

MERISTEM THERAPEUTICS

Una Nueva Economía para las Plantas Cultivadas
November 20, 2006

MERISTEM THERAPEUTICS

From Transgenic Plants to Medicines

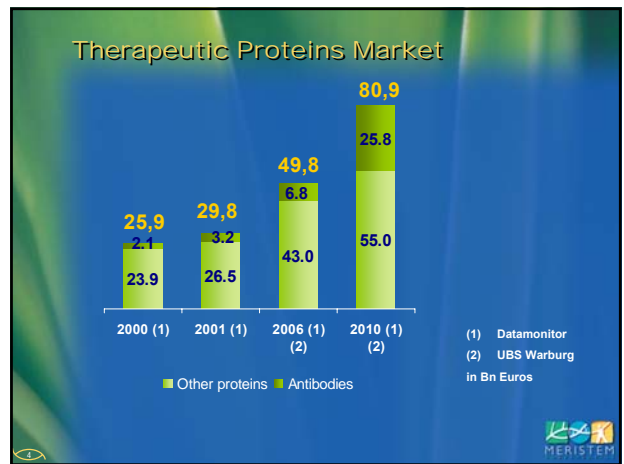
Therapeutic Recombinant Proteins produced in Corn and/or Tobacco

Company Profile

- Established in 1997
- Head Office in Clermont-Ferrand, France
- Labs & Pilot Production

Greenhouse in Veyre-Monton

Plant in Riom

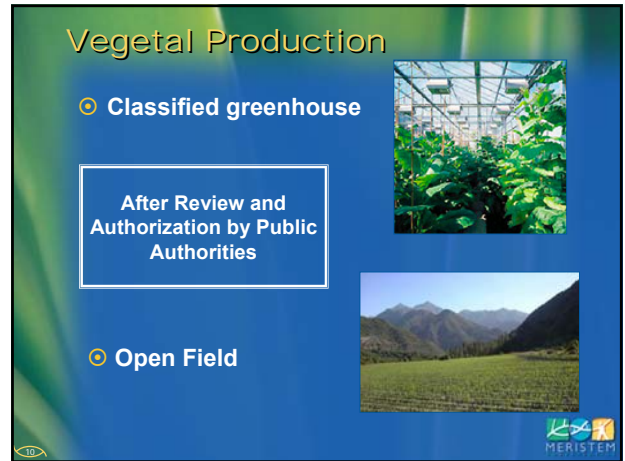
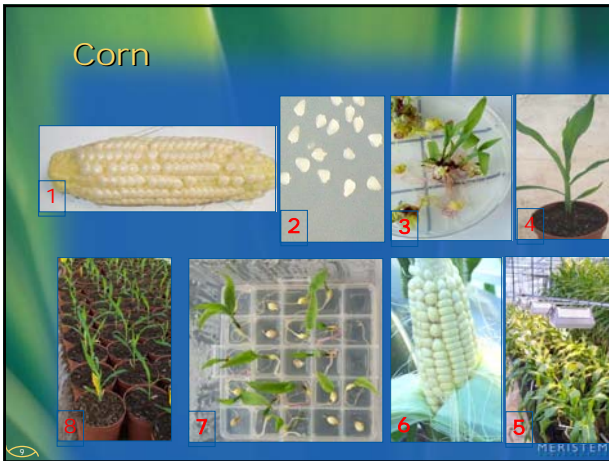
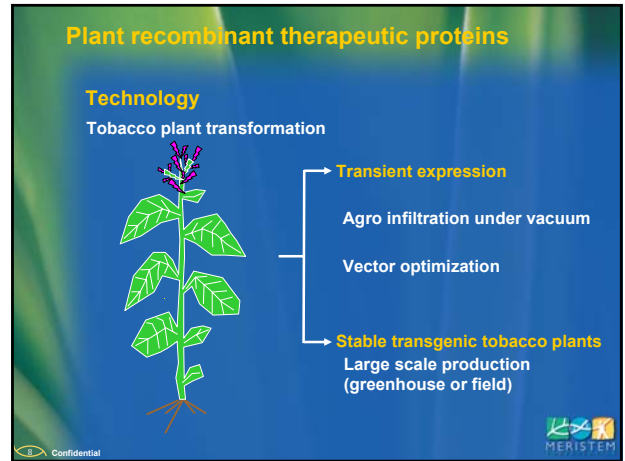
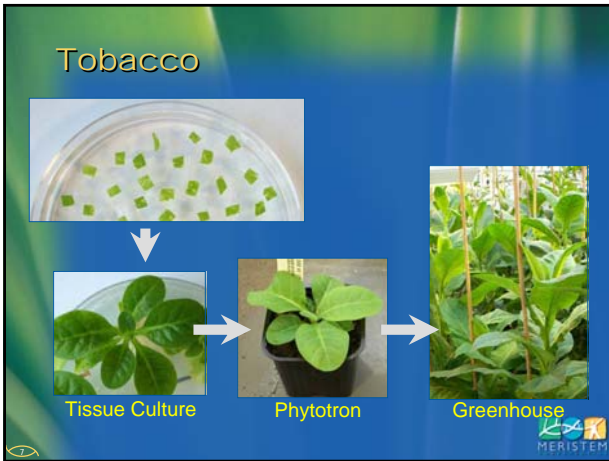


