This communication expressly or implicitly contains certain forward-looking statements concerning Cellectis SA and its business.

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Cellectis SA is providing this communication as of this date and does not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.
Company

- Based in New Brighton, Minnesota – The Green Evolution Company
  - Parent company based in Paris, France (publicly traded)

- Established in March 2010
  - Luc Mathis – CEO
  - Pr. Dan Voytas – CSO – Head of Genome Engineering Department at UMN
  - Feng Zhang – COO
  - Voytas and Zhang are inventors of the TALEN technology

- Targets:
  - Develop plant products obtained through targeted gene editing
  - Develop novel traits and trait combinations in crops of agronomic interest

- Mission: “Crop improvement through targeted gene editing”
DNA-binding TAL domain coupled to FokI (a protein domain without endonuclease activity) to form an endonuclease activity only as a dimer.
Repair of DNA Breaks for Genome Modifications

Non-Homologous End-Joining (NHEJ)

- Self repair by DNA ligation

Homologous Recombination (HR)

- DNA template is used for break repair

Mutagenesis occurs when nucleotides are digested before DNA ligation

Mutagenesis is controlled by the DNA template

Targeted Gene Knock-Outs

Targeted Gene Insertions and Replacements
Technology: Targeted Gene Editing

Meganucleases
Naturally occurring DNA ‘cutters’ found in single-cell organisms

Zinc Finger Nucleases
DNA binding proteins coupled to FokI to form endonucleases

TALEN™
DNA binding proteins coupled to FokI to form endonucleases

CRISPR/CAS
RNA-guided endonuclease

Applications: Gene knock-out, Knock-in and Point Mutations
The Right Tool in the Right Hands
Product Development Overview

- No use of Agrobacterium
- No integration of foreign DNA into the genome
- Highly specific: limited off-target cutting
- No unintended gene silencing
- No bacterial or plant selectable marker

Potato protoplasts → PEG Transformation → \( \text{TALEN}^{\text{TM}} \) → Target Gene (Trait) → Callus Formation → Plant Regeneration

Field selections, phenotyping, field trials, seed bulking

Molecular Genotyping

Plants with no foreign DNA

Trait Validation (Greenhouse)
Acrylamide Reduction in Potato

**Vacuolar Invertase (VInv)**
Cold storage/reduced acrylamide has major commercial value

Bhaskar et al, 2010
Acrylamide Reduction in Potato

Summary of allelic series of VInv mutants

<table>
<thead>
<tr>
<th>Mutant ID</th>
<th>Number of alleles disrupted</th>
<th>Vegetative clones</th>
</tr>
</thead>
<tbody>
<tr>
<td>St116_1</td>
<td>3 (out of 3)</td>
<td>24</td>
</tr>
<tr>
<td>St116_2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>St116_3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>St125_1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>St125_2</td>
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<td>8</td>
</tr>
<tr>
<td>St125_3</td>
<td>1</td>
<td>1</td>
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</table>

Molecular confirmation that all VInv alleles are disrupted in St116_1 potato line
Tobacco Line for Production of Bio-therapeutics

Transformation

<table>
<thead>
<tr>
<th>TALEN</th>
<th>Target</th>
<th>Gene 1/2</th>
<th>Gene 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAL_X3</td>
<td>25.4%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>TAL_X4</td>
<td>57.9%</td>
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<td></td>
</tr>
<tr>
<td>TAL_Y2</td>
<td>NA</td>
<td>27.8%</td>
<td></td>
</tr>
<tr>
<td>TAL_Y4</td>
<td>NA</td>
<td>39.9%</td>
<td></td>
</tr>
<tr>
<td>TAL_Y5</td>
<td>NA</td>
<td>3.9%</td>
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</table>

TALEN cutting efficiency in protoplasts at target loci

Example of Deletions at Genes 1 & 2

Gene1 alleles (two 44-bp deletions) in NB14-29a:

Gene2 alleles (2-bp and 40-bp deletions) in NB14-29a:
Knockouts Give Expected Phenotype

Next Steps:
- Generating 8-allele/4-gene knockout by crossing/selfing
- Monitor post-translational modifications on recombinant proteins in 4-gene knockout
Soybean Oil Composition Improvement

Sample Genotyping Results of T<sub>0</sub> plants

<table>
<thead>
<tr>
<th></th>
<th>GM026-7a</th>
<th>GM026-17</th>
<th>GM026-18</th>
<th>GM026-20</th>
<th>GM026-23</th>
<th>GM027-3</th>
<th>GM027-6</th>
<th>GM027-7</th>
<th>GM027-10</th>
<th>GM027-11</th>
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<tbody>
<tr>
<td>FAD2-1A</td>
<td>WT</td>
<td>WT</td>
<td>+ / -</td>
<td>WT</td>
<td>+ / -</td>
<td>WT</td>
<td>WT</td>
<td>WT</td>
<td>WT</td>
<td>WT</td>
</tr>
<tr>
<td>FAD2-1B</td>
<td>WT</td>
<td>WT</td>
<td>+ / -</td>
<td>WT</td>
<td>WT</td>
<td>WT</td>
<td>+ / -</td>
<td>WT</td>
<td>WT</td>
<td>WT</td>
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</tbody>
</table>

