

# Synovex ONE Grower improves growth performance for at least 200 days in growing beef steers and heifers fed in confinement for slaughter

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## ABSTRACT

Growth-promoting implants are broadly used in the feedlot industry to improve growth performance and to increase production efficiencies. With cattle being fed longer and to heavier weights, there is demand for extended-release implants that payout for at least 200 d. Our objective was to evaluate feedlot growth of Synovex ONE Grower, a moderate potency (150 mg trenbolone acetate [TBA] and 21 mg estradiol benzoate [EB]), extended-release, growth-promoting implant for 200 d. At four locations (Texas, Idaho, California, and Nebraska), 200 steers ( $n = 800$ ; d 0 body weight [BW] =  $320.2 \pm 9.5$  kg) and 200 heifers ( $n = 800$ ; d 0 BW =  $311.5 \pm 9.5$  kg) were blocked by BW and randomized to 1 of 2 treatments: 1) **Control**, empty subcutaneous needle inserted and extracted from the middle third of one ear; 2) **ONE Grower**, 150 mg TBA and 21 mg EB extended-release implant administered in middle third of one ear. Treatments were commingled within pen of the same sex ( $n = 4$ /site; 2/sex/site) in a split plot design replicated across four sites. Cattle were fed finishing ration ad libitum common to each geographical region at least once daily and were observed for any abnormal health events twice daily. Treatments were administered on d 0. Mid-study implant site evaluations were performed on d 35 or 41. Initial BW was recorded on d 0 and final BW was recorded on d 200 to 204. Cattle were harvested from d 201 to 231; however, carcass data were not collected due to slaughter facility complications brought on by the COVID-19 pandemic. Data were analyzed using the PROC MIXED and PROC GLIMMIX procedures of SAS (Version 9.4, SAS Institute, Cary, NC;  $P < 0.05$ ), and animal was the experimental unit. There were no treatment  $\times$  sex interactions ( $P \geq 0.052$ ) for any variable. Final BW on d 200 was greater ( $P < 0.01$ ) for steers and heifers implanted with ONE Grower compared to Control; ONE Grower improved final BW by 5.7% for steers and 3.9% for heifers. Overall average daily gain (ADG) from d 0 to 200 was greater ( $P < 0.01$ ) for ONE Grower steers and heifers compared to Control with an increase in ADG of 13.1% for steers and 8.9% for heifers. For cattle implanted with ONE Grower, implant retention rates at d 35 or 41 were 95.7% and 96.3% for steers and heifers, respectively. There was no difference ( $P \geq 0.32$ ) in percentage deaths, removals, or bullers (steers) between treatments. Synovex ONE Grower improved final BW and ADG in feedlot steers and heifers fed for at least 200 d.

**Key words:** feedlot, implant, ONE Grower, performance, Synovex

## INTRODUCTION

Growth-promoting implants are widely used in the feedlot industry to increase growth performance and improve efficiency, with over 91% of steers and 94% of heifers being implanted at least once in the feedlot (NAHMS, 2013). In the United States, the most recently approved feedlot implants are extended-release products that contain a coating on each implant pellet to slow release of active ingredients into the body for over 200 days. These most recent approvals include Synovex ONE Feedlot (U.S. Food and Drug Administration [FDA], 2014a; Zoetis, Inc., Parsippany, NJ), Revalor XS (FDA 2007; Merck Animal Health, Madison, NJ), Revalor XR (FDA 2017a; Merck Animal Health), and Revalor XH (FDA

2017b; Merck Animal Health). Implants designed and labeled to deliver active ingredients for extended durations (coated implants) can reduce labor costs and production losses associated with disruption of growth performance related to gathering cattle and handling for reimplantation (Cleale et al., 2018).

At the carcass level, implants improve growth performance, increase hot carcass weight (HCW) and longissimus muscle (LM) area, while typically reducing marbling, quality grade and tenderness. However, effects vary with implant strategy, genetics, and sex (Herschler et al., 1995; Duckett and Andrae, 2001; Montgomery et al., 2001). In recent years, beef processors have placed a premium on quality over yield as

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evidenced in the 2016 National Beef Quality audit in which a dramatic increase in the percentage of Prime and Choice carcasses was reported compared to previous audits (Boykin et al., 2017). Lower potency implants have demonstrated lesser negative impacts on carcass quality than higher potency or more aggressive reimplant strategies (Duckett and Pratt, 2014). Feedlots have been placing lighter cattle on feed over the last 20 years which suggests younger, lighter animals could spend greater than 200 d in the feedlot (Smith et al., 2019b). This, in concert with the increase in demand for quality, increases the need for a long-acting implant with moderate potency that will improve growth performance but limit the negative effects on carcass quality.

Synovex ONE Grower was previously approved as Synovex ONE Grass (FDA, 2014b) for increased rate of weight gain for up to 200 days in pasture steers and heifers (stocker, feeder, and slaughter). The purpose of this study was to test the hypothesis that Synovex ONE Grower, a moderate potency (150 mg trenbolone acetate [TBA] and 21 mg estradiol benzoate [EB]), extended-release, growth-promoting implant, would increase rate of weight gain for up to 200 d in growing beef steers and heifers fed in confinement for slaughter compared to a negative control.

## MATERIALS AND METHODS

The current study was conducted in four locations (sites): Texas, Idaho, California, and Nebraska at commercial/research feedlots. The study was conducted under the direction of the study site Institutional Animal Care and Use Committee (IACUC; Nebraska Site, approval #AC19088B; Idaho Site, approval #IC1910) or if the site did not have an IACUC the protocol was reviewed and approved by the Zoetis Ethical Review Board in Kalamazoo, MI (Texas and California sites). All sites followed U.S. standard and international guidance: Good Clinical Practice standards, FDA Guidance No. 85 (FDA, 2001).