Evolution of expression systems

- Extraction / tissues or fluids of human or animal origin
- Production by bacteria / yeasts
- Production par culture of mammalian cells
- Production by transgenic animals
- Production by transgenic plants

Why plants?

	Fermentation		Cells culture	Transgenic	
	E.coli	Yeasts	CHO, PER, C6	Animals	Plants
Protein complexity	-	+/-	++	++	+/-
Cost	+/-	+/-	-	+	++
Time to delivery	+	+	+	-	+/-
Flexibility/capacity	+	+	+/-	+/-	++
Safety (viral, envir.)	+	+	+	+/-	+
Regulatory	++	++	++	+	+



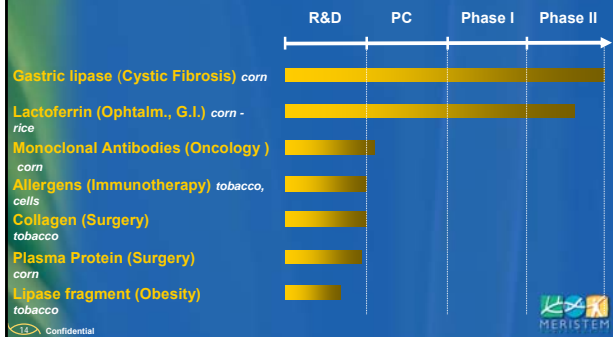
Field Trial Authorizations

- France: 1997, 1998, 1999, 2001, 2003, 2005, 2006
- USA: 1999, 2002, 2003
- Spain: 1997
- Chile: 2001, 2003, 2004, 2005



Plant recombinant therapeutic proteins

Portfolio



Confidential



Recombinant Gastric lipase

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Gastric Lipase: Merispase®

A recombinant lipase, improving lipid absorption in cystic fibrosis patients (exocrine pancreatic insufficiency)

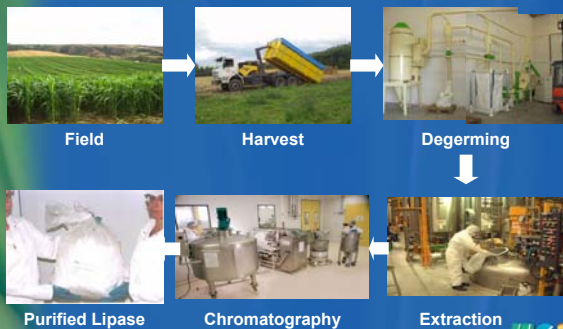
Technology

- ✗ Transgenic corn
- ✗ Endosperm specific
- ✗ Single locus selected
- ✗ No extra vector sequences inserted
- ✗ Expression level: 1mg/g seed

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Merispase® production process

