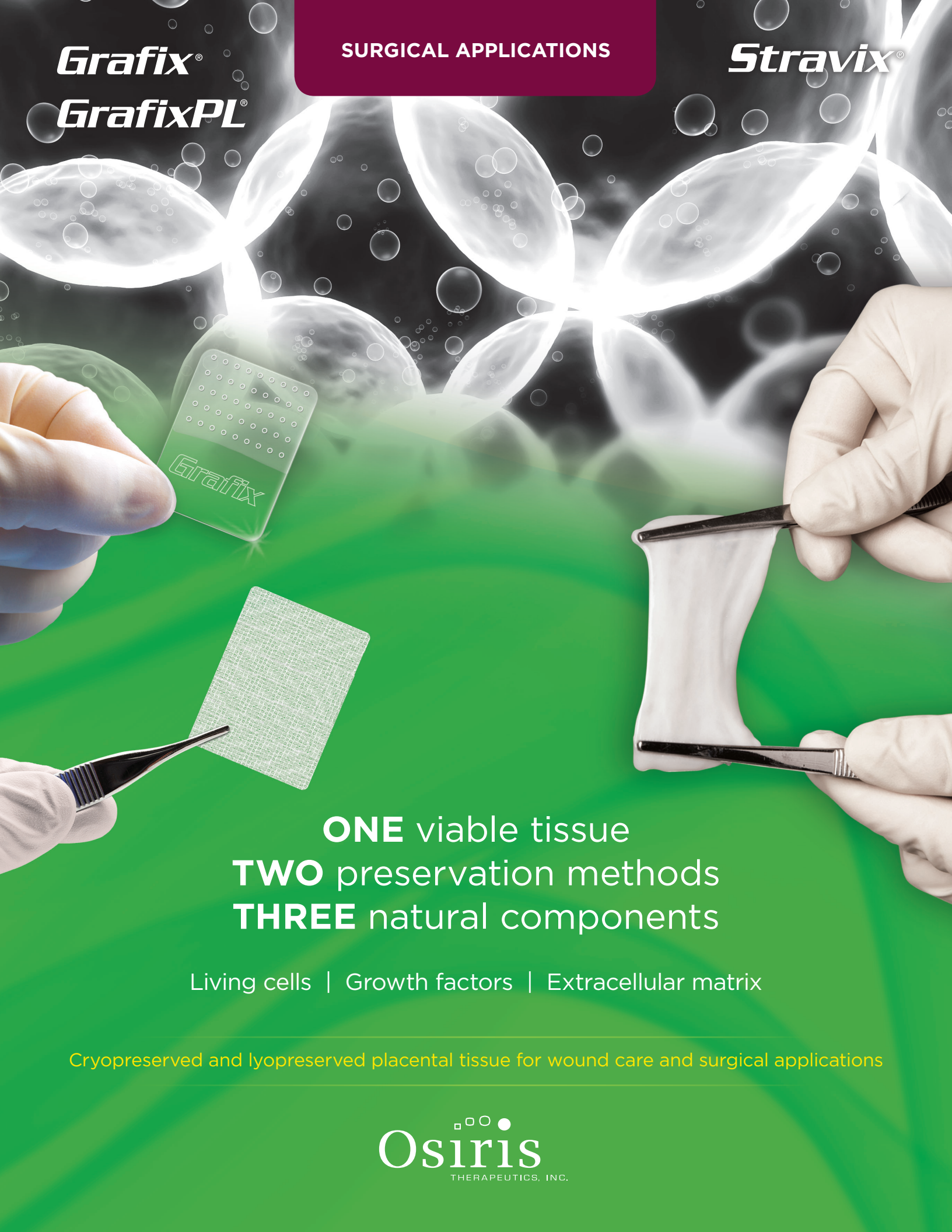


Grafix®
GrafixPL®

SURGICAL APPLICATIONS

Stravix®



ONE viable tissue
TWO preservation methods
THREE natural components

Living cells | Growth factors | Extracellular matrix

Cryopreserved and lyopreserved placental tissue for wound care and surgical applications


Osiris
THERAPEUTICS, INC.