Across the four sites, purebred English, crossbred English, or crossbred continental steers ( $n = 1,018$ ; arrival body weight [BW] =  $288.1 \pm 32.9$  kg) and heifers ( $n = 1,018$ ; arrival BW =  $277.7 \pm 41.9$  kg) were procured from livestock auctions (Texas, Idaho, and Nebraska) or a single source ranch (California). Cattle arrived at each feedlot at least 21 d prior to treatment administration. Cattle were processed upon arrival according to procedures typical of the feedlot industry and the site's geographical location and included vaccinations against respiratory and clostridial pathogens, as well as administration of an antiparasitic product. In addition, cattle were given duplicate, unique identification ear tags with one administered in each ear, and cattle were tagged with a colored tag to denote the pen to which it was assigned; colored pen tags did not denote treatment because cattle on both treatments were commingled within pens. To meet enrollment criteria, both ears of cattle were palpated at arrival processing for the presence of an existing implant, and if an implant was located it was excised by a veterinarian or under the direction of a veterinarian. Ears of animals that were detected previously to have an implant present were rechecked when the randomization BW was collected (d -2 to -1) to ensure complete removal of the implant and that the ear had healed before the animal could be considered for enrollment. Implants were removed at least 21 d prior to d 0 to meet study inclusion requirements. Also, steers were checked at arrival to

confirm sex and to identify bulls or partial castrations; non-steer males were excluded from study. Heifers were evaluated for pregnancy via rectal palpation (California and Nebraska) or ultrasound (Texas and Idaho), and pregnant heifers were excluded from study. Cattle that were noted to be sick or have musculoskeletal abnormalities were not eligible for study enrollment. To be enrolled, cattle had to be healthy with no abnormalities, meet the 21-d absence of implant requirement, be of the correct sex and physiological status and be within the desired weight range of approximately 250 to 364 kg.

Of the 2,036 procured animals, 1,600 animals were enrolled in the study and cattle were administered 1 of 2 implant treatments: 1) **Control**, sham-implanted negative controls where an empty needle was inserted subcutaneously into and extracted from the middle one-third of the ear on d 0 and 2) **ONE Grower**, a single Synovex ONE Grower (150 mg TBA and 21 mg EB, Zoetis, Inc.) administered in the middle one-third of the ear on d 0. All sites utilized ONE Grower implants from the same lot number (Lot number: 309229, expiration date: March 2021). At each site, four pens were used containing 100 animals with both treatments commingled within the same pen (50/treatment/pen). Each site fed two pens (100 animals/pen) of steers and two pens (100 animals/pen) of heifers such that 400 animals were enrolled (200/sex; 200/treatment) at each site for a total of 1,600 animals across all four sites. Day 0 in Idaho was on November 27, 2019; Nebraska on December 17, 2019; Texas on December 20, 2019; and California on January 16, 2020.

Treatments were administered on d 0 with a Synovex SX-10 implant applicator (Zoetis, Inc.). Treatment of Control cattle was by subcutaneous insertion and retraction of the SX-10 implant needle with no implant present in the middle one-third of the caudal aspect of the pinna of the ear. Treatment of ONE Grower cattle involved administration of a single Synovex ONE Grower implant subcutaneously in the middle one-third of the caudal aspect of the pinna of the ear. Cattle with dry ears at time of treatment administration were implanted without cleaning. Cattle ears that were dirty or wet were cleaned prior to treatment administration utilizing either a brush or gauze pads with chlorhexidine (Nolvasan, Zoetis, Inc.); ears were dried with gauze pads or excess moisture was brushed off prior to treatment administration (implantation). Stylets of implant applicators were disinfected in a chlorhexidine solution (Nolvasan, Zoetis, Inc.) after treatment of each animal. In addition, stylets were replaced as needed when they became dull or ineffective. Ears of all study animals were palpated post-treatment on d 35 (Texas, California, and Nebraska) or d 41 (Idaho) to document presence of implant (implant retention rate) and reaction at site of treatment. Implant reactions were defined as local swelling, redness, inflammation, or abscess (i.e., fluid buildup). Treatment administration (d 0) and in-study evaluations (d 35/41) of implants were conducted by unmasked study personnel. All other study activities were performed by masked study personnel that did not know which animals were administered Control or ONE Grower.

Animals were housed per the Guidance for Use of Agricultural Animals (2010) consistent with regional norms to assure optimum performance per pen. Study pens were outdoor, naturally lighted, and ventilated, without shade, and dirt surfaced. Cattle were acclimated to the feedlot environment via introduction of starter feedlot diets upon arrival. During the acclimation phase and after treatment administration on d 0, cattle were fed rations of increasing

proportions of concentrate to roughage until cattle were consuming a final finishing ration which was fed until study completion. Rations utilized ingredients common to the site geographical region. At the Idaho and Nebraska sites, finishing rations were adjusted during the study to accommodate ingredient shortages brought on by COVID-19; however, finishing rations were formulated to meet similar nutrient requirements as previous finishing rations at each site. Ingredients of the finishing ration at each study site are presented in Table 1. Feed was delivered once daily in Idaho, California, and Nebraska and twice daily in Texas. At each site cattle were fed ad libitum and slick bunks were not permitted per the study protocol for this study and never occurred at the Idaho and California sites while occurring infrequently at the Texas and Nebraska sites. Feed delivered

