Precision Breeding for improved Animal Health and Welfare

Regulatory Hurdles for Commercialization of Precision-Bred Food Animals

Mitch Abrahamsen, PhD. Chief Commercial and Scientific Officer
Executive Vice President

Acceligen a division of recombinetics

U.S. Regulatory Pathway for Recombinetics' GE Products

Biomedical / Human Applications

Food Animal Applications

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Pre-Clinical Research	**Regenerative Medicine**	**Animal Agriculture**
Biomedical Models for Developing Human Therapeutics	**Transplantable Cells, Tissues, & Organs**	**Precision Breeding for Animal Health & Productivity**
✓ Regulated by FDA; Process Works Well. Disease Models Approved and for Sale.	✓ FDA Process Exists for Cells, Tissues and Blood Products.	X Regulated as a Drug by FDA under Draft Guidance 187. "*Needs to be regulated based on risk/novelty of the product, not based on process*"

Functional and Defined FDA Process

Unclear/Inhibitory Process

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Food Animal Applications

Animal Agriculture

Precision Breeding for Animal Health, Welfare & Productivity

Innovative Technology - Agriculture

Partnerships with global animal genetics companies to meet industry, retailer and consumer demand for:

Technology looking for a problem

vs.

Problem in need of a technology

t

Accelerating genetic improvement to address critical issues in global farming

- ✓ Naturally-occurring genes
- ✓ Animals not novel
- ✓ Can be achieved through traditional breeding

Who Benefits?

In Europe, These Little Piggies Can't Get to Market.

Precision Breeding Can Provide a Humane Solution for Pork Producers

9TH JANUARY 2018

PIG WELFARE CRISIS CONTINUES: EUROPEAN DECLARATION ON ALTERNATIVES TO PAINFUL SURGICAL CASTRATION FAILS TO DELIVER

European Union Bans Mechanical Castration of Male Pigs Jan. 2018

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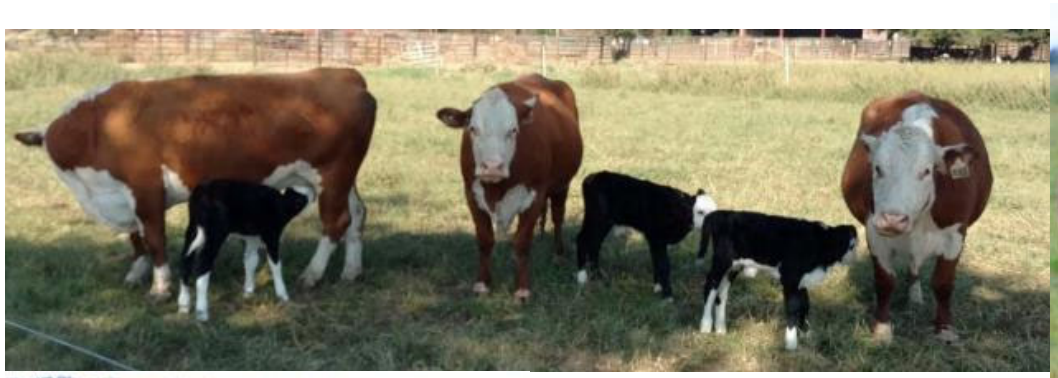
Precision Breeding Solutions for Cattle Health & Welfare

Second Generation of Recombinetics' Gene-Edited Naturally Hornless (Polled) Cattle

Six new healthy precision-bred calves were born in September 2017 including the world's first precision-bred heifer



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Global Livestock Sector & Cattle in the Tropics

- **Elite genetics are not adapted**
- **Breed development takes time**
- **Gene editing can help solve this problem – *precision breeding***

30% of the land	**$1.4 Trillion Global Market**	**1.3 billion employed Long Value Chains**	**53% GDP in IN**	**33% Ag GDP in EE**

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Genselle: First Generation Naturally Cool Calf in the News (SLICK/Heat Tolerant) Born in Brazil July 2018

VIDEO THE WALL STREET JOURNAL.

This Gene-Edited Calf Could Transform the Beef Industry

Is Geneselle Naturally Cool™ in a Brazilian way?

