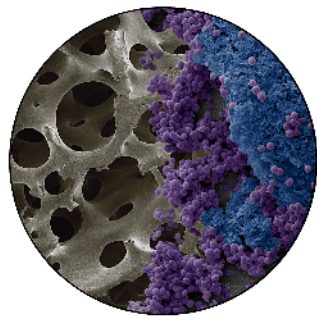
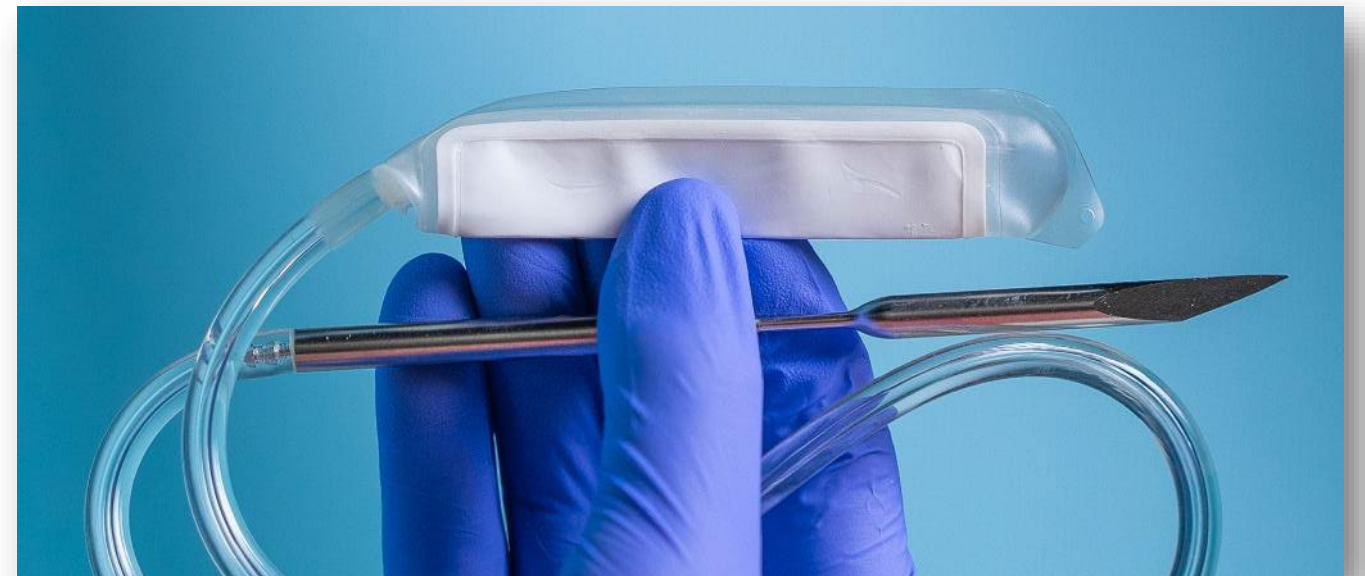


TRANSITIONING A DRUG-LED COMBINATION PRODUCT THROUGH THE FDA: UPDATE ON THE PURGO POUCH, FDA INTERACTIONS, AND MEETING A MAJOR UNMET NEED OF BIOFILM-COMPLICATED, FRACTURE-RELATED INFECTIONS

DUSTIN WILLIAMS, PhD



BONE & BIOFILM
RESEARCH
LABORATORY



DISCLOSURE



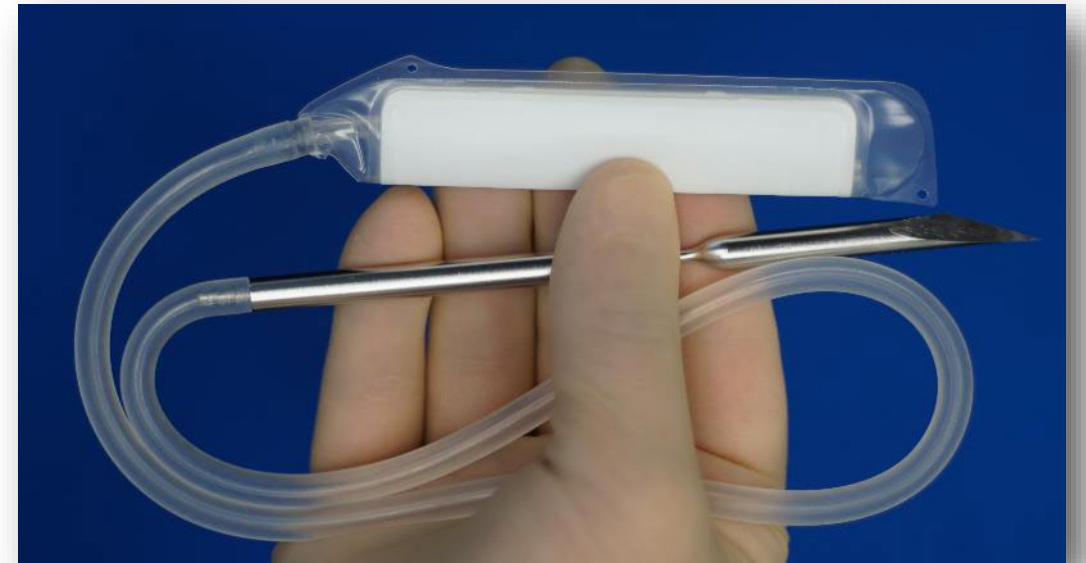
Financial interest

Co-Founder

Board Member

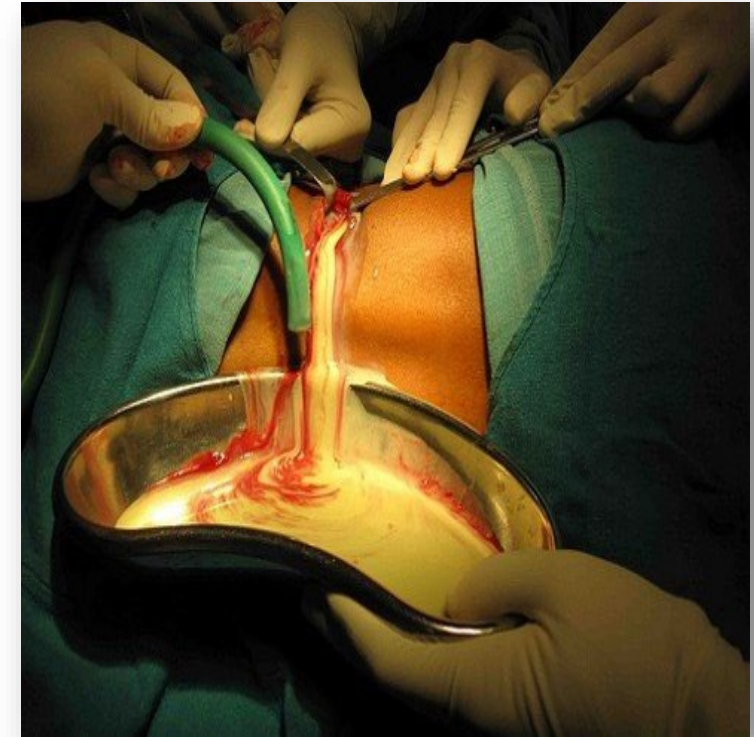
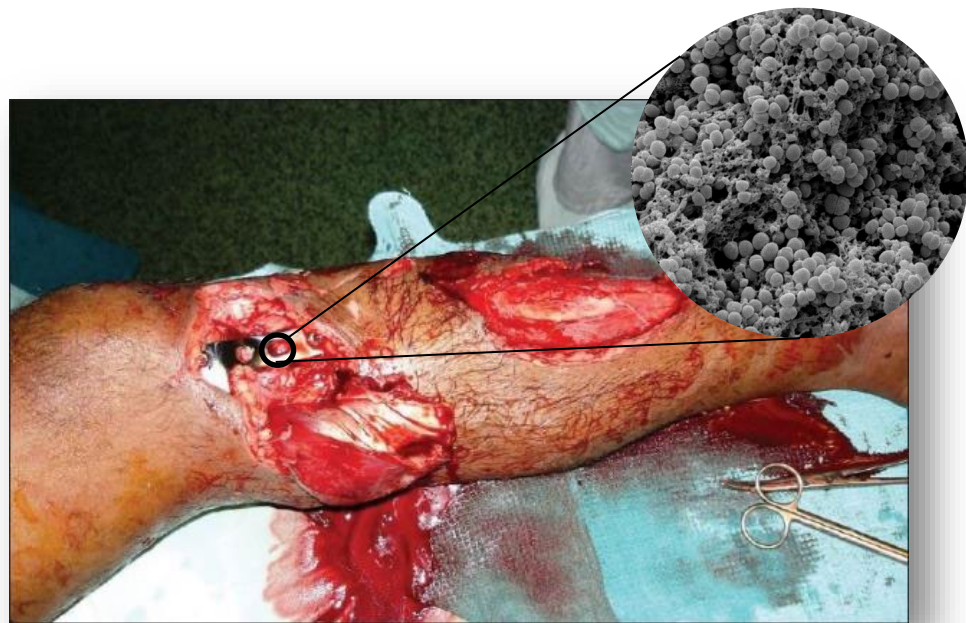
CSO

