CRISPR-Cas
Representing Abundant Potential for Agriculture
Kevin Diehl, Director, Regulatory Strategy and Industry Affairs
Building on Legacy of Crop Improvement Innovation

HYBRIDIZATION, PLANT BREEDING, GERMPLASM

AGRICULTURAL BIOTECHNOLOGY

CRISPR-Cas ADVANCED BREEDING


Pioneer brand Hybrid 307
Pioneer brand Hybrid 3780
Co-develop
HERCULEX Insect Protection
Copper Cross
Pioneer brand Hybrid 312A

First commercialized product developed with CRISPR-Cas**

PROJECTED GLOBAL POPULATION: 9.6 BILLION

** Pending field trials and regulatory reviews.
CRISPR-Cas Enables Targeted DNA Breaks

Guide RNA matches the target DNA sequence

Cas9 nuclease (DNA cutting enzyme)

Target Sequence

Guide RNA is designed to direct Cas9 enzyme to the DNA sequence of interest

Cas9 enzyme binds to the targeted DNA and makes double strand break

DNA double strand break is repaired through a plant’s own cellular process

CRISPR-Cas Applications
How Can We Use CRISPR-Cas?

**DELETE**

The plant *does not* have desired output.
The plant *does* have desired output.

**EDIT**

The plant has *tolerance* to drought.
The plant has *high tolerance* to drought.

**SEARCH/REPLACE**

The plant is *susceptible* to disease.
The plant is *resistant* to disease.
CRISPR-Cas Enables Efficient Introduction of Desired Characteristics

**Drought tolerance example:**

**FROM:** Incorporating desired characteristics in multiple cycles of common breeding practices

**TO:** Incorporating desired characteristics in as little as 1 to 2 cycles via CRISPR-Cas advanced breeding

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- **100% A**
  - Lower quality plant
  - Tolerant to drought

- **100% B**
  - Higher quality plant
  - Sensitive to drought

**GOAL**

100% high quality plant + drought tolerance
DuPont Pioneer Integrating Core Competencies

Understanding Elite Genetics
- High quality DNA sequencing
- Informatics tools and infrastructure

Delivery into Elite Genetics
- Ability to directly introduce targeted improvements to already high-quality plants

Advancing CRISPR-Cas Technology
- Tool with superior activity and targeting specificity
- Incorporating in-house & collaborators’ expertise
CRISPR-Cas Furthers Innovation for Pioneer® Brand Products

CRISPR-Cas has Numerous Potential Agricultural Applications

First Pioneer® Brand Products to Market in as Early as 5 Years

Potential product targets:
- Yield
- Soybean Output Traits
- Disease Resistance
- Drought Tolerance
- Increased Nutritional Value
- Improved Hybrid Systems

Products, benefits and concepts described herein will not be offered for sale or distribution until completion of field testing and applicable regulatory reviews.
# Multi-Platform Approach to Increasing Crop Productivity

## Digital Agronomic Solutions

- **BREEDING**
  - Insect Control*
  - Weed Control
  - Disease Control**
  - Output Traits
  - Yield & Agronomics

- **CRISPR**
- **BIOTECH**
- **CROP PROTECTION**
- **SEED APPLIED TECHNOLOGY**

* Includes Nematode Control
** Includes Bacterial and Fungal Diseases

**Built on a Foundation of**

- **Com**
- **Soy**
- **Canola, Sunflower, & Other Oilseeds**
- **Rice**
- **Fruits/Veg**
- **Other**
## Near-Term Products to Market

<table>
<thead>
<tr>
<th>Waxy Corn Hybrids</th>
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</thead>
<tbody>
<tr>
<td>• Foundational for future product development</td>
</tr>
<tr>
<td>• First commercial agricultural product</td>
</tr>
<tr>
<td>• To market by end of decade</td>
</tr>
</tbody>
</table>

## Broad Agricultural Applications of CRISPR

<table>
<thead>
<tr>
<th>Disease Resistance</th>
<th>Yield &amp; Yield Stability</th>
<th>Drought Tolerance</th>
<th>Output Traits</th>
<th>Maturity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soy</td>
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<tr>
<td>Canola</td>
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<tr>
<td>Rice</td>
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<tr>
<td>Wheat</td>
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<tr>
<td>Sunflower</td>
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**Northern Corn Leaf Blight**

- Devastating global disease with potential to cause $1.68* annual losses in North America alone
- Leveraging germplasm base
- Utilizing native genes, genomic selection, and genome editing
- Providing sustainable grower solutions

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*Source: Internal analysis and USDA.*