CHALLENGES OF COMPROMISED SURGICAL SITES

PATIENT FACTORS THAT CAN IMPACT HEALING¹⁻¹⁰

- Advanced age
- Diabetes
- Obesity
- Smoking
- Prior irradiation or chemotherapy
- Immunosuppression, steroids, or bisphosphonates
- Prior infection or surgery

Surgery for these patients often leads to longer length of stay (LOS), more post-surgical complications, higher readmission rates, and increased costs.¹⁻¹⁰



Image provided by Jenna J. Brimmer, M.D.
Creedon Advanced Wound Center, Alameda, CA

Image provided by Christopher Dress, M.D., F.A.C.S.
Fort Walton Beach Plastic Surgeon, Fort Walton Beach, FL

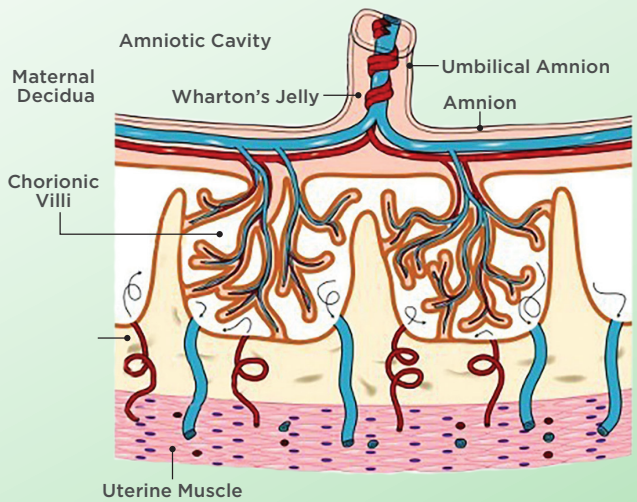
- 4X** higher flap failure rate for patients with prior irradiation undergoing breast reconstructions⁴
- 2X** higher rate of lower-limb vascular graft site infection for obese patients (BMI > 30)⁵
- 2X** higher rate of surgical site infection (SSI) following total joint replacement for comorbid patients⁶
- 2X** greater chance of urethral stricture recurrence for smokers and patients with prior urethral procedures⁷
- 3X** higher rate of fistula formation for patients with prior chemotherapy or radiation⁸
- 5X** higher rate of SSI within tumor field for high-risk cases⁹
- 7X** higher rate of SSI for open abdominal procedures in high-risk patients¹⁰

INHERENT PROPERTIES OF VIABLE PLACENTAL TISSUES

PLACENTAL TISSUES HAVE BEEN SHOWN TO SUPPORT NATURAL HEALING IN THE FOLLOWING WAYS:¹¹⁻¹³

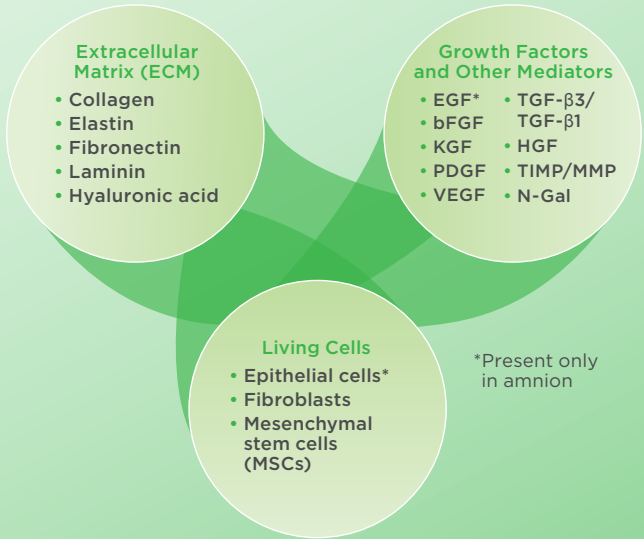
- Serve as a protective barrier and a reservoir for growth factors
- Reduce inflammation
- Promote new blood vessel formation
- Reduce scarring by supporting wound closure without excessive fibrosis
- Inhibit bacterial growth