3M



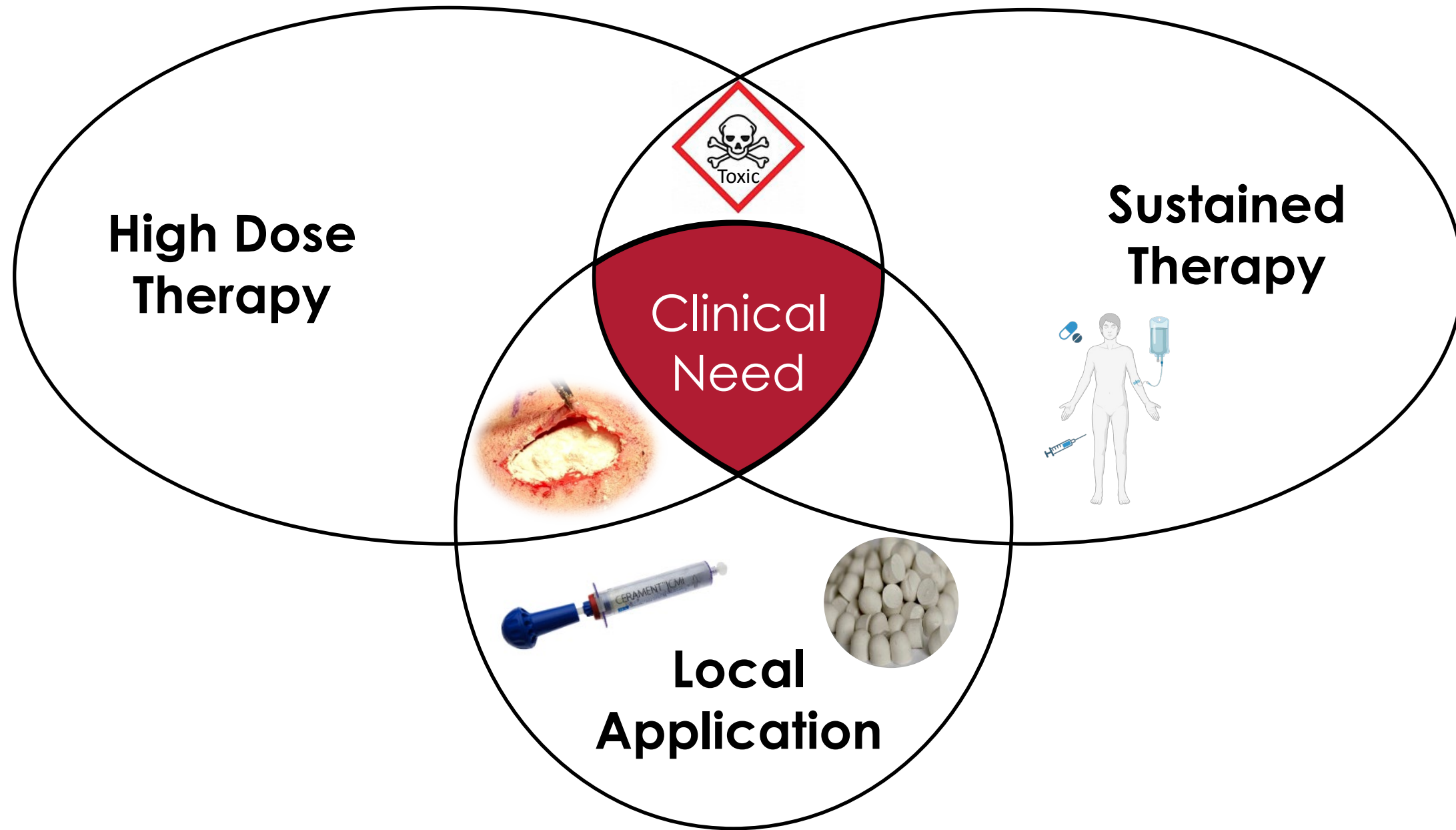
CLINICAL CHALLENGE

- Stubborn fracture-related infection
 - ~50 years no change
 - Unmet need
 - \$40k - \$80k cost



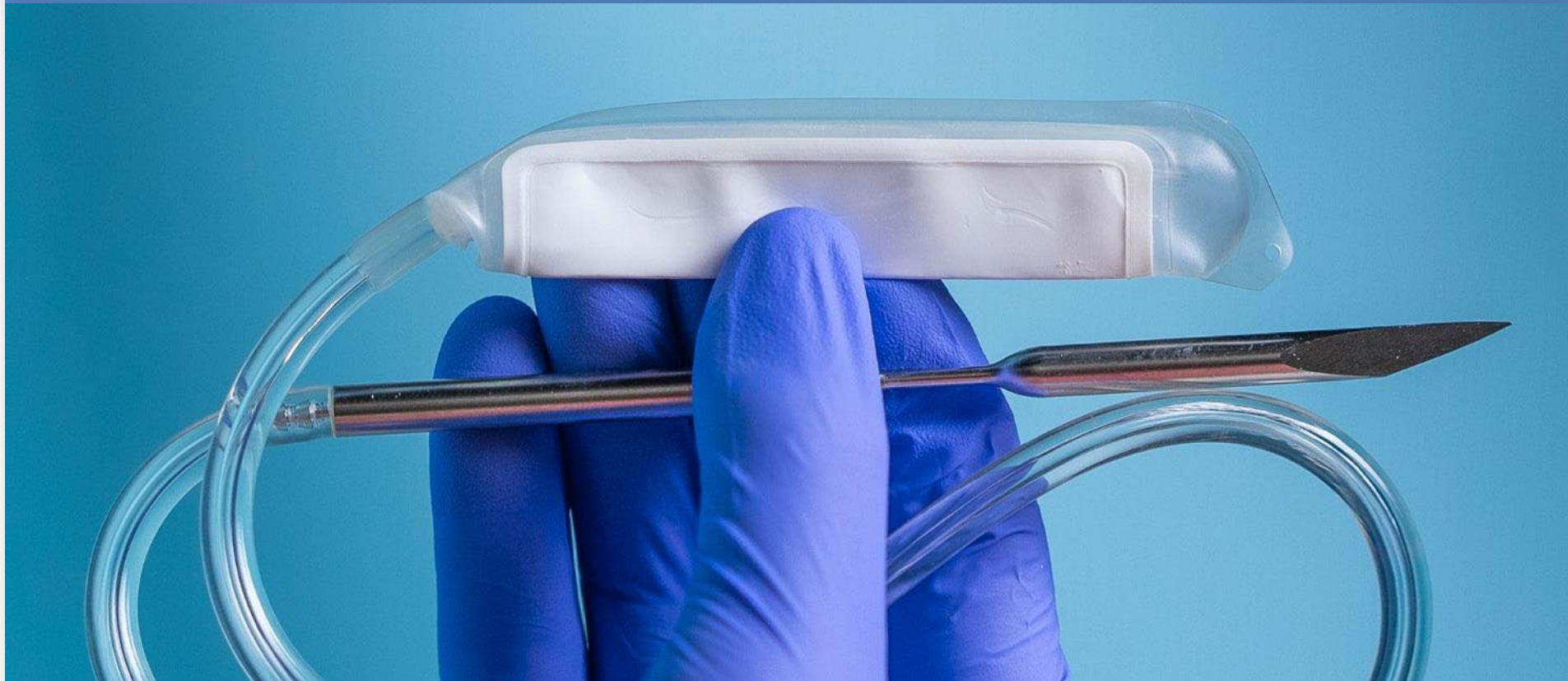
What we're currently doing isn't working well.

TO MEET THE NEED



SOLUTION

- The Purgo Pouch -



Benefits:

- Delivers one or more antibiotics, other drugs
- High dose delivery
 - Max daily dose (failsafe)
- Standalone
 - Placed next to implanted devices or in surgical sites
- Sustained local antibiotic delivery
 - Refillable