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Acceligen's Commercial and Co-Development Progress

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Food Animal Applications

Animal Agriculture

Precision Breeding for Animal Health, Welfare & Productivity

Partnerships with global genetic companies to access:

- ✓ Elite, commercially relevant genetics
- ✓ Animal production systems
- ✓ Developed distribution networks
- ✓ Established customer bases

Bovine – Beef and Dairy

Naturally Hornless (Polled): Partnership with Semex Alliance announced for North America; European partner pending

Heat Tolerant (SLICK): Calves born in Brazil Q2 2018

TB Disease Resistance: $1.3 M development grant received Q1 2018; funding from 3 countries for isolation of disease resistance genes

Swine

Castration-Free Pigs: Partnerships with Hendrix and DNA Genetics announced

PRRSV: Development and commercial partner identified

FMDV: Proof of concept animal developed; semen collection in progress to develop production

Aquaculture

Sterility/Monosexing: Development and commercial partner identified; LOI signed

Contracted Partners

SEMEX Genetics for Life®

Boviteq™

HENDRIX GENETICS

DNA GENETICS Greater gains. Improved performance.

Naturally Hornless (Polled) Commercial Partnership with Semex

Premier North American Dairy Genetics Company (5/29/18)

NUTRITION & HEALTH

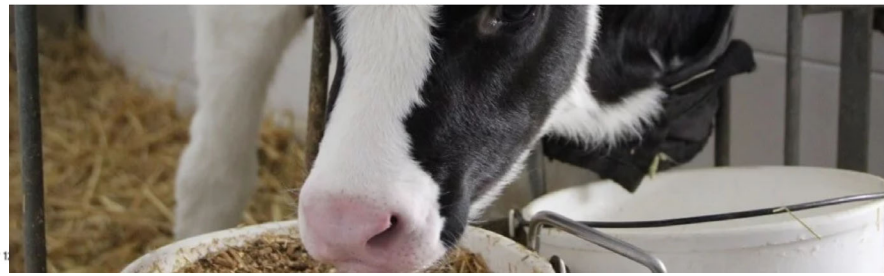
Feedstuffs

Recombinetics, Semex form alliance to improve cattle well-being

SEMEX®
Genetics for Life®

real agriculture

Gene editing allows for polled dairy genetics without the production drag



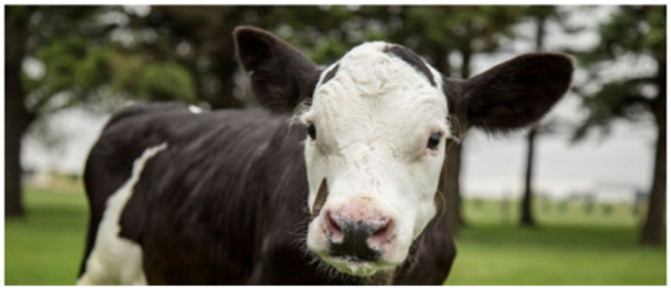
October 1

This Genetics Company Is Editing Horns Off Milk Cows

● Recombinetics says its genetically edited Holsteins are ready to milk, but FDA rules are in flux.

By Adam Piore

Bloomberg Businessweek



Good News

AGDAILY

LIVESTOCK NEWS TECHNOLOGY

Precision breeding partnership will eliminate need to dehorn dairy cows

By AGDAILY Reporters • Published: May 29, 2018

Castration-Free Swine Partnership with Hendrix and DNA Genetics

FFAR Awards $500,000 Grant to Improve Swine Health and Well-Being

Researchers at Recombinetics Will Use Advanced Breeding Techniques to Eliminate Need for Surgical Castration

NEWS

Recombinetics, DNA Genetics form alliance to end surgical castration of swine

Alliance aims to improve swine health and well-being by developing precision breeding technology.

National Hog Farmer

Recombinetics and DNA Genetics form alliance to end surgical castrations of swine

Jan 03, 2018

"Precision breeding includes a range of technologies that will have a strong impact on genetic improvement programs. This specific project is an innovative use of precision breeding techniques that have the potential of improving both animal health and efficiency. We are pleased to be a part of making this technology available to the pork industry," Tom Rathje, Chief Technical Officer, DNA Genetics.

NEWS

Hendrix Genetics joins alliance to end surgical castration of swine

Precision breeding technologies will provide solution for pork producers.

FFAR

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NATIONAL PORK PRODUCERS COUNCIL

U.S. REGULATORY SUPPORT

"NPPC urges the Trump administration to move regulatory oversight of gene editing in animals from the FDA to the USDA's Animal and Plant Health Inspection Service. "

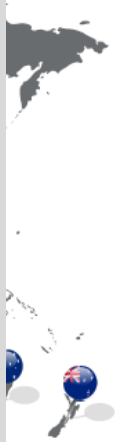
A Global Plan of to Bring Desired Products to Market