First 10 plants yielded three unique individuals with deletions at both genes

Soybean Mutants Produce Intended Phenotypes

Deletion Example at FAD2-1B

ATTTCTCATGGAAAAATAAGCCATCGCCGCCATCACTCCAAACAGGGTTCCCTTGACCGTGATGAAGTGTGTGTCCCA
ATTTCTCATGGAAAAATAAGCCATCGCC---CTTGACCGTGATGAAGTGTGTGTCCCA

---

Project Duration
From TALEN production to T2 seed for phenotypic analysis

18 months

Engineered Diseases Resistance – Gene Editing

1) ID Target

2) Test Transformation

80-90% transformation efficiency in soybean protoplasts

3) Test TALEN™

4) Design Donor

Donor DNA
### Targeted Gene Editing In Soybean

- **Query 421**
- **Query 481**
- **Query 541**
- **Query 601**
- **Query 661**
- **Query 721**
- **Query 781**
- **Query 841**
- **Query 901**
- **Query 961**
- **Query 1021**
- **Query 1081**
- **Query 1141**
- **Query 1201**
- **Query 1261**

<table>
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<tr>
<th>SbjNN</th>
<th>421</th>
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<th>1021</th>
<th>1081</th>
<th>1141</th>
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<tr>
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<td>0</td>
</tr>
<tr>
<td>donor + exTAL1</td>
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<td>1.7%</td>
<td>1.7%</td>
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<td>1.7%</td>
<td>1.7%</td>
</tr>
<tr>
<td>donor + inTAL2</td>
<td>8</td>
<td>6.7%</td>
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</tr>
</tbody>
</table>

- **120 colonies screened**
Shifting Public Perception on GMO Crops

Bill requires labeling genetically modified foods

Associated Press
Saturday, January 4, 2014
(Published in print: Sunday, January 5, 2014)

McDonald's GMO dilemma: why fries are causing such a fuss
Plenty of GMO food probably already makes it on to your plate, and the scientific consensus is that it’s safe to eat. So why are activists so opposed to genetically modified potatoes?

General Mills: Original Cheerios are GMO free
By Aaron Smith @AaronSmithCNN January 3, 2014: 8:37 AM ET

McDonald's already sources other food made from genetically engineered crops.
Regulatory Status

- **United States**
  - Broad opinion letters from USDA for targeted gene editing
  - Opinion from USDA on targeted gene KO with a TALEN
  - Null-segregant is non-regulated (maize, tobacco, sorghum)

- **Japan**
  - Null-segregant is non-regulated (Pioneer SPT maize)

- **Europe**
  - NBT platform, positive trend from the EU commission

- **New Zealand**
  - Gene knockouts using nucleases are exempt from GM regulations
Partnering with CPS
<table>
<thead>
<tr>
<th>Patent Number</th>
<th>Claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>8,586,363</td>
<td>Method for modifying the genetic material of a cell with a FokI endonuclease domain and a TAL effector domain</td>
</tr>
<tr>
<td>8,450,471</td>
<td>Article of manufacture comprising a first TAL effector repeat sequences and a FokI endonuclease domain and second TAL effector repeat sequences and a FokI endonuclease domain</td>
</tr>
<tr>
<td>8,440,431</td>
<td>Method for making an article of manufacture comprising a nucleic acid encoding a first TAL effector endonuclease monomer and a nucleic acid encoding a second TAL effector endonuclease monomer</td>
</tr>
<tr>
<td>8,440,432</td>
<td>Method wherein a first TAL effector endonuclease monomer and second endonuclease monomer form a dimer, and wherein said dimer is capable of cleaving target DNA within a living cell</td>
</tr>
</tbody>
</table>

**Europe**

Received notification from European Patent Office that the examiner has agreed to grant the patent and is expected the end of June (EP 10799163)
Expertise in Partnering

A unique Genome Engineering and Partnering Expertise

- Experienced team, stewardship and LIMS standards
- New process: targeted gene editing – non GMO
- New product opportunities and intellectual property

Platform to Outsource R&D programs

- Develop stacks or non-transgenic products in Soybean, Corn, Canola, Potato, Tobacco
- Value creation in a rapidly maturing field
Conclusions

- Access to unique trait development pipeline
- Cost effective development compared to financing in-house operation
- Strategic non-GMO positioning
- Collaborative partnership enhancing strengths of each partner

Inquiries please contact: whaun@cellectis.com
Thank You