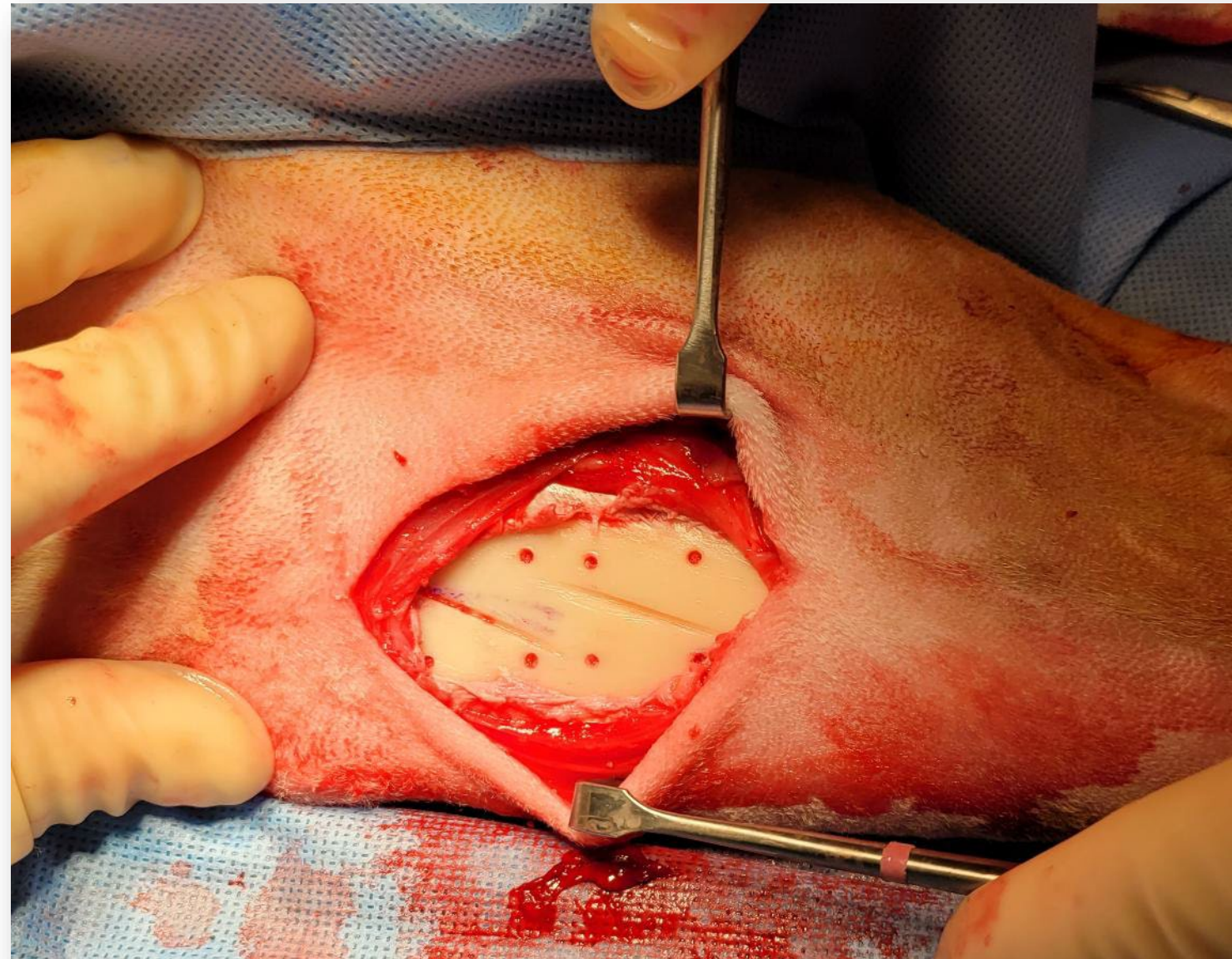
purgo

SCIENTIFIC

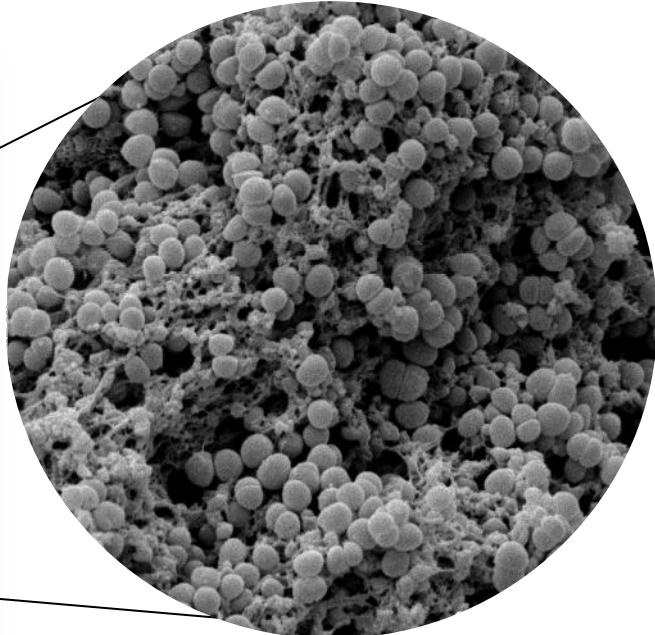
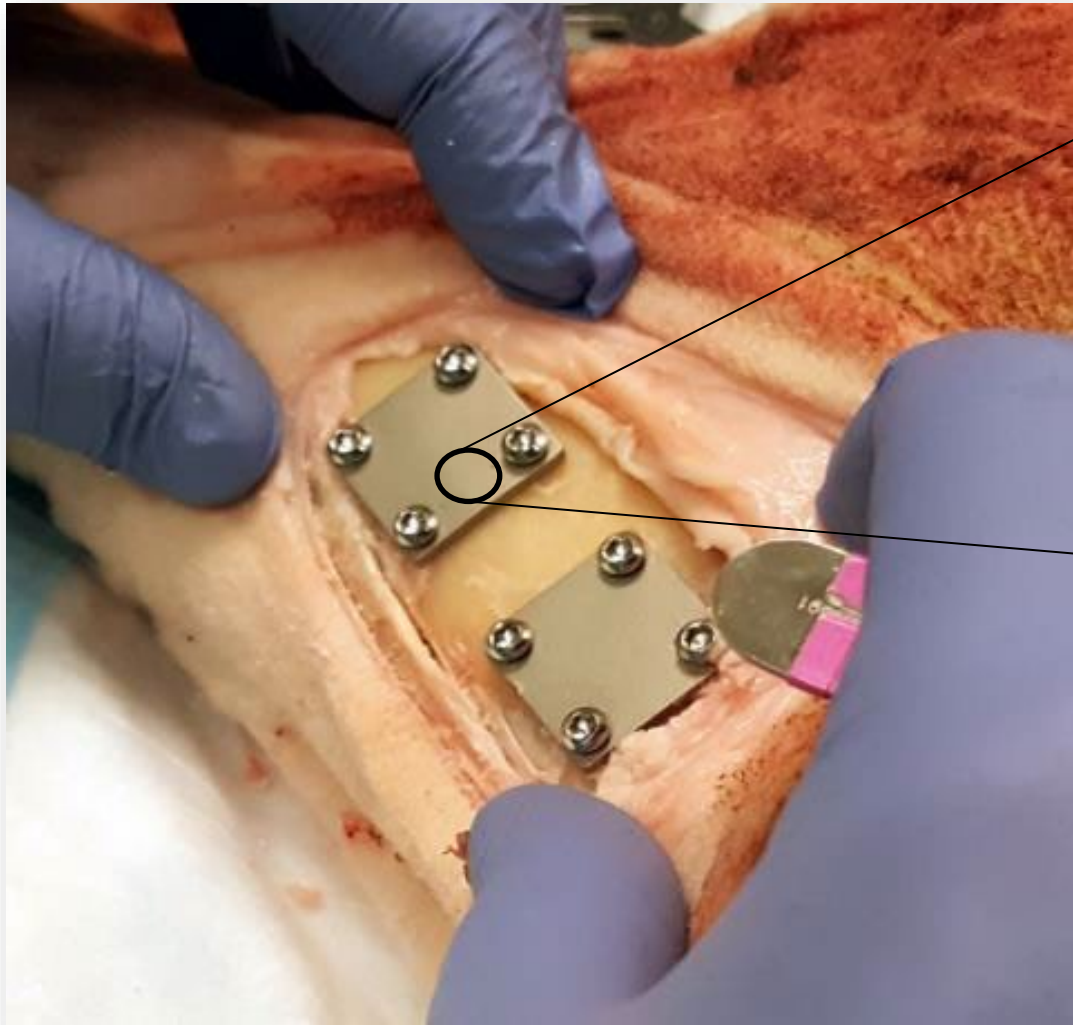
IN VIVO EFFICACY TESTS – SOFT TISSUE TRAUMA



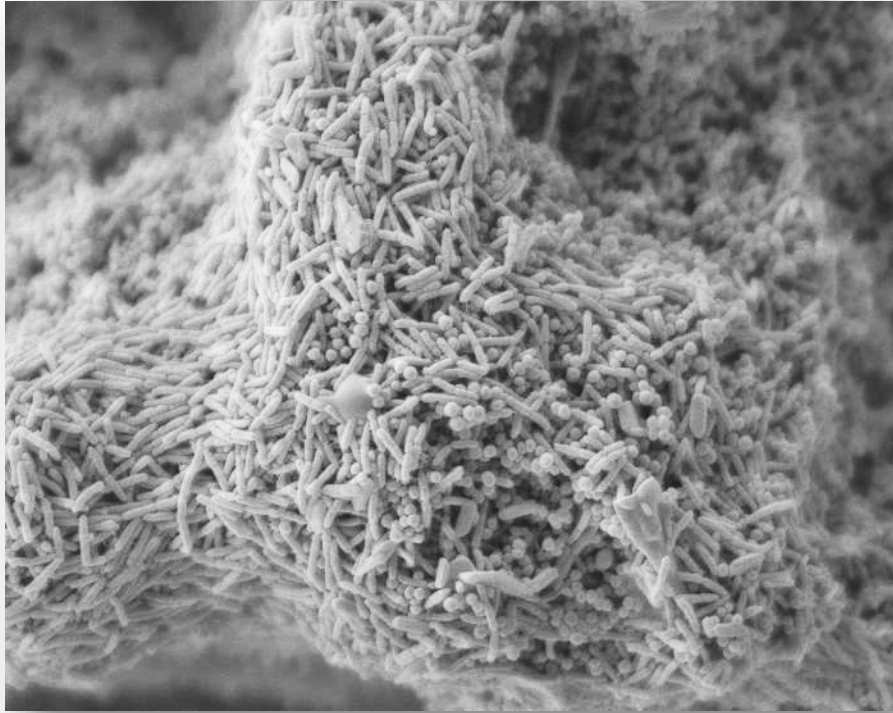
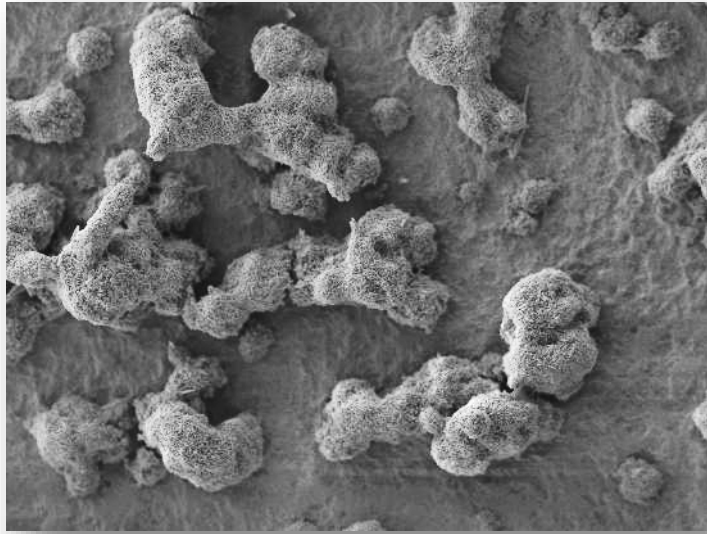
IN VIVO EFFICACY TESTS – OSTEOTOMIZED FRACTURE



IN VIVO EFFICACY TESTS – BIOFILM INOCULA



Monomicrobial



Polymicrobial

IN VIVO EFFICACY TESTS – LOCAL ANTIBIOTICS



Stimulan®

120 mg gentamicin/12 cc beads or
1 g vancomycin + 240 mg tobramycin



Antibiotic powders

1 g vancomycin +
1.2 g tobramycin

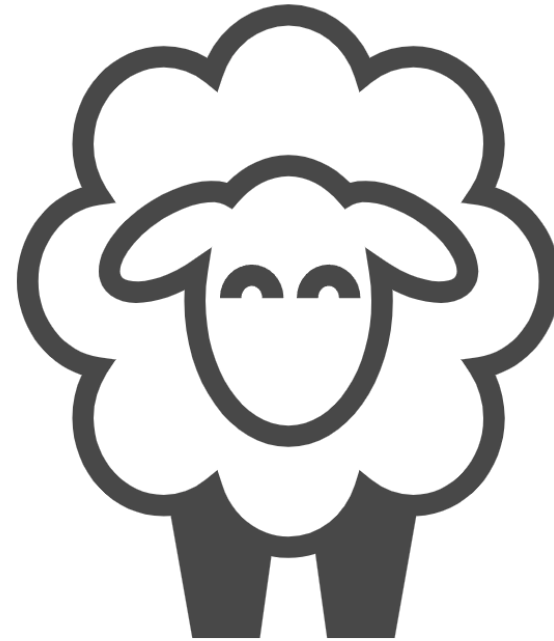
PURGO POUCH PLACEMENT



PURGO POUCH FILLING



MONITORING



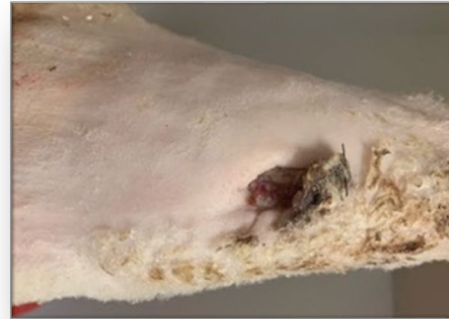
Sheep treated and monitored for up to 30 days
(antibiotic solution in Purgo Pouch changed daily).

Sheep euthanized, tissues collected, bioburden
quantified, bones imaged.