The U.S. Not the First Mover – Need to make sure U.S. is not the last

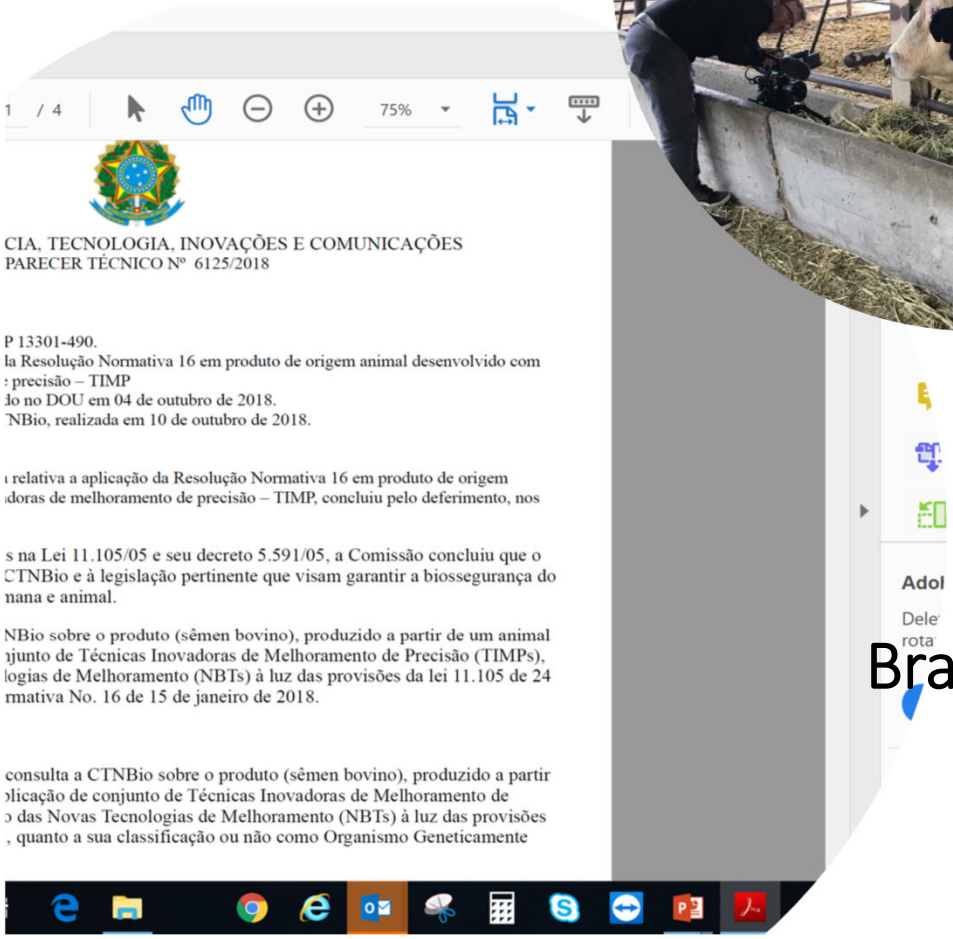
- ✓ Whil
  oppo
  focus
  acce
- ✓ ***Braz***
  favor
  editi
  mon
  comr
  prod
- ✓ ***Japa***
  gene
  of Justice ruled all gene-editing is GMO.

Need to commercialize is driving our efforts to **seek regulatory approval outside the U.S.** for our gene-edited bovine and swine food animals where the pathway is defined and regulated based on product novelty/safety

- ✓ **Focus countries: Argentina; Australia; Brazil; Canada; New Zealand; and Ireland**



