# Precision Breeding for Animal Health and Productivity

**Mitchell Abrahamsen, Ph.D. Chief Commercial and Scientific Officer**

Acceligen a division of recombinetics

# Recombinetics' Single Gene-editing Platform: 3 Products Lines

**Biomedical / Human Applications**

**Food Animal Applications**

| surrogen | regenevida | acceligen |
|---|---|---|
| **Pre-Clinical Research** | **Regenerative Medicine** | **Animal Agriculture** |
| **Biomedical Models for Developing Human Therapeutics** | **Transplantable Cells, Tissues, & Organs** | **Precision Breeding for Animal Health & Productivity** |
| ✓ **World's first sale of a gene-edited cardiac pig model** | ✓ **Mayo Clinic Partnership to grow human cardiomyocytes in pig** | ✓ **World's first gene-edited polled (hornless) cattle** |

**RCI gene-edits animal cells (not human cells)**
**Differentiated and competitive advantage with access to multiple commercial markets**

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Food Animal Applications

**Animal Agriculture**

**Precision Breeding for Animal Health, Welfare & Productivity**

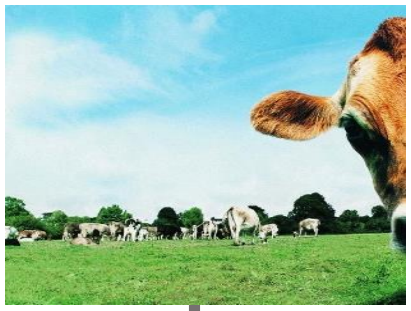
✓ **World's first gene-edited polled (hornless) cattle**

# Strategic Overview

## Gene-Editing to Select Natural-Occurring Animal Traits

**Acceligen partners with key global animal genetics companies based on industry and consumer pull**

- ✓ Societal demand for improved animal welfare
- ✓ Proactive response to animal health challenges and food safety concerns
- ✓ Growing population and limited production resources require improved efficiency
- ✓ Climate change and environmental pressures require improved genetics for sustainable production



### Animal Welfare Traits

Focus on consumer and regulatory acceptance; traits difficult to achieve by conventional breeding

1. Naturally-hornless (polled) cattle
2. Naturally-cool (SLICK/Thermotolerant)
3. Naturally Castration-Free Swine

### Animal Health & Productivity Traits

Focus on key targets for the animal breeding companies; proprietary deployment in genetics company germplasm

1. Limitations within current germplasm (disease resistant)
2. Key factors for production improvement (litter size; growth rate, yield)

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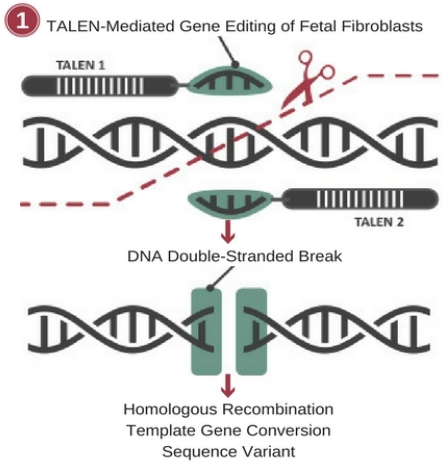
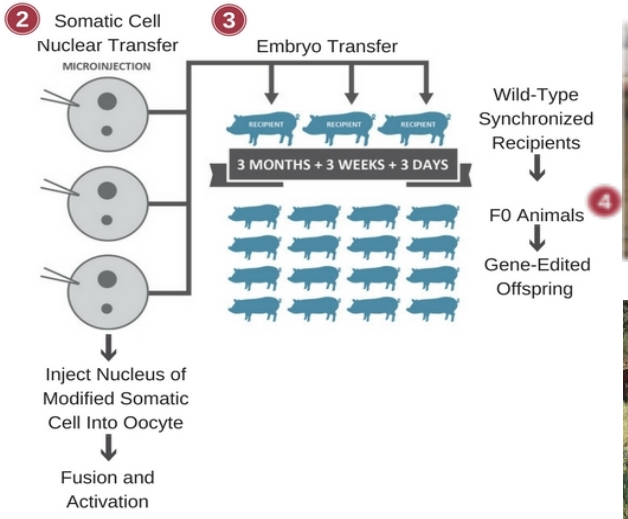
# Biomedical Swine Models + Food Animals on the Ground