**Table 1.** Finishing ration composition at each study location (as-fed basis)

Item	Site			
	Texas	Idaho	California	Nebraska
Ingredient, %				
Steam flaked corn	75.5	—	—	—
Dry rolled corn	—	34.7	78.5	33.3
High moisture corn	—	—	—	20.0
Earlage	—	25.7	—	—
Dried distillers grains	5.5	6.9	—	—
Wet distillers grains	—	—	—	23.8
Sweet Bran 60 <sup>1</sup>	—	—	—	14.0
Alfalfa hay	8.5	-	5.6	—
Wheat	—	8.9	—	—
Wheat straw	—	6.0	—	—
Corn stalks	—	—	—	3.8
Molasses	4.0	5.0	7.4	—
Fat	2.0	—	—	—
Tallow	—	2.2	—	—
Limestone	—	—	0.5	—
Water	—	6.0	-	—
Texas supplement <sup>2</sup>	4.5	—	—	—
Idaho supplement <sup>3</sup>	—	4.6	—	—
California supplement <sup>4</sup>	—	—	8.0	—
Nebraska supplement <sup>5</sup>	—	—	—	5.1

<sup>1</sup>Cargill Animal Nutrition, Wayzata, MN.

<sup>2</sup>35.41% ground cottonseed, 20.09% limestone, 14.49% corn gluten feed, 11.27% urea, 8.25% dolomite, 6.84% salt, 2.55% ammonium sulfate, 0.38% zinc sulfate (36%), 0.32% vitamin A, 0.16% sodium selenite (0.2%), 0.12% manganese sulfate, 0.08% copper sulfate (25%), 0.03% vitamin E, 0.002% cobalt carbonate (46%), and 0.0005% ethylene diamine dihydriodide.

<sup>3</sup>22.94% limestone, 21.79% corn-soy blend, 15.86% urea, 11.25% corn syrup, 10.34% water, 10.00% Attaflow, 7.07% salt, 0.25% zinc sulfate (36%), 0.25% beef tallow, 0.10% manganese sulfate (32%), 0.06% copper sulfate (25%), 0.05% anhydrous ammonia, 0.02% vitamin E premix (60%), 0.01% vitamin A 1000, 0.01% selenium (4%), 0.002% vitamin D3 500, 0.001% cobalt sulfate (32%), and 0.001% ethylene diamine dihydriodide (79.5%).

<sup>4</sup>64.88 soybean meal (47.5%), 11.25% canola pellets, 10.00% almond shells (ground), 3.75% calcium carbonate, 3.75% wheat millrun, 2.00% molasses cane, 1.50% salt, 1.25% dicalcium phosphate, 0.50% fat, 0.50% vitamin ADE, 0.38% calf trace mineral, 0.25% vitamin B premix.

<sup>5</sup>Contained: processed grain by-products, molasses products, calcium carbonate, sodium chloride, zinc sulfate, manganese sulfate, copper sulfate, sodium selenite, copper chloride, ethylene diamine dihydriodide, soybean oil, and cobalt carbonate; individual percentages were not provided by the study site.

was measured daily and feed refusals (orts remaining) were weighed and sampled on d 200 and at times of ration changes at each site. Two samples (~2–3 kg) of the ration being fed at each site, a primary and backup, were taken weekly from arrival through harvest. Primary feed samples were sent to ServiTech Laboratories in Amarillo, TX for proximate analysis. Proximate analysis included: dry matter (%), crude protein (%), nonprotein nitrogen (% of protein), neutral detergent fiber (NDF) (%), crude fiber (%), crude fat (%), ash (%), total digestible nutrients (TDN) (%), Ca (%), P (%), and energy calculations (net energy for gain [NE<sub>g</sub>], net energy for maintenance [NE<sub>m</sub>], digestible energy [DE], and metabolizable energy [ME]). Study rations at each site met or exceeded nutrient requirements for the type and class of cattle on study (NRC, 2016; Table 2). Backup samples were retained frozen (~20 °C) at each site and were not disposed of until review of the ration analysis was performed by the site nutritionist and the Sponsor (Zoetis) nutritionist. Feed refusals were collected from each study pen and composited within site. The analysis of the percentage dry matter of feed refusals was performed at each site. Water was provided ad libitum throughout the study at all sites via automatic waterers. No other feed additives or growth promoters were administered including ionophores, beta-agonists, in-feed antibiotics, or melengestrol acetate.

Dry matter intake (DMI) was not analyzed because steers and heifers of both treatments were commingled within pens of similar sex; overall DMI from d 0 to 200 pooled across sex and treatment averaged 9.0 ± 0.22 kg/d. Overall DMI from d 0 to 200 across both treatments and sites averaged 9.3 ± 0.19 kg/d, and 8.8 ± 0.25 kg/d for steers and heifers, respectively.

BWs were recorded on individual animals upon arrival, d -2 to -1 (randomization BW), d 0, and d 200 (d 200 was used to represent final BW collected, regardless of the actual day of BW collection which was: Texas = d 200, Idaho = d 202, California = d 201, and Nebraska = d 204). BWs on d 0 and 200 were recorded after a 12 h fast at each site. If an animal was removed from the study early or died prior to d 200, that animal's BW was measured on the day of removal or death. Prior to study initiation, weight scales for measuring individual animal BWs were professionally certified. A scale check utilizing a reference range of expected BWs was performed prior to recording animal BW. Final BW post d 200 and directly prior to harvest were not collected due to the COVID-19 pandemic which did not allow for the attainment of carcass data; therefore, the decision was made to not weigh cattle directly before harvest to prevent any additional injuries and reduce shrink or additional antemortem stress. Average daily gain (ADG) was calculated for each animal by subtracting the initial BW taken on d 0 from the final BW taken on d 200 (or day of removal/death) and dividing by the number of days the animal was on study (deads-in calculation).