Non-GLP efficacy
GLP safety

IN VIVO EFFICACY OUTCOMES

Positive control



Infection present, open wound

Stimulan[®] Beads with gentamicin



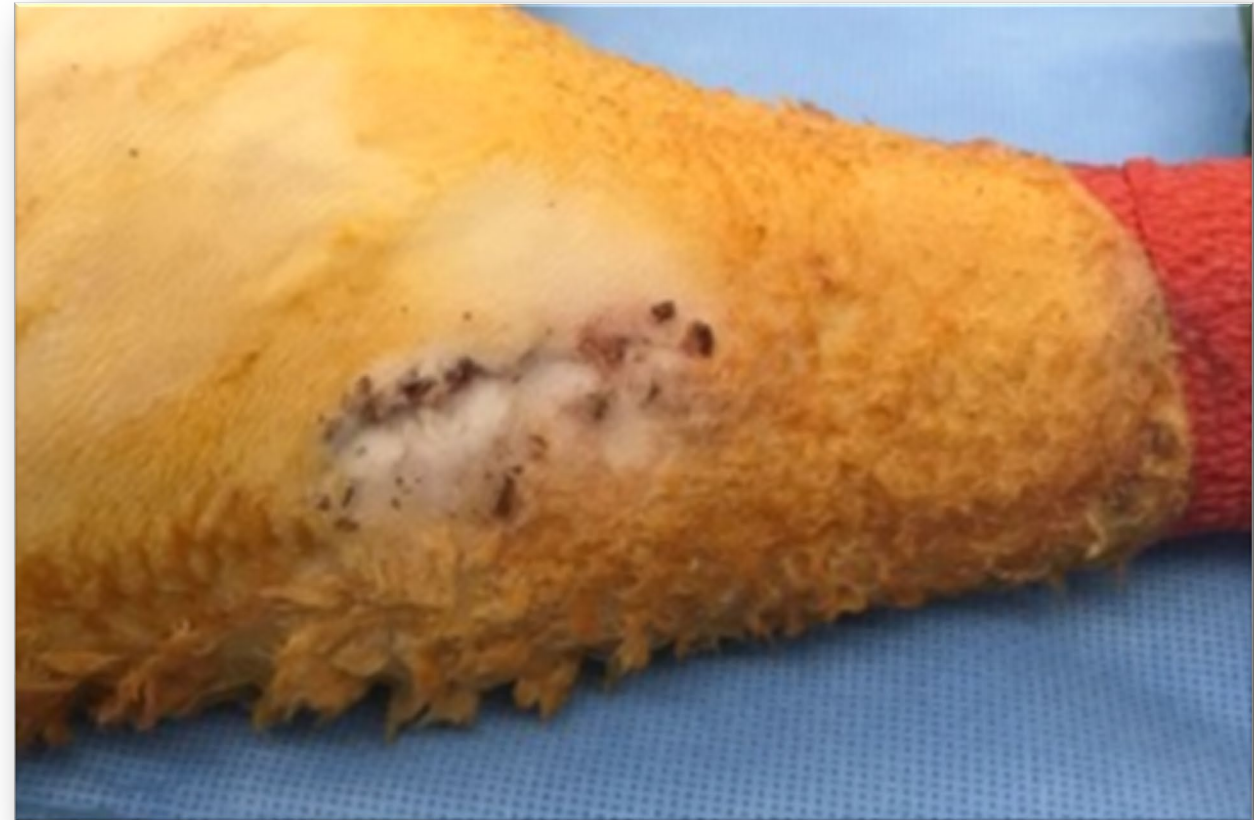
Infection present, open wound

IV Vancomycin IV



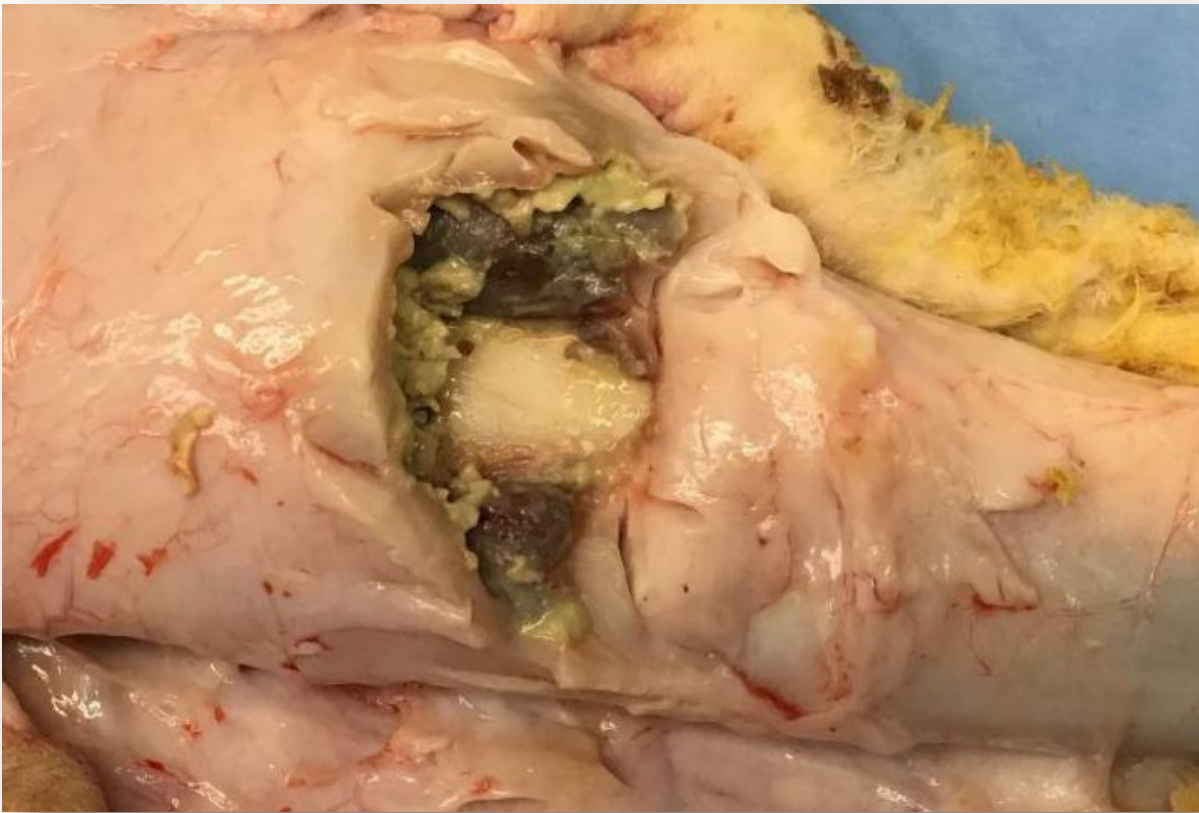
Infection present, open wound

Sheep with Purgo Pouch



Suture line healed and infection managed

IN VIVO EFFICACY – POLYMICROBIAL BIOFILMS



