Global Conference on Sustainable Beef

Innovation in Action

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150 years of innovation
Bayer Animal Health: our shared responsibility drives our actions

Bayer
„Science for Better Life“
people-food-animals

Animal Health
1,5B€ sales
3000 employees
100+ products
CAP&FAP

Beef Group
Parasiticides & BRD
Innovation #1

Customized Parasite Control
External parasites – Why bother?
Economic (in USD), health and well-being impact

USA (Talley 2016)
- Horn fly 1,360M
- Stable fly 672M
- Horse fly 296M
- Face fly 191M
- Ticks 162 M
- Mosquitos 78M
- Lice 56M

Brazil (Grisi et al 2014)
- GI parasites 7,100M
- Ticks 3,240M
- Horn fly 2,558M
- Cattle grub 383M
- Myasis 336M
- Stable fly 335M

Mexico (Rodriguez-Vivas et al 2016)
- Ticks 573M
- GI parasites 445M
- Horn fly 231M
- Liver fluke 130M
- Coccidia 23M
- Stable fly 6 M

Australia (AFI 2015)
- Ticks 156M (N)
- Buffalo fly 99M (N)
- Ephemeral fever 60M (N)
- Intestinal parasites 82M (S)
- Theileria 18M (S)
- Pink eye 11M (S)

Direct health damage + vector borne diseases

+ animal well-being aspects
Challenges to parasite control

Resistance not IF but WHEN?

- Diminishing governmental support
- Environmental safety and pesticide handling
- Limited education
- Rising regulatory requirements and development costs
- Diverse customer preferences by regions
- Climate change and trade facilitating spread of parasites
- Immature alternative parasite control technologies
- Rampant resistance to parasiticides

Constant battle for the cattle industry

Date of introduction

<table>
<thead>
<tr>
<th>Compound Type</th>
<th>Date of Introduction</th>
<th>1st resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>arzenicals</td>
<td>1893</td>
<td>1936 (AUS)</td>
</tr>
<tr>
<td>DDT</td>
<td>1846</td>
<td>1953 (AUS)</td>
</tr>
<tr>
<td>organophosphates</td>
<td>1944</td>
<td>1963 (AUS)</td>
</tr>
<tr>
<td>amidines</td>
<td>1975</td>
<td>1978 (AUS)</td>
</tr>
<tr>
<td>pyrethroids</td>
<td>1977</td>
<td>1981 (AUS)</td>
</tr>
<tr>
<td>macrocyclic lactones</td>
<td>1981</td>
<td>2001 (BRA)</td>
</tr>
<tr>
<td>fipronil</td>
<td>2008</td>
<td>2012 (MX)</td>
</tr>
</tbody>
</table>
Holistic approach required

Product/portfolio development

Pasture management

Resistance monitoring

Collaboration with all stakeholders

Environmental aspects

Safety

Education & training

Customized Parasite Control
Tradition, combined expertise and sustained innovation with Bayer Crop Science and Pharma

Customer need

- Broad spectrum
- Resistance-breaking
- Convenience

Cattle ecto & endoparasitides

- new compound class
- multiple projects progress

**Product development**

- **Registration** (2 years)
- **Development** (3-8 years) 60M€
- **Discovery** (2-4 years) 15-20M€

- 1 development compound
- 5 development candidates
- 10 POC
- 200-2,000 synthetized compounds
- 1M screened compounds

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Discovery (2-4 years) 15-20M€

Development (3-8 years) 60M€

Registration (2 years)
Broad portfolio for rotation

Example: Defense Point (US)

- Pyrethroids
- Organophosphates
- Neonicotinoids

Digital training tool in the works
**Resistance monitoring and diagnostics**

Example: on farm diagnostic (MX)

**Triple Boophilus resistance**

- 1983
  - OP’s
- 1994-1995
  - SP’s
- 2001-2008
  - amitraz

**Tick Control Rules**

1. *Use the right active ingredient*
2. *Follow product label*
3. *Rotate*
4. *Vaccinate*
5. *Strategic control*
6. *Other management tools*
7. *Justified macrocyclic lactone use*

Digital fly counting (in the works)

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\(^1\) SENASICA/SAGARPA
“The hardest thing for most livestock producers to realize is that we are not in the cattle business. We are in the grass business. We are in effect, grass farmers.”