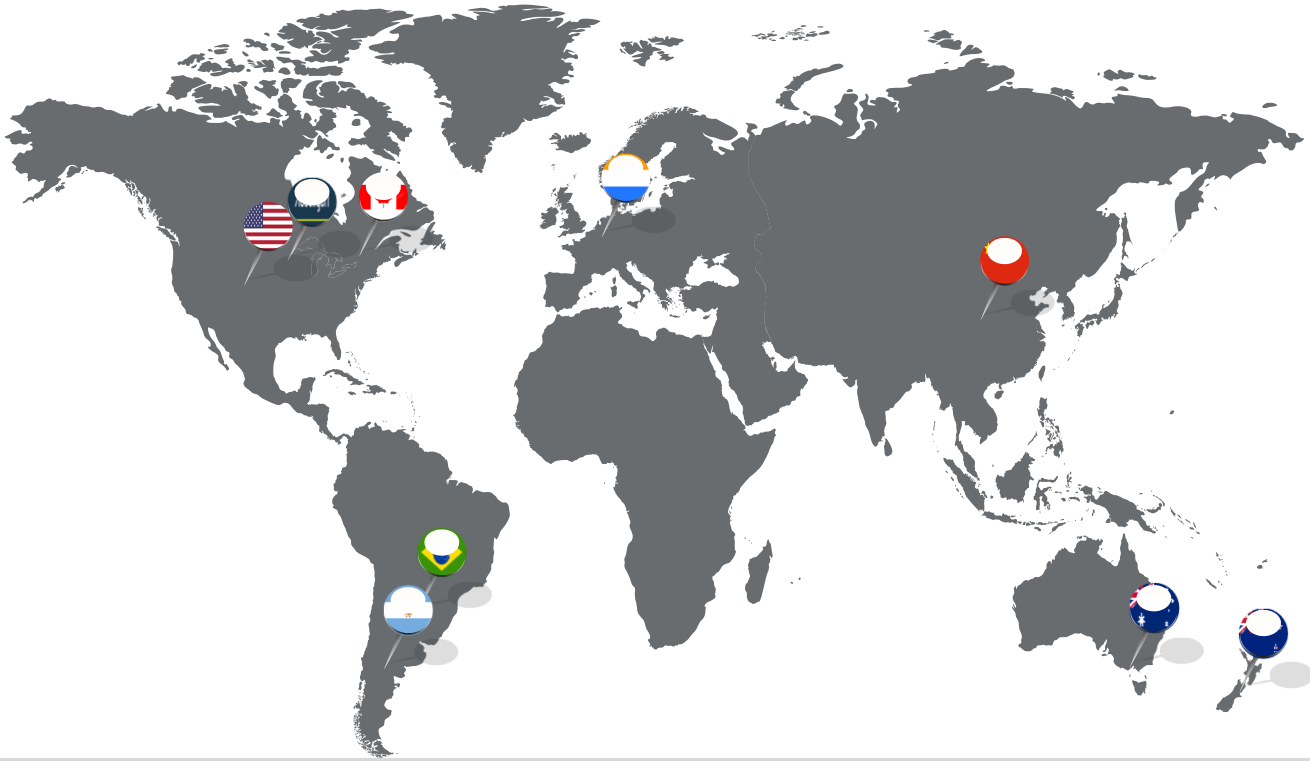
e global
business models
Competitive Advantage/Disadvantage



October 4, 2018: Brazilian Government Declares Buri's Polled Progeny Non-GMO

Brazil is Bullish on Gene-Editing: Non-GMO

Global Partnerships Pave Regulatory Pathways for Commercialization Outside U.S.



Export of Buri's polled semen to Brazil and Australia; commercial development opportunities progressing in New Zealand, Argentina, Ireland and Austria and with global genetics companies

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The cost of regulatory uncertainty in the US

$25 BILLION
ANNUAL MEAT & DAIRY EXPORTS

$14 BILLION
FMD OUTBREAK

$660 MILLION
ANNUAL PRRSv COST

$170 MILLION
ANNUAL BULL SEMEN EXPORTS

$100 MILLION
ANNUAL COST TO DEHORN CALVES

LEADERSHIP STATUS
AUSTRALIA, CANADA, BRAZIL, & IRELAND MAKING STRIDES

Innovation

- ✓ **The challenge - provide genetic improvement of food animals to meet human demands → without compromising animal well-being and the environment**

- ○ **Utilize naturally-occurring gene variants**
- ○ **Can be generated through traditional breeding**
- ○ **Risk-based assessment of product safety**
- ○ **Animals not novel – product not novel**

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NBT's are Scientifically-Sound Breeding Methods: We have been safely eating polled cattle for thousands of years

- Hornless (polled) genetics >5000 years old
  - ancient (*celtic*) allele has been found in an Icelandic bovine skull dating back to 1000 AD
- The *celtic* allele found in polled British beef breeds (i.e. Angus) can be safely bred into all dairy breeds
- RCI has proven capability to introduce polled into a horned genetic line of dairy cattle

Who Supports?

- Holstein USA. Buri (father of our 6 new polled calves) is in registry and qualifies for export status
- Humane Society USA supports gene-editing for animal welfare
- National Pork Producers Council
- Semex Alliance

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Acceligen's Regulatory Position

1. Gene-edited food animals should not be regulated as GMO/transgenic.
   - ✓ Acceligen's gene-edited animals have native traits and are not novel. ***Naturally-occurring genes are not drugs***.
2. Our gene-editing technology and process is precise and safe - no off-target effects.
   - ✓ Naturally-occurring alleles from the same species selected to make hornless cattle. We've been safely eating hornless cows for millennia.
3. Traditional breeding methods are not subject to regulation; Gene-editing accelerates targeted breeding for desired health and welfare traits
   - ✓ Traditional breeding requires ~20 generation backcross from horned to polled to return to high value milk productivity and quality

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New Breeding Techniques for Naturally-Occurring Traits; Bringing Precision-Bred Food Animals to Market

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