PLACENTAL TISSUE ANATOMY

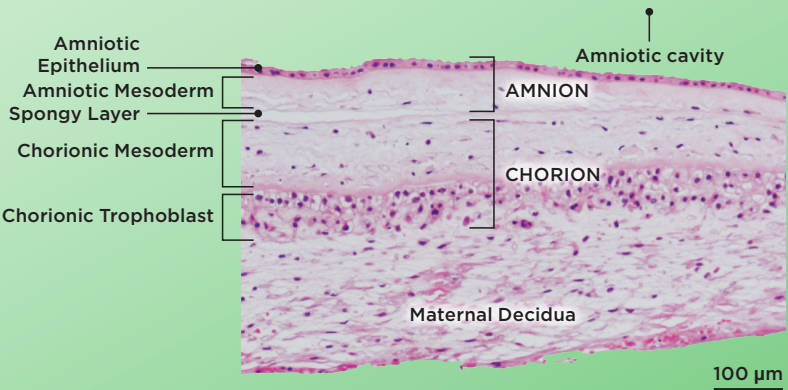


COMPONENTS OF PLACENTAL TISSUE

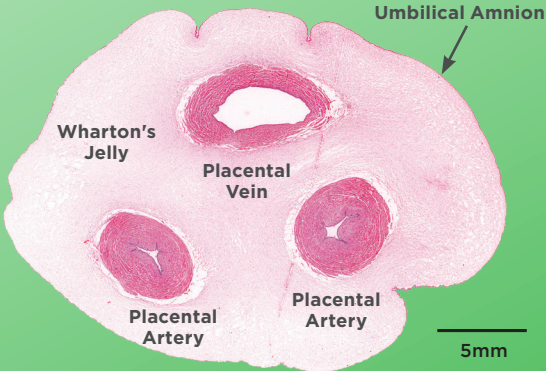
(Within Amnion, Chorion, & Wharton's Jelly)



CROSS-SECTION SHOWING AMNION AND CHORION PLACENTAL MEMBRANES (H&E STAIN)



CROSS-SECTION OF AN UMBILICAL CORD (H&E STAIN)

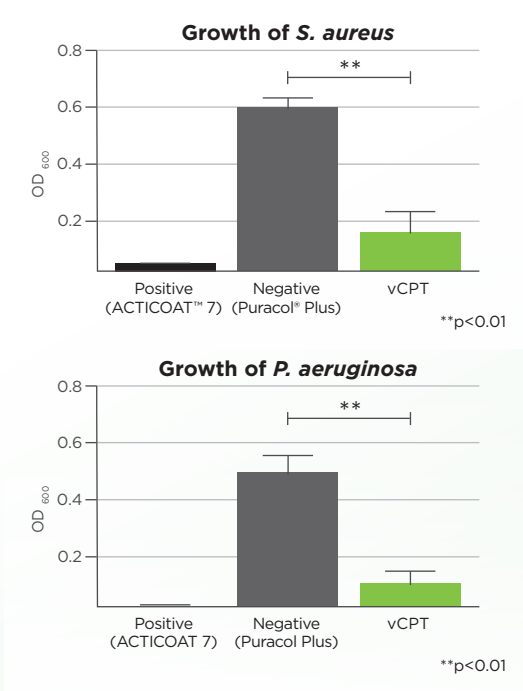


SCIENTIFIC CHARACTERIZATION OF VIABLE CRYOPRESERVED PLACENTAL TISSUE (vCPT)