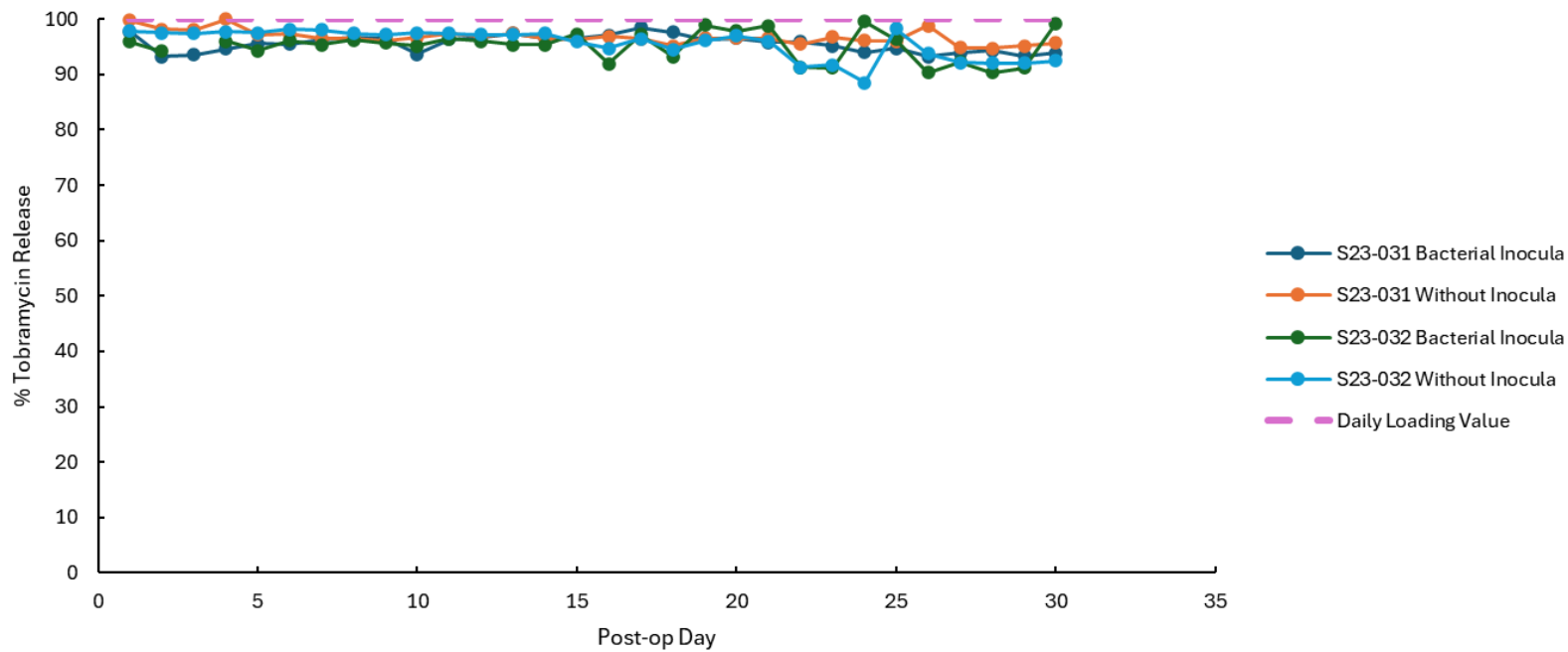
Positive Control



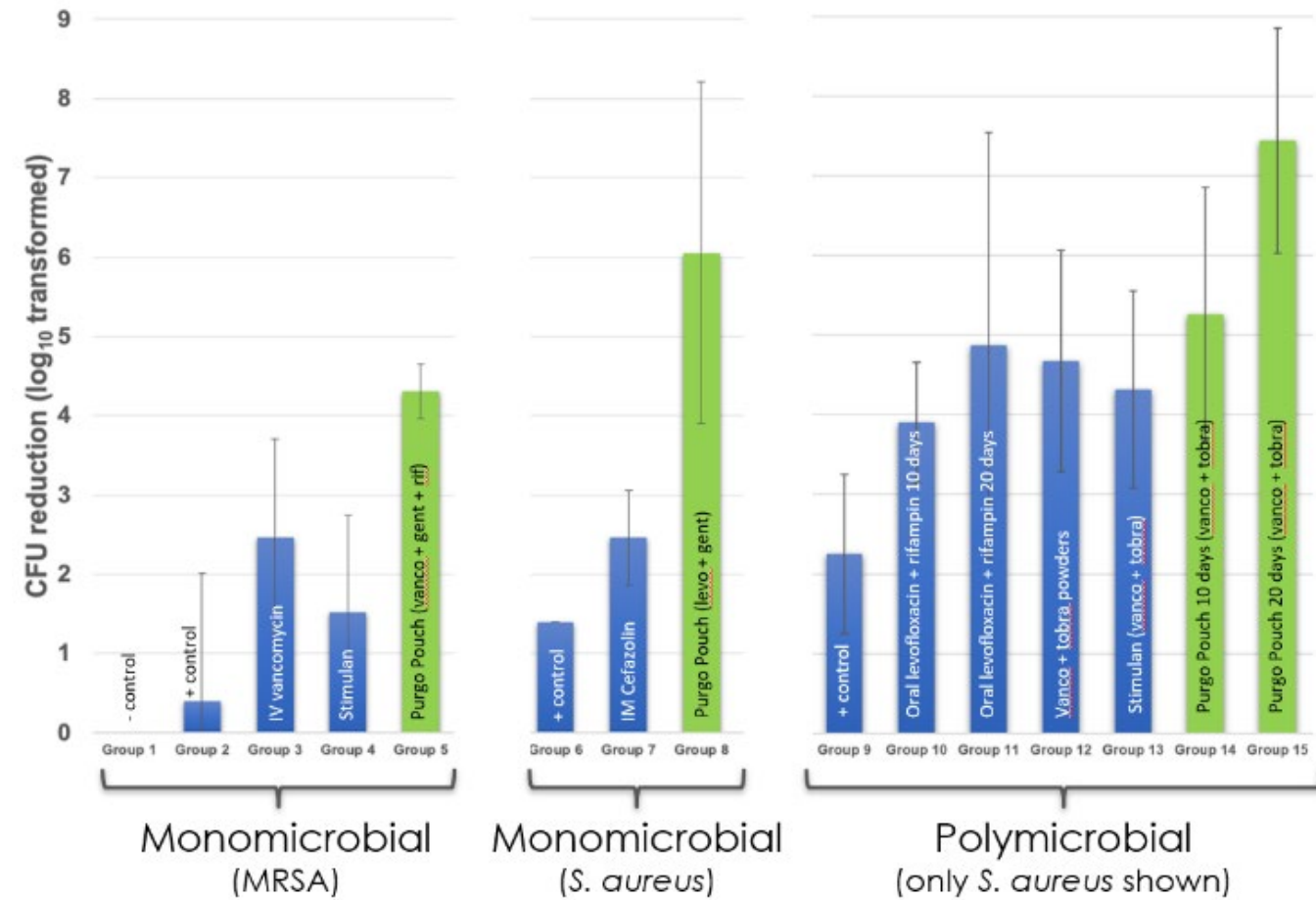
20 Day Pouch
(Vancomycin 33 mg/ml, Tobramycin 20 mg/ml)

SUSTAINS LOCAL DRUG DELIVERY, KILLS BIOFILMS, MAINTAINS HOST BONE

Percent Release of Tobramycin from the Purgo Pouch at 160 mg/day With and Without Bacterial Inocula

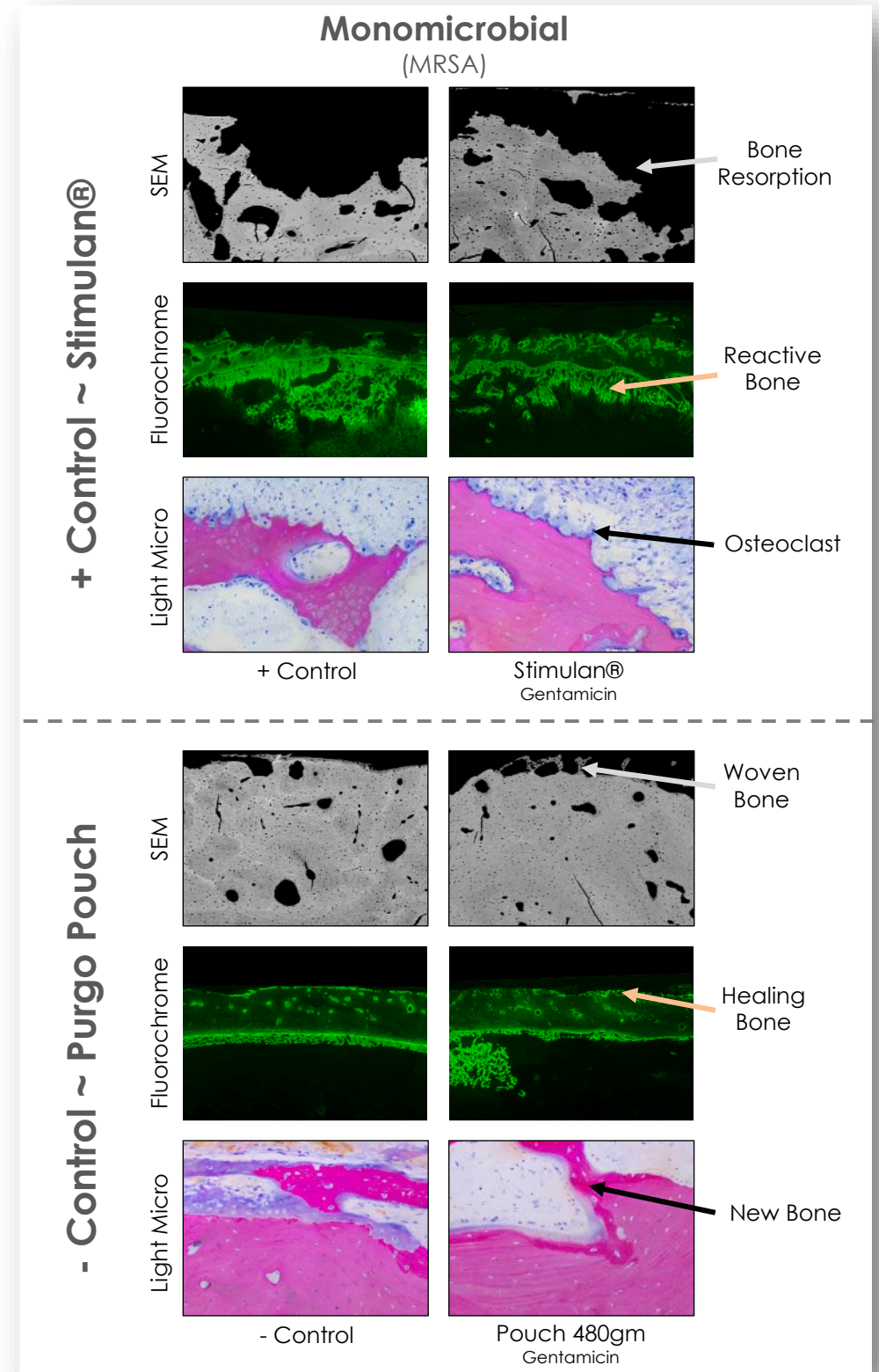
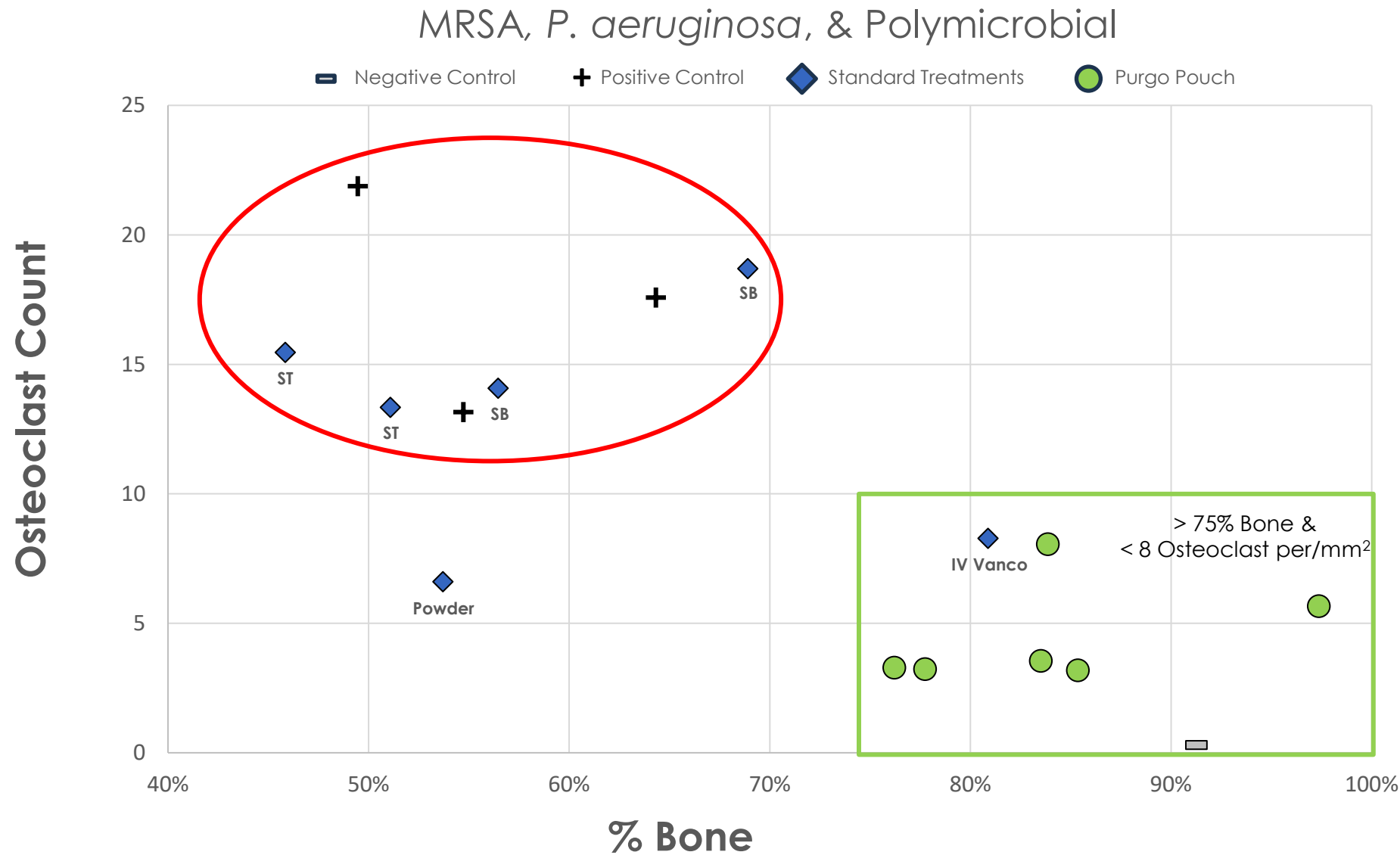