Allan Nation
(editor, The Stockman Grass Farmer)
The challenge

Complex disease

stress + pathogens

M haemolytica, P multocida, H. somnus, Mycoplasma spp, IBR, BVDV, PI3, BRSV

Growing intensification

30% more beef
30% less cattle

feedlot mortality increased from 10.3 to 16.0 per 1000 cattle between 1994-2011

Consumer pressure

on antibiotic use

59.3% of feedlot cattle in US receives AB on arrival

2 2014 Maday, The ongoing battle with BRD, Bovine Veterinarian (September) 30-33 NAHMS 2011
Doing the same thing over and over again and expecting different results?

Focus on the host`s immune status rather on the bugs
Novel Mode of Action

Stimulation of innate immunity\(^1\)

- STING-activation
- effects
- production of type 1 interferon
- antiviral and antibacterial activities
- // counters *Mannheimia haemolytica* LPS effects
- // prevents extensive lung inflammation, fibrosis,…
- // aids in combatting *Mannheimia haemolytica*

\(^1\) Ilg, Investigations on the molecular mode of action of the novel immunostimulator Zelnate: activation of the cGAS-STING pathway in mammalian cells, Molecular Immunology, 90 (2017) 182-189
First licensed immunostimulant with BRD indication

Extract from the USDA label

**Indication**

Aid in the treatment of Bovine Respiratory Disease due to *Mannheimia haemolytica* in cattle 4 months of age or older, when administered at the time of, or within 24 hours after, a perceived stressful event

**Dosage and administration**

2 mL IM single dose

**Withdrawal time**

21 days

Zelnate is based on technology developed by Juvaris BioTherapeutics and is patent protected. Animal health applications are being exclusively developed by Bayer Animal Health and are the subject of Bayer patent applications.
Challenge studies demonstrated high efficacy\textsuperscript{1}

Zelnate as a stand-alone therapy...

\begin{itemize}
  \item \textbf{...significantly reduces lung lesion scores associated with BRD when administered in the face of disease challenge.}
  \item \textbf{...significantly reduces the risk of mortality when administered in the face of clinical BRD.}
\end{itemize}
Field study suggests potential to replace antibiotics on arrivals\textsuperscript{1}

In defined cattle population and in metaphylactic setting

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Micotil Group: 2 mL/100 lbs SC injection (n=1,002 steers) Avg. 501 lbs</th>
<th>Zelnate Group: 2 mL/100 lbs IM injection (n=1,002 steers) Avg. 589.4 lbs</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRD morbidity (%)</td>
<td>7.65</td>
<td>13.84</td>
<td>non-inferior*</td>
</tr>
<tr>
<td>Time to treatment (days)</td>
<td>28.1</td>
<td>22.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BRD repulls (%)</td>
<td>17.90</td>
<td>11.10</td>
<td>0.5929</td>
</tr>
<tr>
<td>BRD chronicity (%)</td>
<td>27.90</td>
<td>29.10</td>
<td>0.9942</td>
</tr>
<tr>
<td>Overall BRD mortality (%)</td>
<td>0.44</td>
<td>0.50</td>
<td>0.7643</td>
</tr>
<tr>
<td>BRD case-fatality (%)</td>
<td>3.95</td>
<td>2.99</td>
<td>0.7287</td>
</tr>
<tr>
<td>ADG (lbs)</td>
<td>2.96</td>
<td>2.91</td>
<td>0.6759</td>
</tr>
<tr>
<td>DMI (lbs)</td>
<td>12.96</td>
<td>12.81</td>
<td>0.3768</td>
</tr>
<tr>
<td>Feed:Gain</td>
<td>4.50</td>
<td>4.55</td>
<td>0.7302</td>
</tr>
</tbody>
</table>

No statistical differences between treatment groups across all clinical and economic parameters.

In this study, Zelnate was shown to be a viable non-antibiotic option for metaphylaxis in medium-risk feedlot cattle.

\textsuperscript{1} Nickell et al. A comparison of clinical and economic outcomes when metaphylactically administering either a novel DNA immunostimulant or tilmicosin to beef calves at medium – high risk of developing bovine respiratory disease in the feedlot; RUAA, Den Hague, 2016

delivering science based products and services

introducing smart digital technologies

enabling collective intelligence of all stakeholders