## *Technology Proven and In Play*




**RCI's DNA Toolbox: Tool Agnostic**

TALENs, CRISPR, other Gene-Editing Methods

**Generation 2: Three naturally polled calves and their polled mothers 6 new calves born September 2017**

**RCI's Competitive Advantage: Broad IP in Animal Gene Editing**

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# Acceligen Strategic Deployment: How We Go to Market

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**Precision Breeding for**
**Animal Health, Welfare & Productivity**

**Acceligen rapidly enhances genetic improvement in food animals to address critical issues in global farming systems.**

**Animal Welfare Traits**
- Build consumer confidence
- Regulatory clarity

**Animal Health Traits**
- Disease resistance
- Key Industry Driver

**Animal Productivity Traits**
- Key factors for production improvement (litter size; growth rate, yield)

**Macro Traits**
Industry Wide Acceptance Drivers
First Movers Preferences
Dominant Traits Impacting all Genetic Stocks

**Micro Traits**
Proprietary
Competitive Advantage
Unique to Specific Genetic Stocks

# Why deploy gene editing in animals?

- Technology looking for problems vs. problems in need of technologies/solutions
- Animal Breeding companies have done a great job
  - Significant progress for easy to measure economic traits (e.g. Growth, FCR, yield, productivity)
  - Implementation of Genomic Selection - driving improved rates of genetic progress
- Health and Welfare traits
  - Not a focus of selection programs until recently
  - Can't always express the phenotype within pedigree populations
- Long pipeline (3 -4 years)
  - Pedigree animals long gone before offspring are in the commercial environment
- Cross-bred products
  - 2, 3 and 4 unique purelines contributing to commercial product depending on species
- Genetic variation in a species that may be missing in commercial pureline/pedigree stocks

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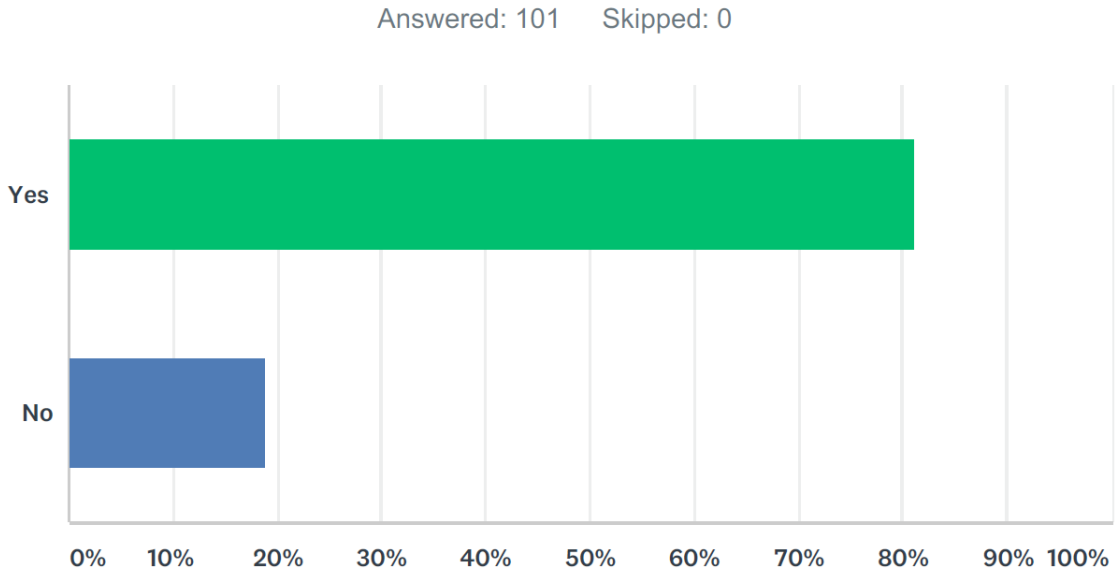
# Should Irish researchers develop elite genetically polled animals?