vCPT RETAINS INHERENT ANTIMICROBIAL PROPERTIES†

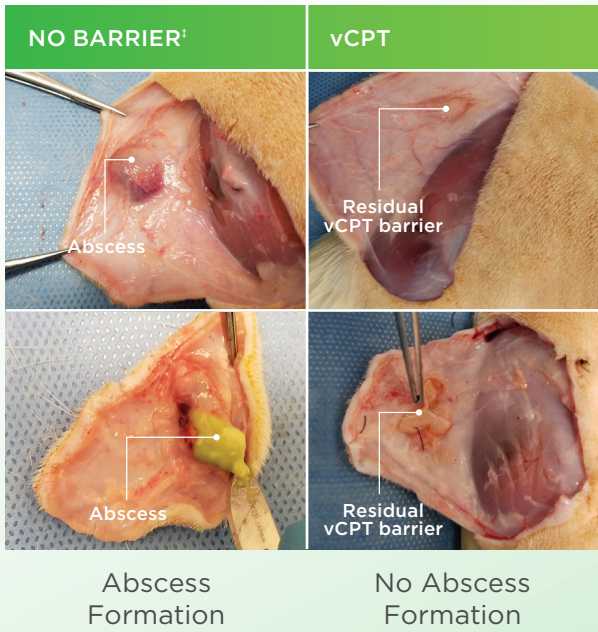
IN VITRO ACTIVITY¹⁴

Viability cryopreserved placental tissues inhibit the growth of common wound-related bacteria.



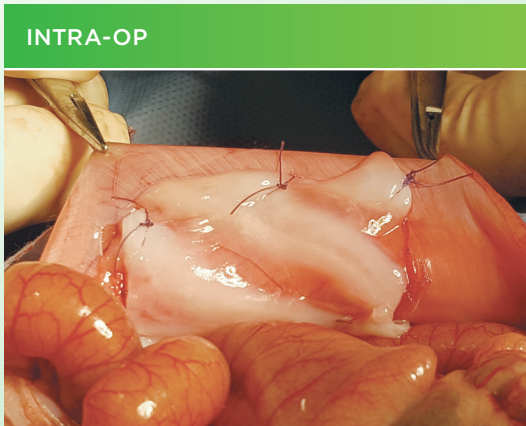
IN VIVO ABSCESS MODEL AT WEEK 4†

Rats received an injection with a known dose of bacteria.



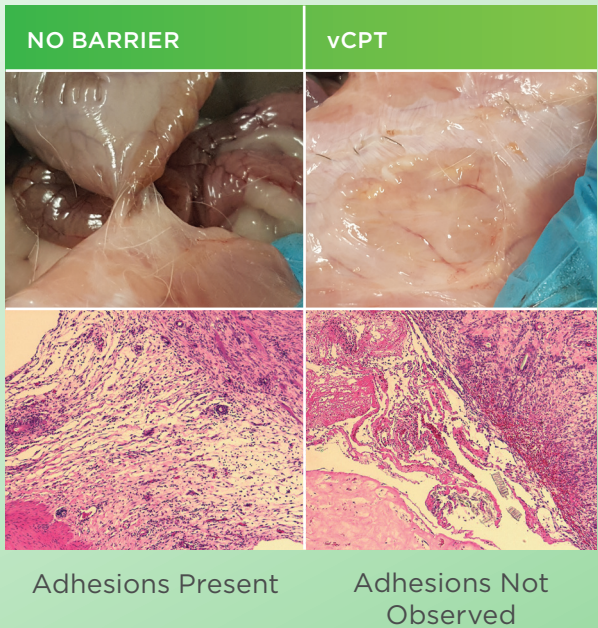
vCPT RETAINS INHERENT ANTI-ADHESION PROPERTIES IN VIVO¹⁵

vCPT was sutured to the abdominal wall in rabbits to assess adhesion formation over 10 weeks.



Gross Appearance at Day 67

Hematoxylin and Eosin Staining



STRAVIX: PLACENTAL TISSUE FOR COMPROMISED SURGICAL SITES

Stravix®
Cryopreserved Placental Tissue

- Cryopreserved umbilical amnion and Wharton's jelly from the human umbilical cord
- Blood vessels removed to prevent immune response
- Can be used as a wound cover or surgical wrap