Biofilm reduction in fracture sites of various treatment groups

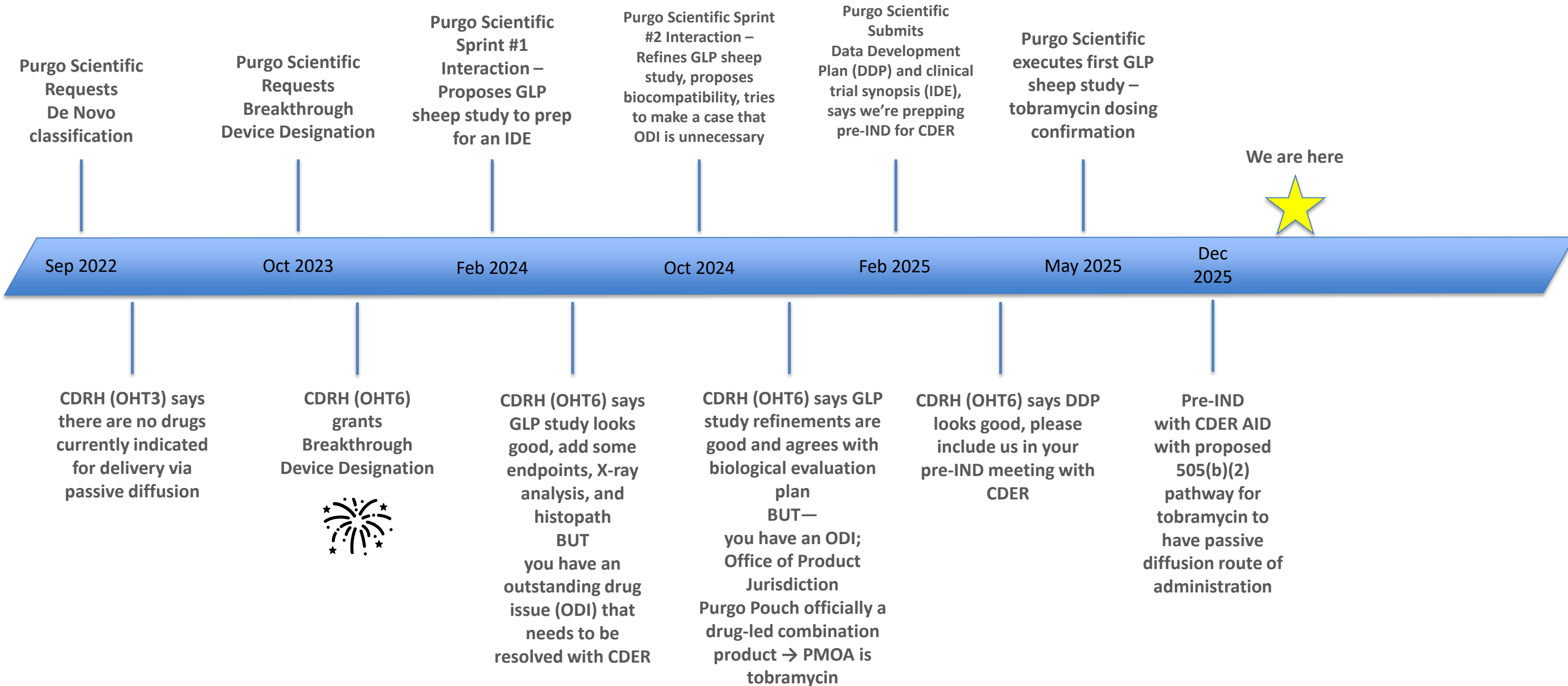


HISTOLOGICAL SUMMARY

- Purgo Pouch manages bone infection, minimizes bony destruction & osteoclasts



FDA EXPERIENCE AND TIMELINE



TOBRAMYCIN

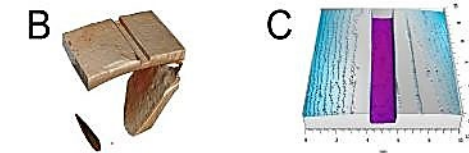
Rationale:

- Fairly broad spectrum; most organisms that cause FRI (*S. aureus*, *E. coli*, *P. aeruginosa*)
- Common in local release technologies (OstealTx, EP Granules, CaSO₄ beads)
- IM injectable
- Single isomer
- Stable – not quickly hydrolytically or enzymatically degraded
- Highly soluble (>94 mg/mL)
- Reasonably priced
- Target protein synthesis – good for biofilms
- Layers well with other therapies, e.g., beta lactams or fluoroquinolones
- Familiar to ortho surgeons

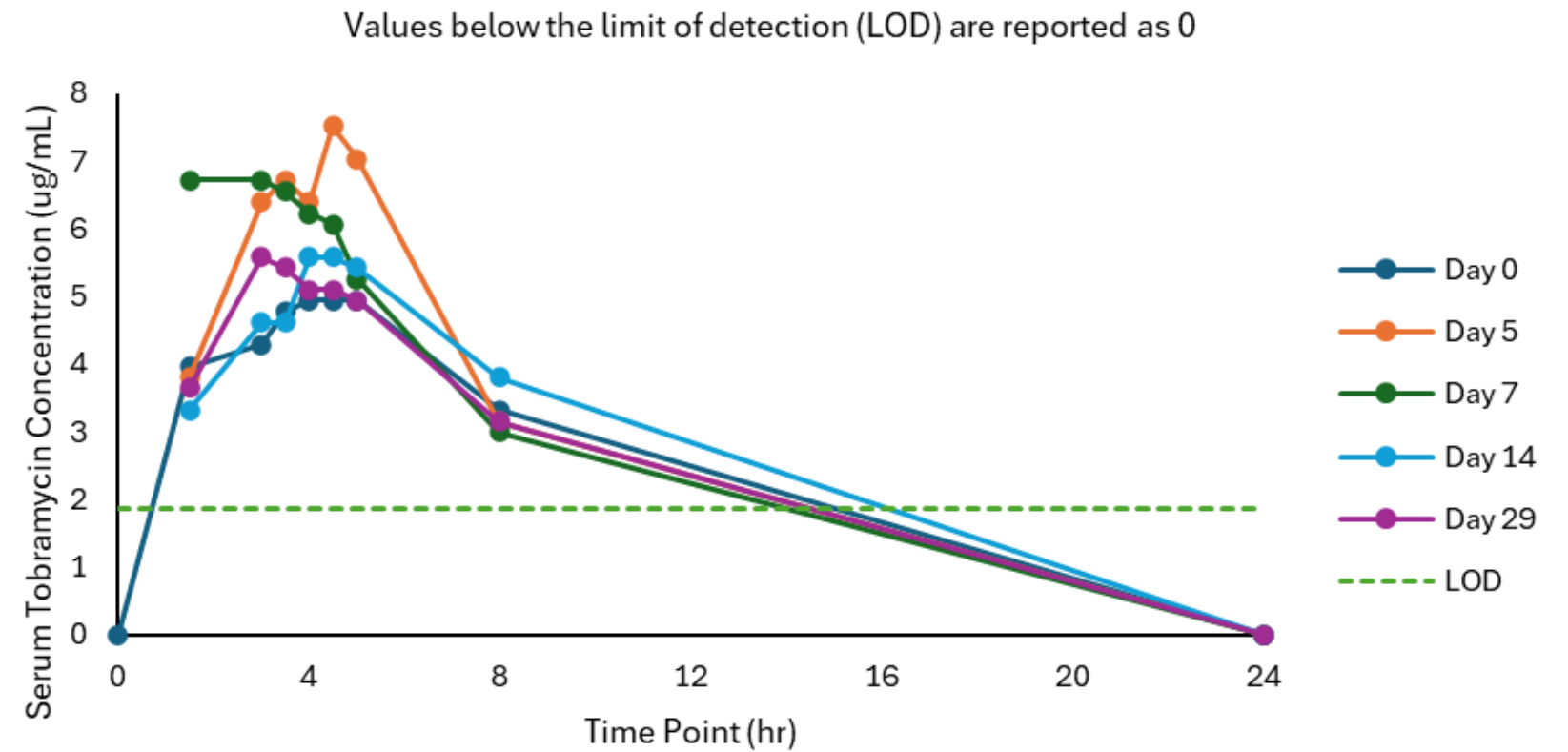
GLP SHEEP STUDY – TOBRAMYCIN DOSING CONFIRMATION

Setup:

- n=4 sheep (2 male (wethers), 2 female))
- Right tibia Purgo Pouch, left tibia sham surgery
- Purgo Pouch refilled daily 352 mg tobramycin
 - Residual fluid collected daily
- X-rays collected Day 0 and Day 30
- Blood collection at various timepoints for CBC, blood chem, and haptoglobin per ISO 10993-11; serum tobramycin quantification
- 30-day endpoint
- Tier 1 end organs collected along with popliteal and inguinal lymph nodes; histopath in process per ISO 10993-11 and 10993-6