## This will be done using precision breeding technology to change the horned gene to a polled gene.

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# The Solution – Speed Breeding Polled Dairy and Beef Cattle

- **Speed Breeding:** a safe, no risk gene editing method to introgress polled genetics into elite dairy genetic lines
- The natural allele found in polled beef breeds (i.e. Angus) can be bred into all diary breeds
- **Ancient DNA:** this allele has been found in an Icelandic bovine skull dating back to 1000 AD
- We have been eating this allele safely for a long time
- RCI has proven capability to introduce polled into a horned genetic dairy line of cattle
- Holstein USA supports this technology and will register gene edited polled cattle – Buri is registered

Spotigy & Buri pictured at 1 mo, produced by NT cloning

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# Use of New Breeding Techniques (NBTs) to create genetic improvement in livestock and fill market needs:

- ✓ Benefits for Animal Health and Welfare
- ✓ Benefits for Producers
- ✓ Benefits for Consumers

## The Challenge:
## Mechanical Dehorning is Difficult for Animals and Producers

# Animal Welfare Problem: Painful Dehorning of Dairy and Beef Cattle

1. **Population problem:** High Merit dairy animals generally have horns, which must be removed.
2. **Procedure:** ~15 million calves polled each year in US
3. **Animal welfare imperative:** Dehorning is proven painful, increases risk of infection and death; unpleasant for producers and animals
4. **Cost:** Minimum cost to mechanically poll ~ $5-$20 per animal; increased risk of health and wellness. Eg.~$US138M mortality loss from polling in Australia
5. **Growing consumer and retailer pressure to address animal welfare in modern supply chains.**

Image from http://www.fwi.co.uk/livestock/buyers-guide-calf-disbudders-on-test.htm

Nestlé Walmart Save money. Live better. McDonald's

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# Benefits for Animals, Producers and Consumers: Naturally Hornless Calves

- ✓Benefit to her:  no painful, dehorning process
- ✓Benefit to the farmer: avoids unpleasant dehorning process; farmer could spend additional **$5-$20 on polled semen** and break even on the cost of dehorning
- ✓Benefit to consumers and retailers: Naturally Hornless animal welfare trait provides “guilt free” milk and meat

**Commercial Partners (Global Genetics Companies) On Board**

**U.S. Regulatory Framework Lags Science**

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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

Spotigy & Buri pictured at 1 month,

# Naturally Hornless (Polled) Commercial Partnership with American Dairy Genetics Company Semex (5/29/18 )

real agriculture

Gene editing allows for polled dairy genetics without the production drag

NUTRITION & HEALTH

Feedstuffs

Recombinetics, Semex form alliance to improve cattle well-being

SEMEX® Genetics for Life®

Good News

AGDAILY

LIVESTOCK NEWS TECHNOLOGY

Precision breeding partnership will eliminate need to dehorn dairy cows

By AGDAILY Reporters . Published: May 29, 2018

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

# *The rules are changing: How do Breeding companies respond?*

**Progress Report: Castration of Pigs in the EU**

05 December 2016

**EU - For centuries, surgical castration has been performed on pig farms across Europe. Until recently, the procedure was performed without the use of anaesthesia or analgesia. But now, the EU has proposed an outright ban on surgical castration, effective 1 January, 2018. While some member states have taken great steps in the right direction, progress in other countries has been slow or non-existent, writes Melanie Epp for The Pig Site.**

Porcine Health Manag. 2016; 2: 29.
Published online 2016 Dec 20. doi: 10.1186/s40813-016-0046-x

PMCID: PMC5382460
PMID: 28405455

## Pig castration: will the EU manage to ban pig castration by 2018?

Nancy De Briyne,[2][1] Charlotte Berg,[2] Thomas Blaha,[3] and Déborah Temple[4]

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### Abstract

Go to:

### Background

Go to:

In 2010, the 'European Declaration on alternatives to surgical castration of pigs' was agreed. The Declaration stipulates that from January 1, 2012, surgical castration of pigs shall only be performed with prolonged analgesia and/or anaesthesia and from 2018 surgical castration of pigs should be phased out altogether.

9TH JANUARY 2018

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

# Benefits for Animals, Producers and Consumers: Castration-Free Swine

- ✓Benefit to piglets:  no painful, castration process
- ✓Benefit to the farmer: avoids unpleasant castration process; male pigs less aggressive; legally-compliant with EU regs
- ✓Benefit to consumers and retailers: Naturally avoids boar taint concern

**Mechanical Castration Banned in EU as of Jan. 2018**

9TH JANUARY 2018

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

**RCI's Precision Breeding Technologies Solve Problems for Global Genetics Companies**

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# Castration-Free Swine Partnership: 2 International Genetics Companies and Recombinetics Plus NPPC Advocacy

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

POSTED ON DECEMBER 14, 2017 CATEGORIES: GRANT, NEWS NO COMMENTS YET

*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.

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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.

NATIONAL PORK PRODUCERS COUNCIL

DNA GENETICS


NEWS

**Hendrix Genetics joins alliance to end surgical castration of swine**

Precision breeding technologies will provide solution for pork producers.