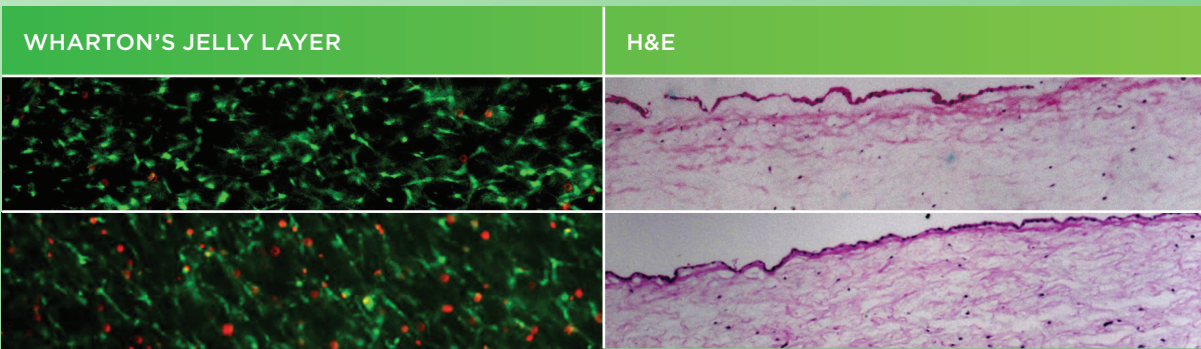
NATIVE COMPONENTS ARE PRESERVED^{15†}

	Fresh Placental Tissue	Stravix		Fresh Placental Tissue	Stravix
Epithelial cells	●	●	IL-10	●	●
Fibroblasts	●	●	IL-1RA	●	●
Mesenchymal Stem Cells	●	●	TIMPs	●	●
Hyaluronic Acid	●	●	TGF-β3	●	●
Collagen	●	●	HGF	●	●
bFGF	●	●	N-Gal	●	●
VEGF	●	●	LL-37	●	●
PDGF	●	●	RNase 7	●	●
EGF	●	●	Defensins	●	●
SDF-1	●	●	Elafin	●	●

ENDOGENOUS CELLS REMAIN VIABLE^{15†} 3-D MATRIX REMAINS INTACT^{15†}

Fresh Umbilical Tissue, Prior to Processing

Stravix, Post-Thaw



EASILY MANIPULATED AND SUTURED FOR USE IN CONVENTIONAL OR LAPAROSCOPIC SURGICAL SETTINGS

Durable	1 mm to 3 mm thick
Strong	10x tensile strength compared to amnion alone†
Barrier	Intimately adapts to injured tissue to form adhesion barrier

[†]Data on file at Osiris.

[‡]Control animals received an injection with a known dose of bacteria, but no vCPT was applied.

[†]Data on file at Osiris.