General health observations were performed twice daily to identify any abnormal health events, including adverse reactions to treatments, and to ensure feed and water were considered "normal." Abnormal health events were defined as any unfavorable or unintended observations for any animal, regardless of whether or not they were considered related to treatment. Each abnormal health event was further classified according to the main system organ class it affected (cardiovascular, digestive tract, eye, musculoskeletal, reproductive

**Table 2.** Analyzed nutrient composition of feedlot rations fed to steers and heifers at each site<sup>1</sup>

Item <sup>2</sup>	Site			
	Texas	Idaho	California	Nebraska
Dry matter, %	81.09 ± 1.02	71.09 ± 2.69	81.76 ± 0.96	61.98 ± 5.01
Crude protein, %	13.27 ± 0.91	13.69 ± 1.12	11.12 ± 0.78	14.65 ± 0.87
NPN, % of crude protein	2.14 ± 0.43	3.06 ± 0.44	0.17 ± 0.09	0.75 ± 0.17
Crude fiber, %	6.94 ± 1.74	11.27 ± 6.59	4.42 ± 0.69	6.13 ± 0.84
NDF, %	16.52 ± 3.65	21.99 ± 9.39	10.94 ± 0.70	19.21 ± 1.31
TDN, %	88.02 ± 2.11	81.52 ± 10.01	90.45 ± 0.89	89.56 ± 1.06
Crude fat, %	4.88 ± 0.82	5.94 ± 1.87	3.06 ± 0.21	3.99 ± 0.35
Ash, %	5.21 ± 1.69	5.07 ± 1.23	3.72 ± 0.57	4.89 ± 0.34
Calcium, %	0.68 ± 0.14	0.60 ± 0.17	0.47 ± 0.21	0.72 ± 0.07
Phosphorus, %	0.31 ± 0.03	0.36 ± 0.04	0.32 ± 0.03	0.50 ± 0.03
NE <sub>m</sub> , Mcal/kg	2.18 ± 0.07	1.98 ± 0.31	2.25 ± 0.02	2.23 ± 0.02
NE <sub>g</sub> , Mcal/kg	1.50 ± 0.04	1.32 ± 0.29	1.57 ± 0.02	1.54 ± 0.02

<sup>1</sup>Multiple ration types (i.e., starter, transition, finisher) included in summary for each site. Rations did not contain medicated feed additives, including ionophores, antibiotics, beta agonists, or melengestrol acetate.

<sup>2</sup>NDF, Neutral detergent fiber; NE<sub>g</sub>, Net energy for gain; NE<sub>m</sub>, net energy for maintenance; TDN, total digestible nutrients.

system, respiratory tract, skin and appendage and systemic disorders). Routine estrus behavior was considered normal and was not documented for heifers because estrus suppression was not implemented (i.e., melengestrol acetate).

A total of 46 animals were removed from the study posttreatment. Of these animals, 23 died and 2 were euthanized. Two required euthanasia during the study, one at the Texas site due to chronic pneumonia (ONE Grower) and one animal at the Idaho site due to a broken leg (ONE Grower). Neither was related to treatment. Euthanasia was performed by qualified personnel under supervision of a licensed veterinarian in a humane manner consistent with the AVMA Guidelines (2013). Animals that died during the study ( $n = 23$ ) and the two euthanized animals were examined post-mortem by a licensed veterinarian, or person(s) under veterinary supervision trained in bovine medicine to determine the cause of death; no animal deaths were determined to be related to treatment. Twenty-one animals were removed from study (other than the animals that died or were euthanized) and returned to the herd (removed from study but not died or was not euthanized). Eight of the 21 animals removed from study were removed after the final BW collection and prior to harvest which included 6 animals that were healthy but removed due to lameness concerns regarding trucking to harvest.

Cattle were intended to be harvested shortly after the d 200 BW measurement and for carcass data to be collected by the West Texas A&M Beef Carcass Research Center (WTAMU BCRC); however, the COVID-19 pandemic caused delays in the marketing and harvesting of cattle. Additionally, all harvest facilities prohibited access for non-personnel. Thus, there was not a path forward for WTAMU BCRC to collect carcass data. Furthermore, the inability of beef processors to match individual identification to individual carcasses prohibited collection of camera data. Cattle continued to be observed and adequately managed post d 200 until harvest. Heifers at the Texas site were harvested on d 201 and steers on d 208 at Tyson Foods in Amarillo, Texas (United States Department of Agriculture [USDA] Establishment #: M245E). Idaho steers

were harvested on d 230 and heifers on d 231 at Washington Beef in Toppenish, Washington (USDA Establishment #: M235). California steers and heifers were harvested on d 208 at One World Beef Packers in Brawley, California (USDA Establishment #: M21488). Steers and heifers from the Nebraska site were harvested on d 204 at JBS, USA in Grand Island, Nebraska (USDA Establishment #: 969G).

### Statistical Analysis

The study was a split plot design replicated across multiple sites. Sex was the whole plot factor and treatment was the subplot factor. The whole plot was a completely randomized design with pen as the experimental unit. The subplot was a generalized randomized block design. Blocking was based on BW at pre-enrollment (d -2 to -1) and pen. Animal was the experimental unit for treatment. Within site and sex, animals of similar pre-enrollment BWs were randomly assigned to a pen. Within a pen, animals were randomly assigned to treatments with an equal number of animals assigned to each treatment. All statistical analyses of data utilized SAS Release 9.4 (SAS Institute, Cary, NC).