GLP SHEEP STUDY – TOBRAMYCIN DOSING CONFIRMATION



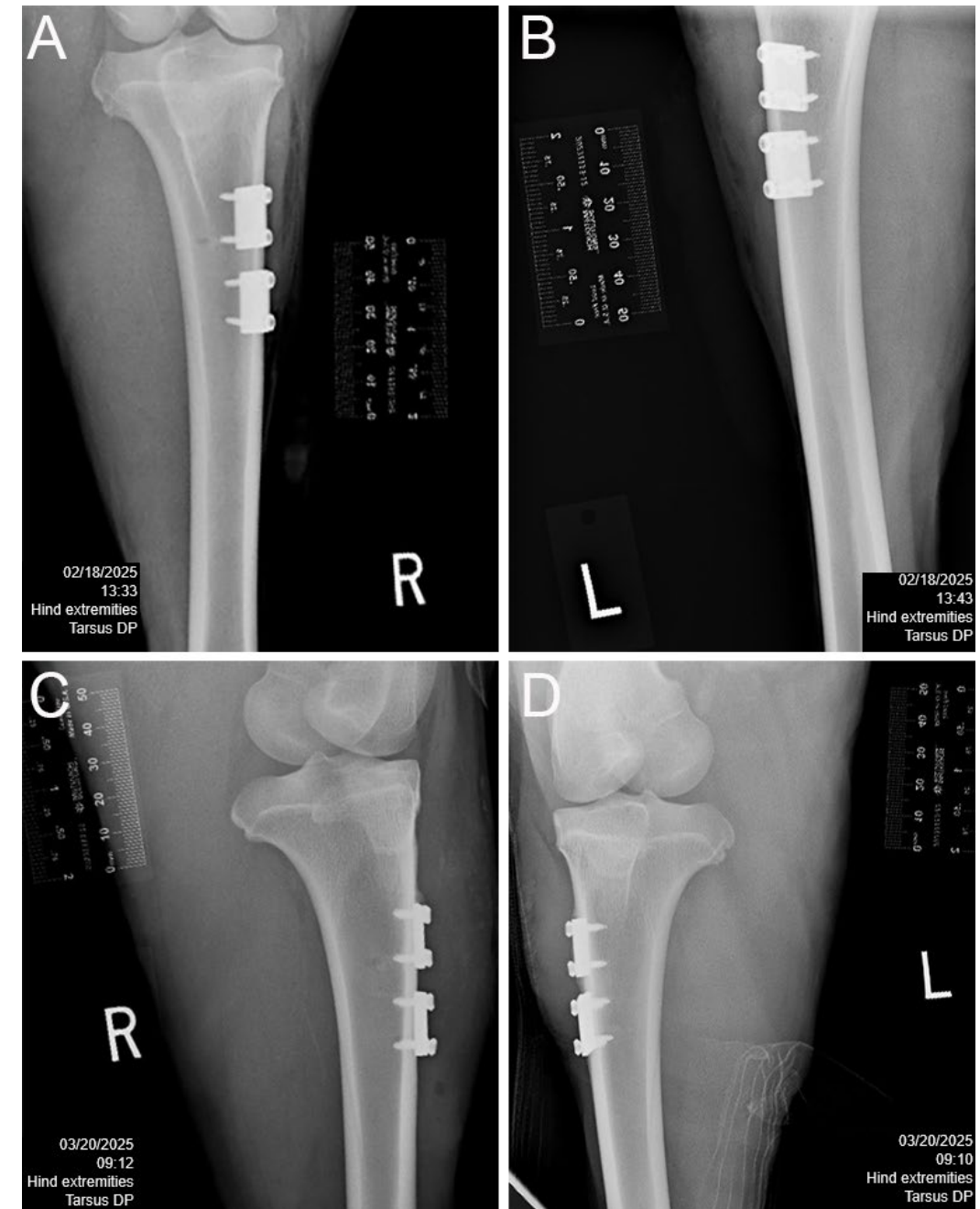
GLP SHEEP STUDY – TOBRAMYCIN DOSING CONFIRMATION

	S25-110_T0	S25-110_T1	S25-110_T5
ALP (U/L)	104	116	170
AST (U/L)	79	121	64
ALT (U/L)	17	24	16
Creatine kinase (U/L)	608	288	91
Albumin (g/dL)	3.7	3.7	3.4
Total Bilirubin (mg/dL)	0.1	0.1	0.1
Total Protein (g/dL)	6.5	6.5	6.1
Globulin (g/dL)	2.8	2.8	2.7
Bilirubin - Conjugated (mg/dL)	0.0	0.0	0.0
BUN (mg/dL)	14	12	16
Creatinine (mg/dL)	0.7	0.5	0.7
Cholesterol (mg/dL)	29	35	32
Glucose (mg/dL)	143	71	51
Calcium (mg/dL)	9.9	9.9	10.1
Phosphorus (mg/dL)	3.6	5.9	5.2
Bicarbonate TCO2 (mmol/L)	26	26	24
Chloride (mmol/L)	108	111	114
Potassium (mmol/L)	3.3	4.6	4.4
ALB/GLOB ratio	1.3	1.3	1.3
Sodium (mmol/L)	143	147	150
BUN/Creatinine Ratio	20.0	24.0	22.9
Bilirubin - Unconjugated (mg/dL)	0.1	0.1	0.1
NA/K Ratio	43	32	34
Haptoglobin (mg/mL)	0.9	1.4	1.1
Hemolysis Index	Normal	Normal	Normal
Lipemia Index	Normal	Normal	Normal

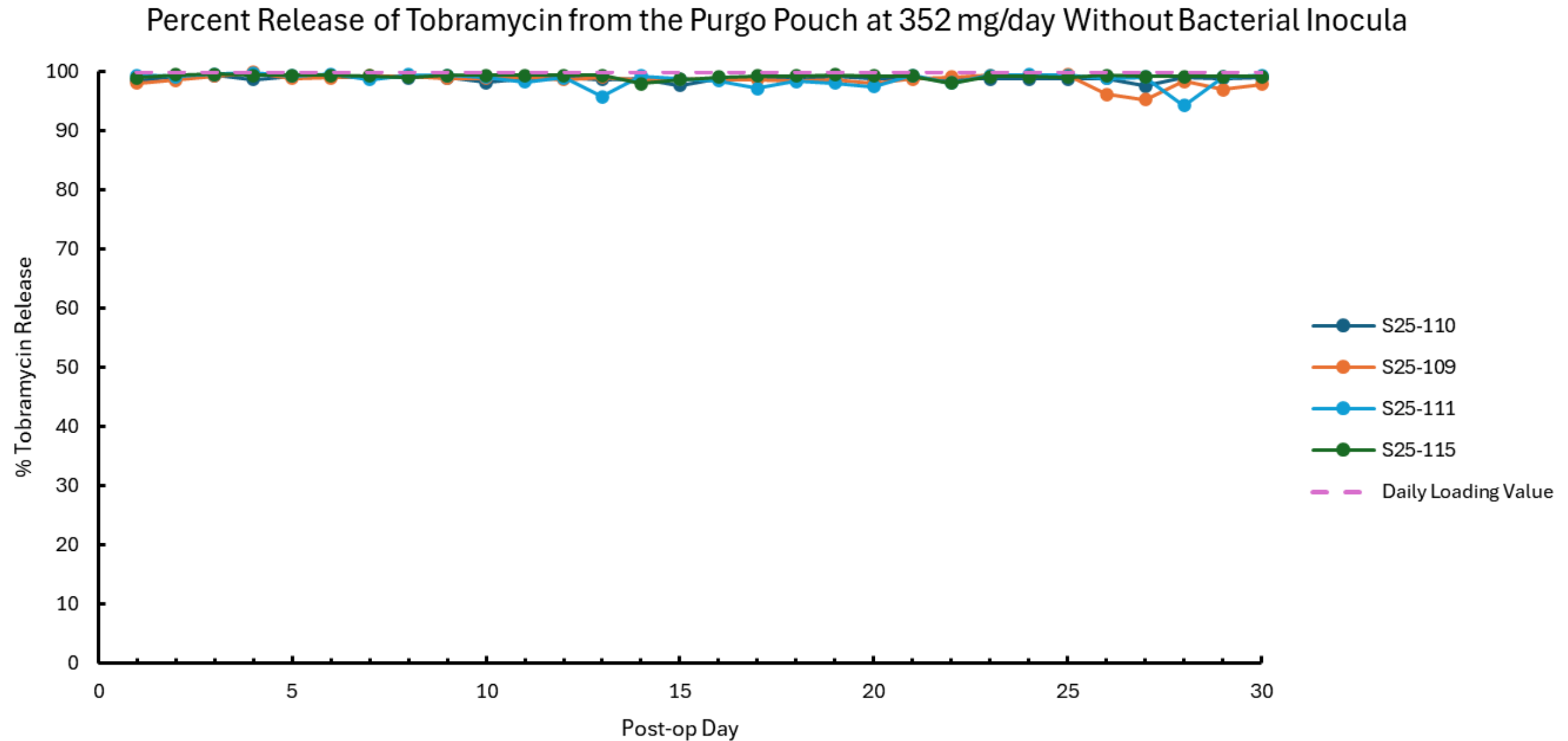
Day 0 (surgery day)