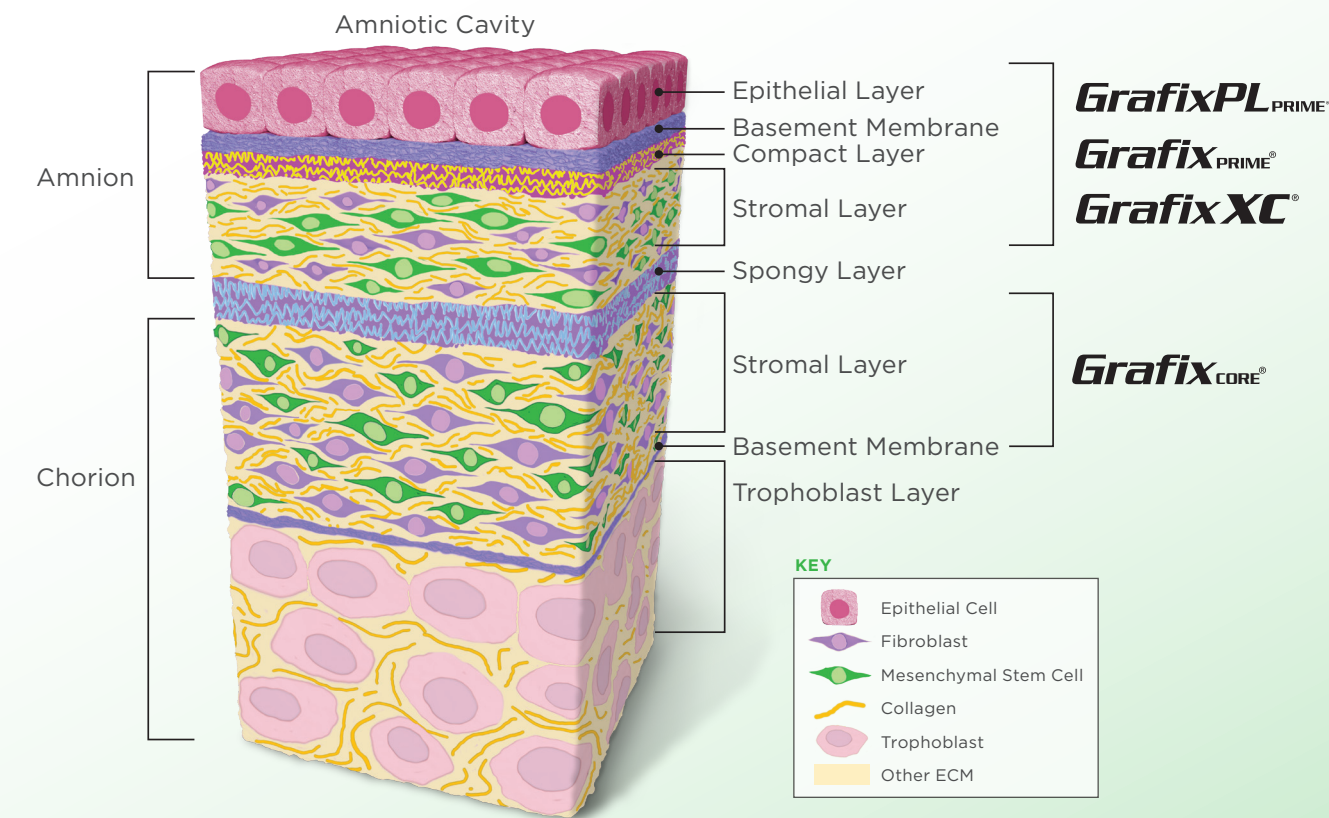
GRAFIX AND GRAFIXPL: PLACENTAL MEMBRANES FOR COMPROMISED SURGICAL SITES

ENGINEERED BY NATURE, OPTIMALLY PRESERVED BY OSIRIS, AVAILABLE ON DEMAND



- Cryopreserved and lyopreserved placental membranes derived from the amnion or chorion placental membranes
- Trophoblast layer and maternal components removed to prevent an immune response
- Can be used as a wound cover or surgical wrap

CROSS-SECTION OF THE PLACENTAL MEMBRANES



NATIVE GROWTH FACTORS ARE RETAINED¹⁶

	Fresh Placental Amniotic Membrane	Grafix PRIME, Post-Thaw	GrafixPL PRIME, Post-Rehydration
IL-10	•	•	•
IL-1RA	•	•	•
PDGF-BB	•	•	•
FGF-B	•	•	•
SDF-1α	•	•	•
Angiopoietin-1	•	•	•

ENDOGENOUS CELLS REMAIN VIABLE¹⁶

3-D MATRIX REMAINS INTACT¹⁶

	EPITHELIAL LAYER	STROMAL LAYER	H&E
Fresh Amnion, Prior to Processing			
Grafix, Post-Thaw			
GrafixPL, Post-Rehydration			