BW and ADG were analyzed using a generalized linear mixed model (PROC MIXED) that evaluated fixed effects of treatment, sex, and treatment by sex interaction. Random effects included site, pen within site and sex, site by treatment interaction, site by sex interaction, site by treatment by sex interaction, and error. Treatment least squares means, ranges, and 95% confidence intervals (CIs) are presented by sex. Treatment comparisons were performed within sex as there were not any treatment by sex interactions.

Occurrence of abnormal health events was analyzed separately by sex using a Cochran-Armitage test adjusting for site. Treatments were compared using contrasts.

Occurrence of deaths and removals was analyzed using a generalized linear mixed model (PROC GLIMMIX) with binomial distribution and logit link. The model included fixed effects of treatment, sex, and treatment by sex interaction.

Random effects included site, pen within site and sex, site by treatment interaction, site by sex interaction, and site by treatment by sex interaction. Treatment least squares means and 95% CIs are presented by sex. Treatment comparisons were performed within sex. Occurrence of bullers (steers) was analyzed using a Cochran Armitage test adjusting for site. Treatments were compared using contrasts.

Implant retention rate (yes/no) and reaction rate were summarized by treatment, both within and across sex, using frequency distribution tables for the mid-study evaluation (d 35 or 41).

Treatment comparisons were assessed using two-sided tests at the 5% level of significance ( $P \leq 0.05$ ).

### Animals Excluded From Analysis

A total of five animals were not included in the growth performance (BW and ADG) analysis. Steer 6096 (ONE Grower, Texas Site) was removed from the growth analysis because the animal died from ruminal bloat (not related to treatment) within the first week of the study. Heifer 6334 (Control, Texas Site) who was incorrectly identified as open during the preenrollment check was removed from the efficacy analysis because she died during calving and thus the heifer did not meet the inclusion requirement of being open at time of study start. Animals 7067 (Control, Idaho Site) and 7258 (Control, Idaho Site) were not included in the efficacy analysis because the animals were noted as displaying bull-like behavior and upon examination were determined to be cryptorchid bulls; thus, they did not meet the inclusion requirements. Bull 7254 (Control, Idaho Site) was misidentified as a steer during physical examination

and was not included in the efficacy analysis. Animals 6334 (heifer), 7067 (cryptorchid bull), 7258 (cryptorchid bull), and 7254 (bull) were also removed from the abnormal health event/necropsy data because reason for removal data was related to exclusion criterion (calving, cryptorchid bull or intact bull).

## RESULTS

### Pooled Feedlot Data

Pooled steer and heifer growth performance data are presented in Table 3. There was no treatment  $\times$  sex interaction for BW on d 0 ( $P = 0.42$ ); however, there was tendency ( $P = 0.07$ ) for a treatment  $\times$  sex interaction for Day 200 BW with ONE Grower steers being 34.4 kg heavier compared to Control while ONE Grower heifers were only 22.2 kg heavier than Control heifers. In addition, no main effect of sex was detected for BW on d 0 ( $P = 0.51$ ). There was a main effect of sex ( $P = 0.05$ ) for d 200 BW with steers (615.9 kg) being 41.5 kg heavier on d 200 compared to heifers (574.4 kg). Pooled main effect of treatment for BW was not different ( $P = 0.74$ ) on d 0 as expected. Pooled d 200 BW was greater ( $P < 0.01$ ) for ONE Grower cattle compared to Control with final BW on d 200 of 609.3 and 581.0 kg for ONE Grower and Control, respectively.

There was a tendency ( $P = 0.052$ ) for a treatment  $\times$  sex interaction for ADG from d 0 to 200 as ONE Grower steers outgained Control steers by 0.18 kg/d while ONE Grower heifers outgained Control heifers by 0.11 kg/d. A main effect of sex was significant ( $P = 0.01$ ) with an increase in ADG for steers (1.46 kg/d) compared to heifers (1.30 kg/d). Overall

**Table 3.** Growth performance of steers and heifers fed for at least 200 days

Item	Treatment <sup>1</sup>		SEM <sup>2</sup>	P-value			
	Control	ONE Grower		ONE vs. CON <sup>3</sup>	Treatment	Sex	Treatment $\times$ Sex
N <sup>4</sup> , head							
Pooled	796	799	—	—	—	—	—
Steers	397	399	—	—	—	—	—
Heifers	399	400	—	—	—	—	—
Body weight, kg							
Day 0							
Pooled	316.0	315.7	7.52	0.74	0.74	0.51	0.42
Steers	320.6	319.7	9.50	0.43	—	—	—
Heifers	311.3	311.7	9.50	0.72	—	—	—
Day 200							
Pooled	581.0	609.3	7.16	<0.01	<0.01	0.05	0.07
Steers	598.7	633.1	9.78	<0.01	—	—	—
Heifers	563.3	585.5	9.78	<0.01	—	—	—
Average daily gain, kg/d							
Day 0 to 200							
Pooled	1.30	1.45	0.02	<0.01	<0.01	0.01	0.052
Steers	1.37	1.55	0.02	<0.01	—	—	—
Heifers	1.24	1.35	0.02	<0.01	—	—	—

<sup>1</sup>Control = sham implant (empty needle administered subcutaneously in middle one-third of the ear); ONE Grower = single Synovex ONE Grower (150 mg trenbolone acetate and 21 mg estradiol benzoate; Zoetis, Inc.) implant administered in the middle one-third of the ear.

<sup>2</sup>SEM, standard error of the mean.

<sup>3</sup>Orthogonal contrast of ONE Grower vs. Control.

<sup>4</sup>Number of head included in growth analyses.