Day 1

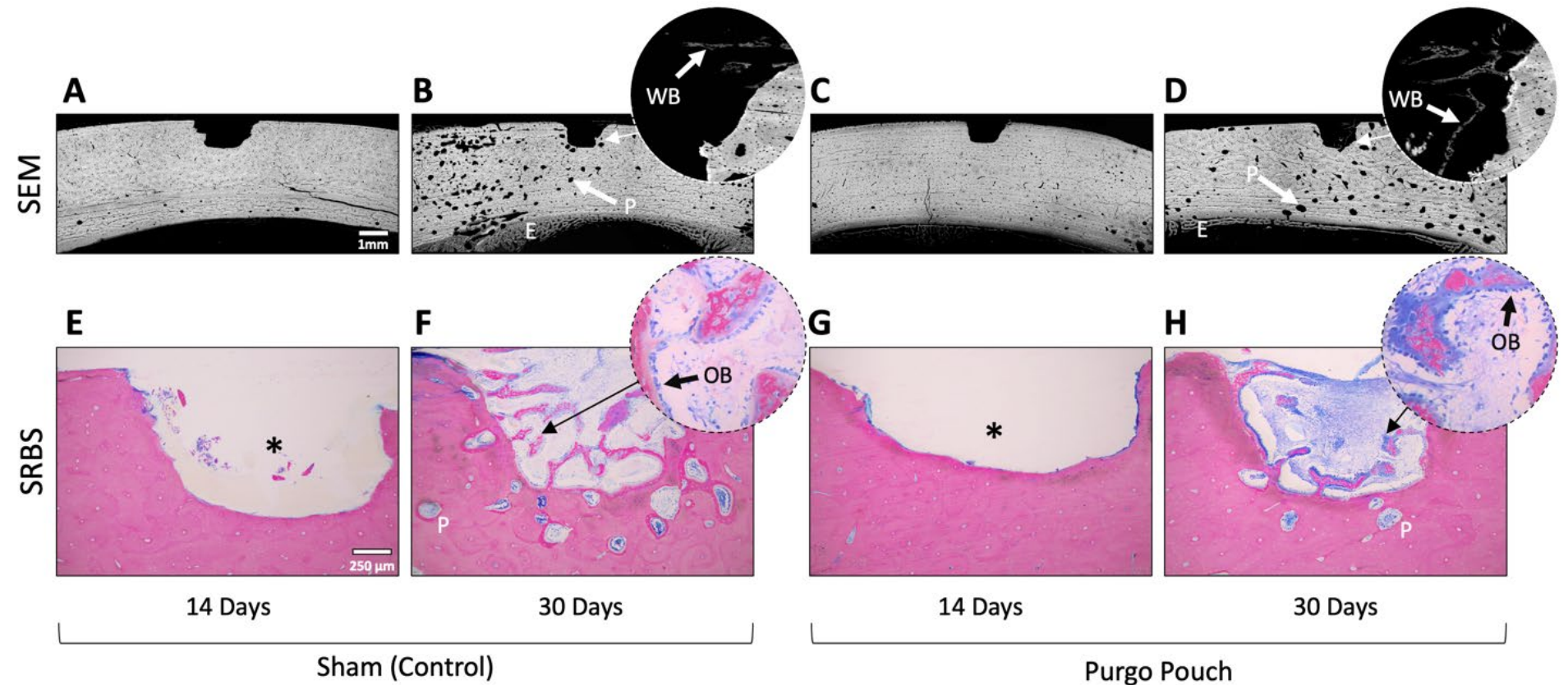
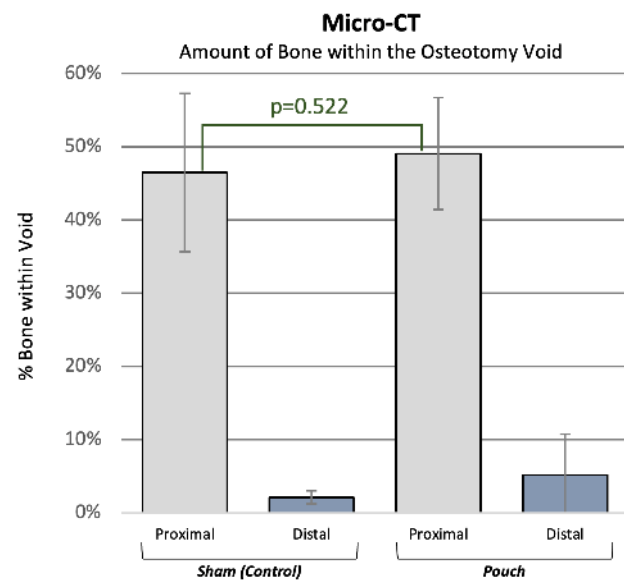
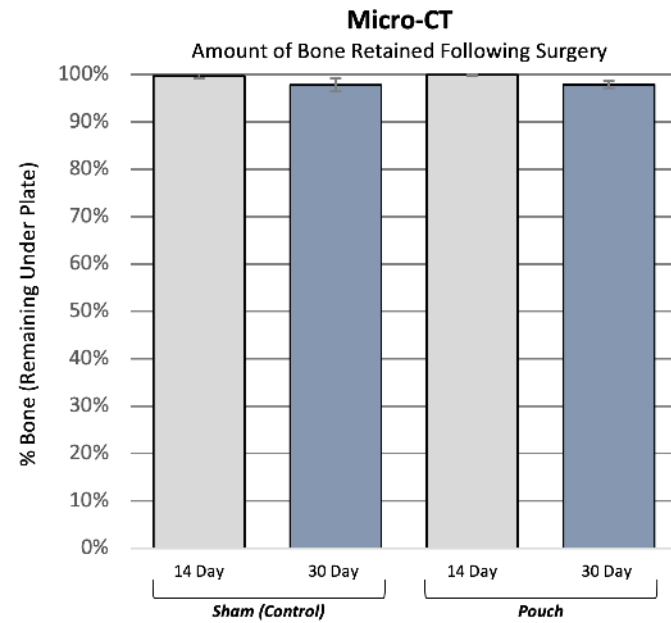
Day 30



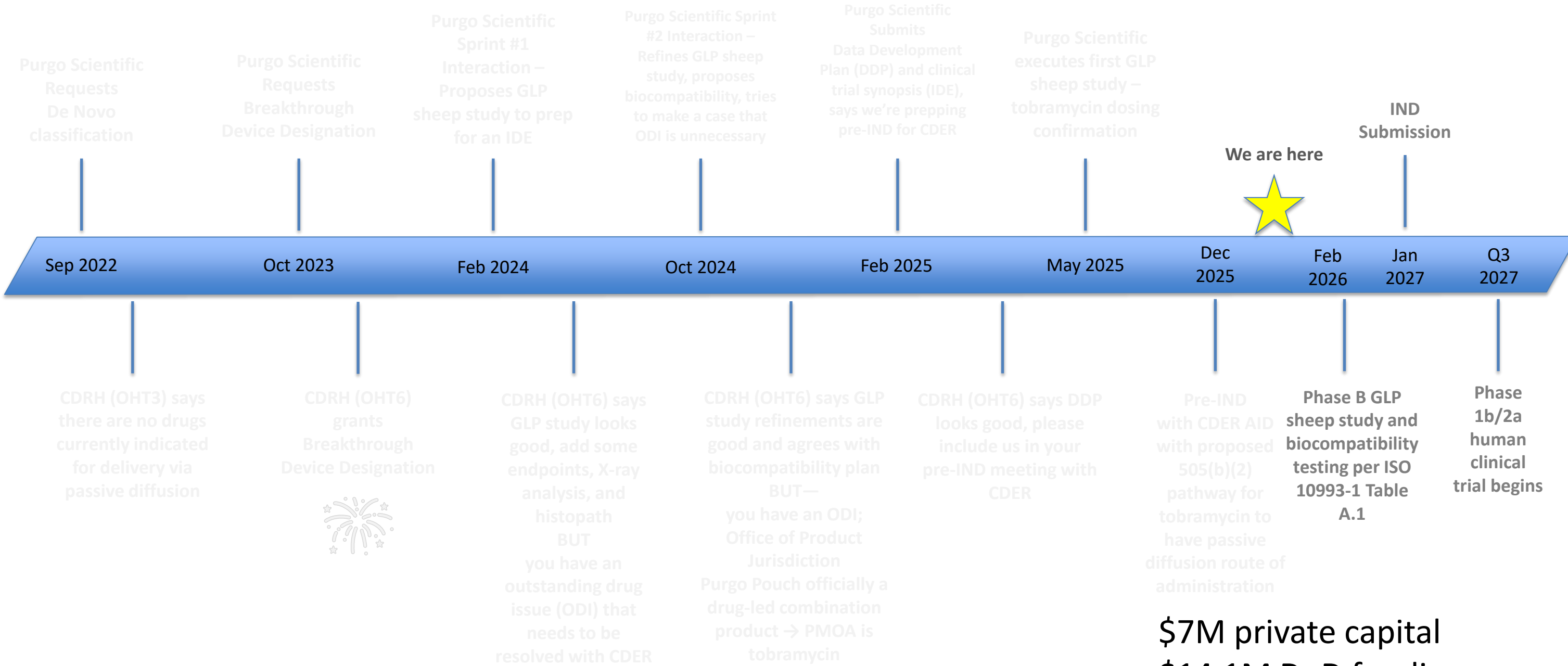
GLP SHEEP STUDY – TOBRAMYCIN DOSING CONFIRMATION



PILOT SHEEP STUDY – TOBRAMYCIN DOSING CONFIRMATION



FDA EXPERIENCE AND TIMELINE



\$7M private capital
\$14.1M DoD funding
Raising \$12 for clinical trial

WHAT I WISH I KNEW BEFORE ENGAGING THE FDA

- Hire a competent regulatory consultancy
 - Pay cash if possible; if equity, make it weighted milestone-driven!
- Intended use defines the technology
 - The words you use matter
- **Primary mode of action (PMOA)!!**
- Understand definitions of and differences between device, drug, combination products (device-led or drug-led)
- Engage FDA earlier than you think you should: we should have done an informational long ago
 - Our first meeting with FDA, they didn't have a clue what we were talking about
- **Make ISO and/or ICH standards your friend!!**
- FDA reviewers are humans and part of your team...treat and approach them as such



Daily Reloadable Antibiotic Delivery

Current Veterinary Markets

- 200+ veterinary hospitals nationwide
- 500+ active veterinary users worldwide
- In 19 veterinary colleges and universities
- Diverse infection treatment and prevention

"... outperformed the antibiotic beads spectacularly."

Caleb Hudson, DVM, MS

Nexus Veterinary Specialists



dog
Skin grafting a degloving injury



dog
Chronic perianal wound



Recurring ear infection

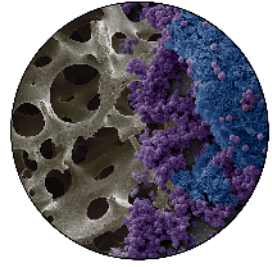


horse
Fistulous Withers



Daily Reloadable Antibiotic Delivery

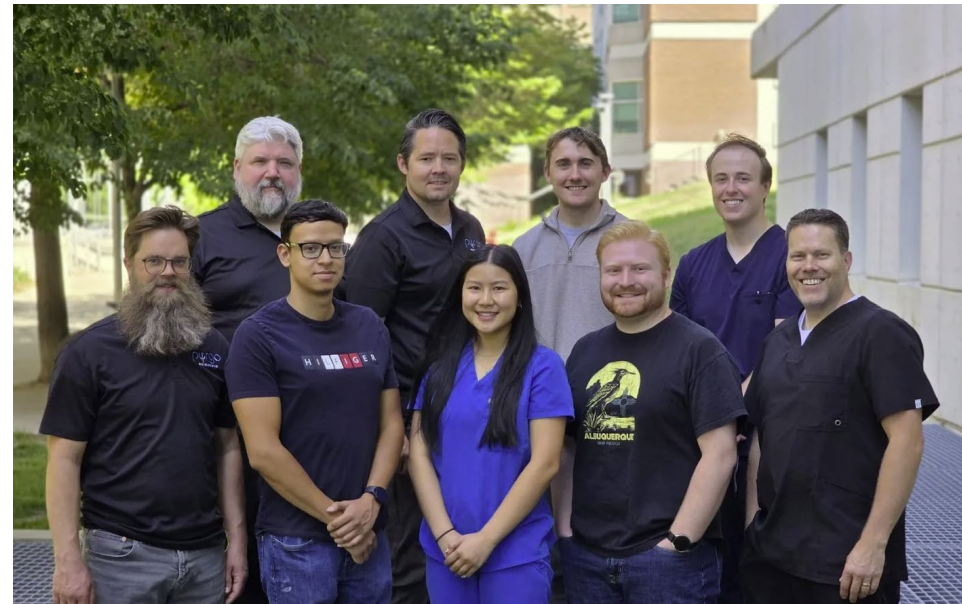




BONE & BIOFILM
RESEARCH
LABORATORY



ACKNOWLEDGMENTS



THANK YOU