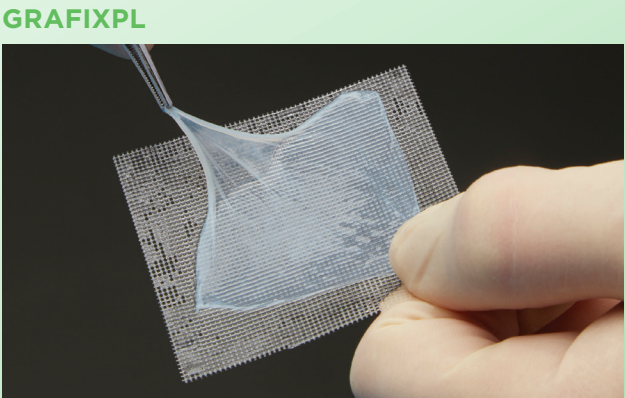
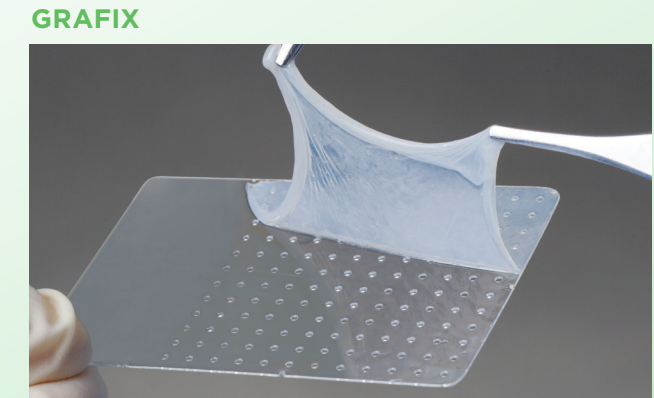
LIVE AND DEAD CELL STAINING

The presence of viable cells in Grafix and GrafixPL was independently confirmed by researchers at Rutgers University, Montana State University, and the University of Texas Southwestern.[†]

EASILY APPLIED IN OPEN SURGICAL PROCEDURES WHERE EXCESS BULK IS NOT WARRANTED

Low Profile	Average 110 μm ¹⁷
Conforming	Precisely contours to any wound or flap [†]
Versatile	Bury under incision lines or cover larger areas

[†]Data on file at Osiris.

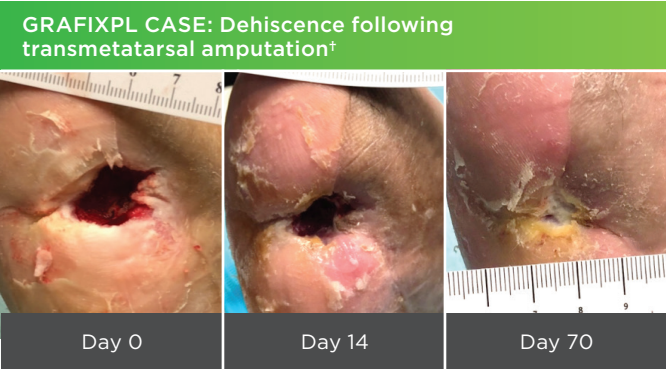


CLINICAL RESULTS WITH GRAFIX, GRAFIXPL, AND STRAVIX

CLOSURE OF DEHISCENCE WOUNDS FOR HIGH-RISK PATIENTS



Images provided by Brad Bailey, M.D.
Palomar Pomerado Wound Care Center, San Diego, CA



Images provided by Charles Ananian, D.P.M.
New Hope Podiatry Group, Los Angeles, CA

LIMB SALVAGE FOR HIGH-RISK EXTREMITY WOUNDS

In a prospective, open-label study of complex wounds in high-risk patients (n=27), 96.3% of wounds achieved 100% granulation and 59.3% of wounds achieved complete closure in 16 weeks when Grafix was applied weekly in addition to standard of care.¹⁸ In a retrospective study of Stravix in the surgical management of large defects in patients (n=10) with gas gangrene, all patients achieved complete closure in 13.4 weeks (mean) with one application of Stravix.¹⁹ The mean length of hospital stay was 9 days compared to 31.1 days on average in a database review of 11,666 patients with gas gangrene of the foot.^{19,20}



Images provided by Robert G. Frykberg, D.P.M., M.P.H.
Phoenix Veterans Affairs Health Care System, Phoenix, AZ



Images provided by Kristen McGinness, D.P.M.
Northeast Medical Group Bridgeport Podiatry Center, Bridgeport, CT

CLOSURE OF FISTULAE²¹

In a retrospective case series (n=2), a single application of Grafix, in conjunction with standard of care, was used to cover two chronic low-output enterocutaneous fistulae. On day 3 post-op, both fistulae had closed and both patients returned to clear liquid diets. Both fistulae remained closed at 2 months follow-up.