**Table 4.** Mid-study evaluation (d 35 or 41) of implant site retention rate and reaction rate in feedlot steers and heifers

Item	Treatment <sup>1</sup>			
	Control		ONE Grower	
	N <sup>2</sup>	%	N <sup>2</sup>	%
Implant retention rate, %				
Pooled	797	0.0	799	96.0
Steers	399	0.0	399	95.7
Heifers	398	0.0	400	96.3
Implant reaction rate, %				
Pooled	797	0.0	799	2.0
Steers	399	0.0	399	3.0
Heifers	398	0.0	400	1.0

<sup>1</sup>Control = sham implant (empty needle administered subcutaneously in middle one-third of the ear); ONE Grower = single Synovex ONE Grower (150 mg trenbolone acetate and 21 mg estradiol benzoate; Zoetis, Inc.) implant administered in the middle one-third of the ear.

<sup>2</sup>N = number of total animals.

**Table 5.** Summary of the percent of deads and removals in feedlot steers and heifers

Item	Treatment <sup>1</sup>			P-value		
	Control	ONE Grower	ONE vs. CON <sup>2</sup>	Treatment	Sex	Treatment × Sex
Deads and removals, %						
Pooled	2.35	3.06	0.55	0.55	0.34	0.43
Steers	2.21	2.19	0.99			
Heifers	2.48	4.25	0.33			

<sup>1</sup>Control = sham implant (empty needle administered subcutaneously in middle one-third of the ear); ONE Grower = single Synovex ONE Grower (150 mg trenbolone acetate and 21 mg estradiol benzoate; Zoetis, Inc.) implant administered in the middle one-third of the ear.

<sup>2</sup>Orthogonal contrast of ONE Grower vs. Control.

ADG pooled across sex was greater ( $P < 0.01$ ) for Synovex ONE Grower cattle compared to Control cattle with an overall ADG of 1.45 and 1.30 kg/d for ONE Grower and Control, respectively.

Pooled implant retention and reaction rates are summarized in Table 4. Pooled implant retention rates on d 35 (Texas, California, and Nebraska) or 41 (Idaho) for steers and heifers implanted with ONE Grower was 96.0% with 767 out of 799 animals possessing a palpable implant at time of evaluation. No implants were detected in Control cattle (0 out of 797). Pooled implant reaction rates for Synovex ONE Grower steers and heifers were 2.0% (16 out of 799 animals) with no reactions for Control cattle (0 out of 797 animals).

Pooled analysis across sex for deads and removals is presented in Table 5. There was no treatment × sex interaction ( $P = 0.43$ ) for the percentage of deads and removals nor was there a main effect of sex ( $P = 0.34$ ). The main effect of treatment for deads and removals was not significant ( $P = 0.55$ ) with 2.35% and 3.06% of deads and removals for Control and ONE Grower, respectively.

**Table 7.** Summary of the percent of abnormal health events in feedlot heifers

Item	Treatment <sup>1</sup>		P-value
	Control	ONE Grower	
Heifers with abnormal health events, %	5.8	9.0	0.07
Proportion by system organ class, %			
Cardiovascular disorders	0.0	0.5	0.16
Digestive tract disorders	1.0	2.0	0.25
Eye disorders	0.3	0.0	0.32
Musculoskeletal disorders	0.5	1.3	0.25
Reproductive system disorders	0.3	0.0	0.32
Respiratory tract disorders	2.5	4.5	0.12
Skin and appendages disorders	0.5	1.5	0.15
Systemic disorders	0.8	0.0	0.08

<sup>1</sup>Control = sham implant (empty needle administered subcutaneously in middle one-third of the ear); ONE Grower = single Synovex ONE Grower (150 mg trenbolone acetate and 21 mg estradiol benzoate; Zoetis, Inc.) implant administered in the middle one-third of the ear.

## Steer Feedlot Data

Growth performance of feedlot steers fed for at least 200 d is summarized in Table 3. As expected, initial BW were not different ( $P = 0.43$ ) on d 0 between treatments (Control = 320.6 kg; ONE Grower = 319.7 kg). Final BW was greater ( $P < 0.01$ ) for steers implanted with ONE Grower (633.1 kg) compared to Control (598.7 kg). ADG from d 0 to 200 was greater ( $P < 0.01$ ) for steers implanted with ONE Grower compared to Control (1.55 vs. 1.37 kg/d).

Implant retention and reaction rates of steers are presented in Table 4. Ears palpated on d 35 (Texas, California, and Nebraska) or 41 (Idaho) yielded a retention rate of 95.7% with 382 out of 399 steers implanted with ONE Grower still possessing a palpable implant at time of mid-study evaluation. As expected, none out of the 399 Control steers (0.0%) had palpable implants on d 35 or 41. Twelve out of 399 steers (3.0%) implanted with ONE Grower had an implant site reaction at time of evaluation. Zero of 399 Control steers had an implant site reaction at time of mid-study evaluation.

Summary of the percentage of deads and removals feedlot steers is presented in Table 5. There was no difference ( $P = 0.99$ ) between treatments for the percentage of deads and removals (Control = 2.21%; ONE Grower = 2.19%) in steers.

The analysis of bullers and for abnormal health events in feedlot steers is summarized in Table 6. There was only one buller identified, and it was a Control steer; therefore, there was no difference ( $P = 0.32$ ) between treatments on the percentage of bullers (Control = 0.3%; ONE Grower = 0.0%). In addition, there was no difference ( $P = 0.47$ ) between treatments for the percent of steers with an abnormal health event nor was there a difference ( $P \geq 0.08$ ) between treatments for the proportion of abnormal health events for any of the system different organ classes in steers.