HENDRIX GENETICS

# *Public Perception: How do Breeding companies respond?*

FOOD FOR THOUGHT

## 'Environmental Nightmare' After Thousands Of Atlantic Salmon Escape Fish Farm

August 24, 2017 · 10:52 AM ET

COURTNEY FLATT JOHN RYAN

Aboard the fishing vessel Marathon, Nicholas Cooke (left) and Nathan Cutlee unload 16 farm-raised At container on Tuesday in Bellingham, Wash.

Megan Farmer /KUOW

Commercial fishing boats are scrambling to cat
after a net pen broke near Washington's Cypre
the non-native fish jumping in the water or wa

FROM EARTHFIX

## Grieg Seafood says 21,700 salmon escaped in Loch Snizort

20 February 2018 Share

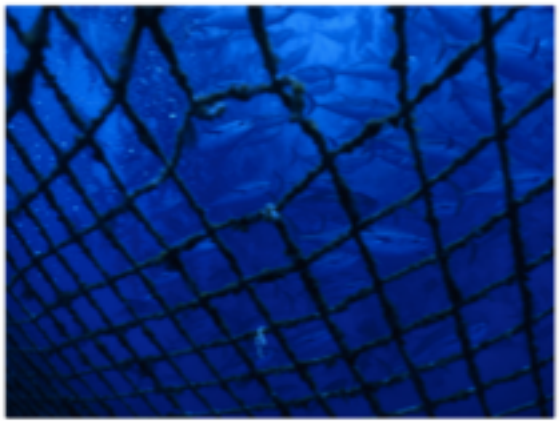
Grieg Seafoods said it believed about 21,700 fish had esca

A salmon farming company has admitted a maj
cages anchored in Loch Snizort, near the Isle o

### Deliberate sex reversal of farmed fish is common

Deliberate sex reversal is a common practice in aquaculture of some popular fish such as tilapia and halibut. The primary purpose is produce fish of the sex that is larger at maturity or otherwise has more desirable commercial characteristics. Sex change is accomplished using a combination of testosterone and other androgens, estrogens, and aromatase inhibitors such as Femara at various life stages of the fish. Efforts are made to keep the hormones to a low enough level to avoid obvious deformities in the fish or compromise their survival. Although use of such hormones does not necessarily mean that the fish themselves have high hormone levels when slaughtered, the safety of this practice has not been established.

# Benefits for Animals, Producers and Consumers: Sterile Fish



## Keeping Wild Stocks Wild

When fish or shrimp are kept in pens or ponds that are connected to natural waterbodies, some can escape. This isn't as harmless as you might think. In some cases, escapees can impact wild populations by competing with them for food, habitat and spawning partners.

- ✓Benefit to fish: no chemicals
- ✓Benefit to the farmer: no risk of escape or need to add chemicals
- ✓Benefit to consumers and retailers: Solves concerns about environmental impact and chemical additives

# Acceligen's Elite Traits: Commercialized with Partners

**Partnerships with leading global genetic companies allow for efficient deployment of key welfare and economic traits with minimal capital constraints and maximized revenue capture.**

- ✓ No need to "own" genetic stocks; access to established elite and commercially relevant genetics
- ✓ No need to own production systems
- ✓ Exploit developed distribution networks
- ✓ Exploit established customer bases and relationships

## Bovine – Beef and Dairy

- **Naturally Hornless (Polled)**
  - ✓ Three global genetics companies as commercial partners based in North America and Europe
- **Heat Tolerant (SLICK)**
  - ✓ Animals to be born 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 Swine**
  - ✓ Commercialization development grant received; Agreements with two major swine genetics companies focused on animal development
- **PRRSV Resistance**
  - ✓ Development and commercial partner identified
- **FMDV Resistance**
  - ✓ Proof of concept animal developed; 2nd generation animals due in April

## Aquaculture

- **Male Sterility and Mono-sexing**
  - ✓ Development and commercial partner identified; LOI signed

# Acceligen's Regulatory Position

1. Non-transgenic food animals should be regulated by USDA, not FDA.
   - ✓ Acceligen's gene-edited animals have native traits and are not GMO. Naturally-occurring genes are not drugs.
2. Our gene-editing technology and process is precise and safe, with 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 just accelerates desired traits
   - ✓ Traditional breeding requires ~20 generation backcross from horned to polled to return to high value milk productivity and quality

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a division of

recombinetics