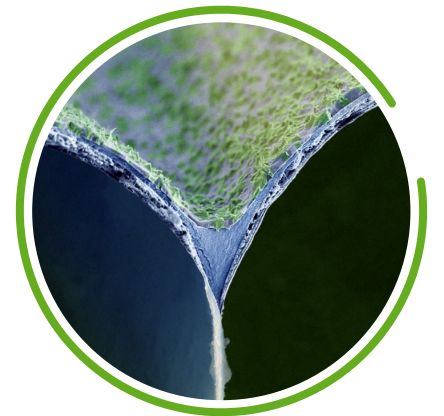
Favorable  
environmental profile



Control of  
resistant fungi



Independent of  
weather conditions



Long-lasting  
performance

- Revysol® enables farmers to protect their crops and farm sustainably
  - ▶ Yield protection and resource efficiency: up to **1/3 less active ingredient per wheat hectare**
  - ▶ Productive land use and protection of natural habitats: **4% less wheat area** needed
  - ▶ Beyond wheat, Revysol® was optimized on more than 40 crops

- Successful market introductions across the globe confirm blockbuster potential of **> €1 billion projected peak sales**
- Strong support of our target of reduce CO<sub>2</sub> emissions per ton of crop by 30%





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