**Table 6.** Summary of the percent of abnormal health events in feedlot steers

Item	Treatment <sup>1</sup>		P-value
	Control	ONE Grower	
Steers with abnormal health events, %	6.0	7.3	0.47
Proportion by system organ class, %			
Behavioral disorders	0.3	0.0	0.32
Digestive tract disorders	2.3	3.0	0.50
Eye disorders	0.0	0.3	0.32
Musculoskeletal disorders	0.5	0.3	0.56
Respiratory tract disorders	2.5	2.8	0.82
Skin and appendages disorders	0.5	0.8	0.65
Systemic disorders	0.8	0.0	0.08
Uncoded signs	0.0	0.3	0.32
Bullers, %	0.3	0.0	0.32

<sup>1</sup>Control = sham implant (empty needle administered subcutaneously in middle one-third of the ear); ONE Grower = single Synovex ONE Grower (150 mg trenbolone acetate and 21 mg estradiol benzoate; Zoetis, Inc.) implant administered in the middle one-third of the ear.

### Heifer Feedlot Data

Table 3 summarizes growth performance of feedlot heifers over at least 200 d. Initial BW on d 0 for feedlot heifers was not different ( $P = 0.72$ ) between treatments (Control = 311.3 kg; ONE Grower = 311.7 kg). There was an improvement ( $P < 0.01$ ) in the final BW of heifers implanted with ONE Grower (585.5 kg) compared to Control (563.3 kg). Overall study ADG was greater ( $P < 0.01$ ) for heifers implanted with ONE Grower (1.35 kg/d) compared to Control (1.24 kg/d).

Implant retention and reaction rate for feedlot heifers are summarized in Table 4. There was a 96.3% (385 out of 400 heifers) implant retention rate for heifers implanted with ONE Grower at the time of the evaluation on d 35 or 41. Zero out of 398 Control heifers (0.0%) had an implant present at time of mid-study evaluation. Only 4 out of 400 heifers implanted with ONE Grower had implant site reactions at the time of evaluation which equated to a reaction rate of 1.0% of heifers on ONE Grower. Zero out of 398 Control heifers had an implant site reaction at time of mid-study evaluation.

The occurrence of deaths and removals in feedlot heifers is summarized in Table 5. There was no difference ( $P = 0.33$ ) between treatments for percentage deaths and removals, with 2.48% and 4.25% for Control and ONE Grower, respectively.

The percentage of abnormal health events and proportion of abnormal health events by system organ class is presented in Table 7. Percentage of heifers with an abnormal health event was not different ( $P = 0.07$ ) between treatments. In addition, each system organ class of abnormal health events in feedlot heifers was not different ( $P \geq 0.08$ ) between treatments.

## DISCUSSION

Growth-promoting implants are a technology that provides a great improvement in feedlot cattle performance and

a substantial return on investment to feedlot operators (Duckett et al., 1996) which has resulted in over 90% of feedlot cattle being implanted at least once (NAHMS, 2013) during the feedlot period. Cattle implanted with TBA and estradiol (either estradiol-17 $\beta$  [E<sub>2</sub>] or EB) were shown to repeatedly improve ADG, DMI, and feed conversion while reducing marbling score and USDA yield grade (Smith et al., 2019b, 2020).

Lee et al. (2000) reported composition and methods of coating on growth-promoting implants and that in vitro and in vivo release of TBA and EB was slowed when implants were coated with a polymeric, porous coating. The use of coating technology to extend the payout of implants has increased in prevalence with recent regulatory approvals of implants with this technology. Cleale et al. (2012) reported that eliminating the need to handle cattle multiple times in an effort to reimplant for cattle fed up to 200 days by using a single, long-acting implant represents an opportunity to minimize stress while reducing handling cost and not negatively impacting feed intake following handling.

Synovex ONE Grower was previously approved as Synovex ONE Grass (FDA, 2014b) with the same dose of 150 mg TBA and 21 mg EB in six extended-release pellets and was labeled for increased rate of weight gain for up to 200 days in pasture steers and heifers (stocker, feeder, and slaughter). Cleale et al. (2015) reported a 19.5% improvement in ADG in stocker steers and a 10.9% improvement in ADG in stocker heifers implanted with Synovex ONE Grass compared to sham-implanted negative controls. Results from the pasture trials are similar to what was found in these feedlot studies, where Synovex ONE Grower improved rate of weight gain by 13.1% and 8.9% in feedlot steers and heifers compared to sham-implanted controls. Synovex ONE Feedlot, which is approved for use in feedlot steers and heifers fed in confinement for slaughter, contains the same polymeric, porous film on each implant pellet as Synovex ONE Grower, but with two additional pellets, resulting in a 25% more potent implant totaling 200 mg TBA and 28 mg EB. Cleale et al. (2012) reported a 15.4% improvement in ADG for feedlot steers and a 12.0% improvement in ADG for feedlot heifers implanted with Synovex ONE Feedlot fed in confinement for slaughter for 200 d. The primary outcome of ADG for cattle in the present study implanted with ONE Grower was only 2.3% to 3.1% less than the ADG response for cattle implanted with Synovex ONE Feedlot despite a 25% lower dose of TBA and EB.