NORTHERN CORN LEAF BLIGHT

**READINESS:**
**First half of next decade**
Waxy Corn is a High Amylopectin Starch Corn

<table>
<thead>
<tr>
<th>No. 2 Yellow Dent Corn</th>
<th>Waxy Corn</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Translucent appearance</td>
<td>• Candlewax-like appearance</td>
</tr>
<tr>
<td>• Feed / ethanol / food</td>
<td>• Food / industrial</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Starch</th>
<th>Starch</th>
</tr>
</thead>
<tbody>
<tr>
<td>75% Amylopectin</td>
<td>&gt;97% Amylopectin</td>
</tr>
<tr>
<td>25% Amylose</td>
<td></td>
</tr>
</tbody>
</table>
CURRENT WAXY CORN PRODUCT
• Change in **WAXY GENE** responsible for amylose production
• Originated from >100 year old corn variety
• Challenges:
  — Some yield drag
  — Lags elite genetics

NEXT GENERATION WAXY CORN PRODUCT
• Change in **WAXY GENE** responsible for amylose production
• Accomplished directly in elite inbred lines - parents of commercial hybrids
• Efficient solution to current waxy product challenges

**WAXY GENE**
- Partial deletion of **WAXY GENE**
- Full deletion of **WAXY GENE**

Starch
>97%
Amylopectin
Maize Lethal Necrosis Disease

Range of symptoms
- Vascular discoloration
- Even “clean” plants may show:
  - Sterile tassels
  - No ears
  - High cob rot/ predisposed to other challenges

• MLN first observed in Kenya in 2011; spread to neighboring countries in less than five years

• Average reduction in maize production: 3% in drylands; 32% in moist environments; yield reduction at individual farms can be as high as 90% (de Groot et al., CIMMYT)

• In Kenya, MLN affects nearly a quarter of total maize production; yearly losses ~$US110 million (Biosciences for Framing In Africa, 2016)
Vast Potential for Wide Array of Applications

Developing solutions to the toughest agricultural challenges
Listening to Full Range of Stakeholders

- Recognize that all new technologies require a “social license”
- Asking traditional and non-traditional stakeholders about their hopes and fears of CRISPR-Cas and how to balance the two
- Using insights as we develop our plans and as we work with others in agriculture and with those applying CRISPR-Cas across industries
- On-going discussion
CRISPR-Cas is one of many tools DuPont uses to deliver improved products and value to customers.

Safety and product stewardship are foundational to any DuPont product offering. See more here

When using CRISPR-Cas for advanced plant breeding, DuPont will only work with genetic material from the target plant/crop.

DuPont is committed to open, transparent, and timely communications about its use of CRISPR-Cas.

DuPont is committed to responsible development and application of CRISPR-Cas to help ensure consumer confidence.

- DuPont supports appropriate, science-based regulatory oversight for plants developed with CRISPR-Cas advanced plant breeding, consistent with plants developed through other plant breeding methods.

- DuPont intends to enable others wanting to develop agricultural products using CRISPR-Cas through access to intellectual property (IP), technology capabilities, infrastructure and scientific expertise.

- DuPont will consider diverse viewpoints in its decision-making process for products developed with CRISPR-Cas advanced plant breeding.

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1 "CRISPR-Cas" is derived from naturally occurring “CRISPR” found in many bacteria that naturally protect themselves against bacteriophage. DuPont has used this natural CRISPR for many years to improve dairy product manufacturing and to make food safe and last longer.

2 These principles refer to the DuPont use of “CRISPR-Cas” as a plant breeding technique. If CRISPR-Cas is used to more efficiently develop GMOs, DuPont will follow all applicable GMO regulations and the DuPont Biotechnology Guiding Principles. See more here
Vision for CRISPR-Cas at DuPont Pioneer

HALO MESSAGE
CRISPR-Cas is a more efficient way to improve plants and help farmers produce more and better food, with fewer resources.

Why?
Farmers face real challenges because plants are under constant stress from things like climate change, drought and disease. This, coupled with rapid population growth and changing diets, requires agricultural innovation to keep pace. CRISPR-Cas is a more efficient and targeted means to developing agricultural solutions to these evolving challenges.

What?
Based on a natural system, CRISPR-Cas can precisely improve a plant without incorporating DNA from another species. It’s a continuation of what people have been doing since plants were first domesticated – selecting plants for their desired characteristics like higher yields, disease resistance, longer shelf life or better nutrition. It’s one tool that could help keep pace with the growing demand for more sustainable agricultural solutions.

DuPont’s Commitment
DuPont is committed to transparent and timely communications about our use of CRISPR-Cas and intend to enable others wanting to develop agricultural products using CRISPR-Cas. We believe in the responsible development and application of CRISPR-Cas. We support appropriate, science-based regulatory oversight and will consider diverse viewpoints in our decision making.