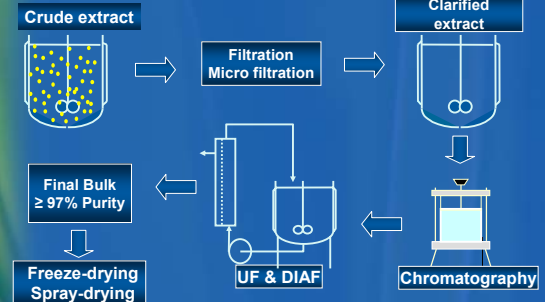


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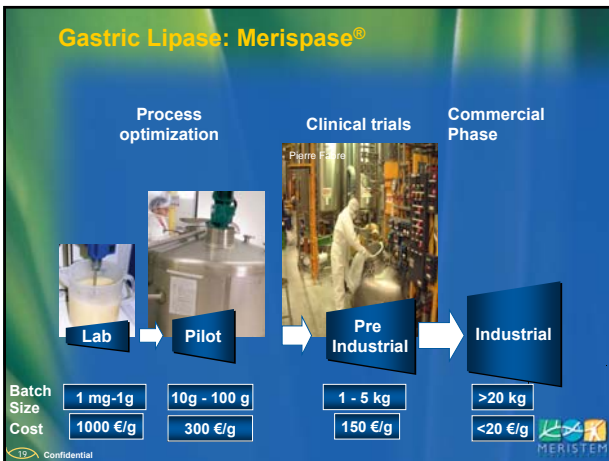
Gastric Lipase: Merispase®

Process



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Recombinant allergen

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Dust mite allergen

Der p1 allergen

- Major allergen of the house dust mite
- Glycoprotein with cysteine protease activity (25kDa)
- Expression in other systems (bacteria, yeast, mammalian cells) not successful
- Alternative production required for immunotherapy treatments

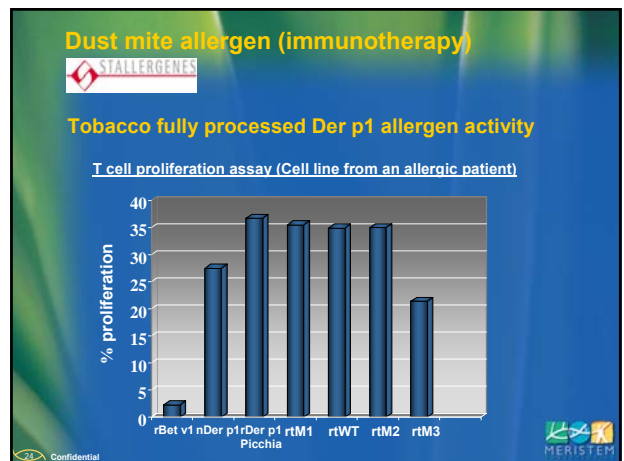
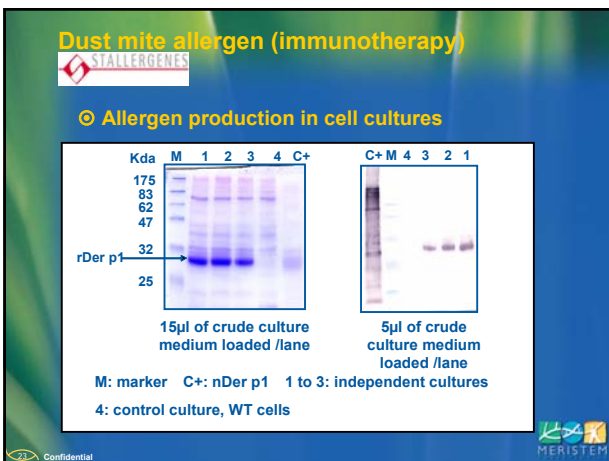
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Dust mite allergen

Technology

X Transgenic tobacco
 X Constitutive expression
 X Expression level: 0.05=>1 mg rDer p1 / g of leaf

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Conclusions

- The technology has demonstrated its capability to produce active proteins in transgenic plants
- It can drive down the manufacturing costs of future medicines
- It can succeed in obtaining proteins difficult or impossible to obtain in other systems
- Both tobacco and corn can be used, with specific advantages



8, rue des Frères Lumières 63100 Clermont-Ferrand France
T 33 473 98 68 10 - Fax 33 473 98 68 19
www.meristem-therapeutics.com