Steers in the current study administered ONE Grower were 34.4 kg heavier than sham-implanted controls on d 200 which represents a 5.8% improvement in BW over 200 d. Heifers implanted with ONE Grower were 22.2 kg heavier at D 200 than their Control counterparts which represented an increase of 3.9% in BW response with the use of ONE Grower in heifers fed for at least 200 d. Thus, data from this study demonstrated that ONE Grower improved BW response over intervals of at least 200 d in both feedlot steers and heifers. In steers, there was a 0.18 kg/d improvement in ADG over 200 d resulting in a 13.1% response in ADG to implantation of ONE Grower compared to Control. Heifers saw an 8.9% response in ADG after implantation of ONE Grower over a 200-d feeding period which resulted in a 0.11 kg/d improvement in ADG. As evidenced in this study, the use of long-acting implants such as ONE Grower greatly improved final BW and ADG through 200 d. Although

not researched in this study, with treatments commingled within pen, historical data utilizing implants suggest that use of ONE Grower for at least 200 d would likely increase DMI and gain efficiency compared to Control (Smith et al., 2019a, 2020). This is further supported by the Synovex ONE Feedlot approval work which resulted in a 4.7 and 4.5% increase in DMI for steers and heifers, respectively, while seeing an 8.0% and a 7.0% increase in gain efficiency for steers and heifers, respectively (Cleale et al., 2012).

Growth performance results from the current study support use of a single, long-acting implant for at least 200 d without the need of reimplantation. McLaughlin et al. (2013) reported no difference in growth performance including ADG in steers implanted with either long-acting Synovex ONE Feedlot (all implant pellets coated), Revalor XS (6 out of 10 implant pellets coated), or short-acting Synovex Plus (no implant pellets coated) in a 161 or 200 d study. Nichols et al. (2014) reported no difference in growth performance of cattle implanted with a long-acting partially coated implant compared to steers implanted with an initial implant followed by terminal reimplant with both treatments receiving the same total hormone concentration and were fed for the same duration. Similarly, Ohnoutka et al. (2020) described those heifers implanted with a long-acting implant; regardless of whether it was partially coated or fully coated, had similar growth performance to a single; short-acting implant with the same hormonal concentration given on d 1 or delayed until d 70 in a 198 d study. Schumacher et al. (2019) reported that feedlot heifers administered Synovex ONE Feedlot had growth performance comparable to heifers implanted with Synovex Choice on d 0 followed by reimplant with Synovex Plus on d 95 with all heifers being fed for 182 d.

Less aggressive implant strategies have demonstrated less of a negative impact on carcass quality; specifically marbling and thus quality grades (Duckett and Pratt, 2014). Cleale et al. (2012) reported that Synovex ONE Feedlot (25% greater TBA and EB than ONE Grower) increased HCW and LM area; however, also reduced marbling score by 5.5% in steers and 6.8% in heifers while also decreasing the percentage of carcasses grading USDA Choice or Prime compared to sham-implanted negative controls. Because ONE Grower is 25% less potent than Synovex ONE Feedlot, the authors hypothesize that animals implanted with ONE Grower may have greater marbling scores and USDA quality grades when compared to cattle implanted with Synovex ONE Feedlot. More research is needed to determine the effect of Synovex ONE Grower on carcass quality and composition. A meta-analysis of implants in feedlot steers by Reinhardt and Wagner (2014) reported that a moderate potency implant does not negatively affect marbling score and quality grades as much as a more potent single combination implant. Duckett and Pratt (2014) reported in a review article that a single combination (testosterone and estrogen analogs) implant reduced marbling scores on average by 4.62%; however, a two implant, reimplant strategy using combination implants reduced marbling scores by 9.34% on average. Johnson et al. (1996) reported that a moderate potency (120 mg TBA and 24 mg E<sub>2</sub>), short-acting implant (Revalor-S; Merck Animal Health) had no effect of marbling score or quality grades; however, it should be noted the sample size in that study was relatively small. Synovex ONE Grower is a long-acting implant but of similar potency with 20 mg more TBA and the equivalent of 9 mg less E<sub>2</sub> than Revalor-S which supports the hypothesis

that ONE Grower may minimally impact marbling score and quality grades. Given our inability to collect carcass data as part of this study, more research is needed to determine the effect of Synovex ONE Grower on carcass quality and composition. A long-acting implant may improve growth performance with minimal negative implications on carcass quality, which would be of great benefit to producers and packers, who place a premium on carcass quality but do not want to give up the benefits of a long-acting implant on growth performance.

Finally, implants have been repeatedly reported to be safe since their first adoption in the 1950s. Results from this study showed that implant retention rates were high with close to 96% retention rates at the mid-study implant site evaluations. This, in concert with the minimal implant site reactions noted, shows that the implant pellets are not only being retained but are not causing irritation or reactions when administered subcutaneously in the ear. Some growth-promoting implants have shown to have an effect on the proportion of bullers as evidenced by warning indications placed on certain implant labels by the FDA; however, ONE Grower did not have an effect on the proportion on bullers in the current study. Cleale et al. (2012) reported that Synovex ONE Feedlot (25% more pellets than ONE Grower) had no effect on the percentage of steers or heifers with an abnormal health event which coincides with results from the current study as there was no difference between steers and heifers implanted with ONE Grower compared with Control for the percentage of steers and heifers with an abnormal health event. Lastly, Synovex ONE Grower was observed to be safe with a similar percentage of deaths and removals occurring in both treatments (ONE Grower and Control) throughout the duration of the current study.

In conclusion, growth-promoting implants are one of the most effective and widely used technologies in the feedlot industry to improve growth performance and efficiencies. Synovex ONE Grower was observed to be safe and improved growth performance including final BW and ADG for up to 200 d. Feedlot producers can utilize Synovex ONE Grower as a moderate potency, long-acting single implant that will improve growth performance for up to 200 d.

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## Conflict of Interest Statement

Jase J. Ball, Patrick C. Taube, John W. Hallberg, Stacey L. Wood-Follis, Carleen R. Dykstra, Angela N. Nadrasik, Nicole L. Eberhart, Shelby L. Jones, Karmella D. Borchers, and Jordan A. Scramlin are employed by Zoetis, Inc., which funded the research projects. The other authors declare no conflict of interest at the time the research was conducted, analyzed, and summarized.

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