†Data on file at Osiris.

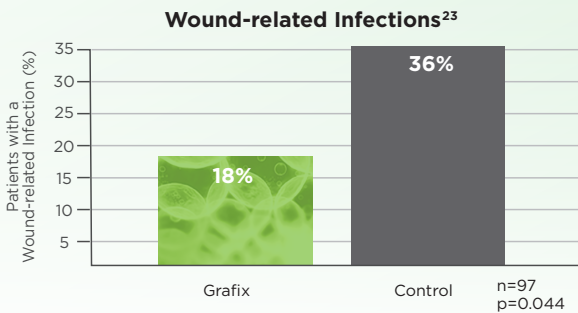
ADJUNCTS TO NERVE REPAIR²²

In a retrospective case series (n=7), Grafix was used to wrap nerve repair sites following nerve decompression and neurolysis revision. A collagen nerve conduit was then wrapped around the nerve over the Grafix. At 7 months follow-up, all patients demonstrated improved nerve conduction velocities, and 5 of 7 achieved full recovery of motor function (MRC grade 5/5).

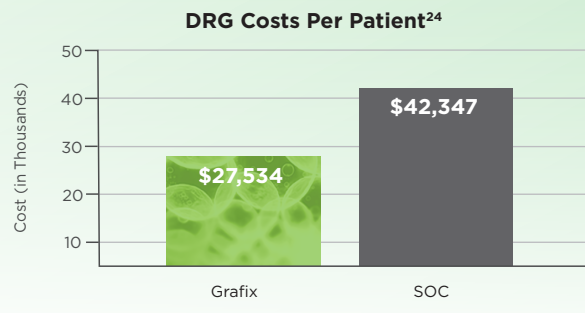
SIGNIFICANTLY FEWER INFECTIONS, FEWER COMPLICATIONS, AND LOWER COSTS

IN A RANDOMIZED, CONTROLLED TRIAL, MANAGEMENT OF WOUNDS WITH GRAFIX LED TO:^{23,24}

- **50%** drop in wound-related infections compared to standard of care
- An average of **35%** reduction (\$14,813) in diagnosis-related group (DRG) costs per patient



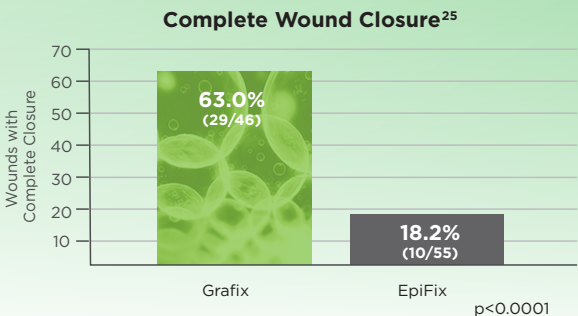
Infection rate with Grafix was significantly lower



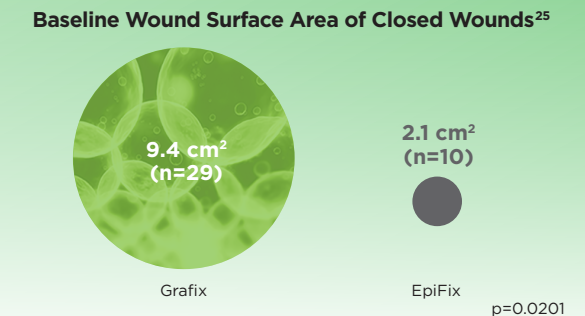
35% reduction in DRG costs

GRAFIX DEMONSTRATED SUPERIOR CLINICAL OUTCOMES VERSUS EPIFIX

In an investigator-initiated, retrospective, single-center study, 79 patients and 101 wounds were treated with Grafix, an intact cryopreserved placental membrane, or EpiFix, a dehydrated human amnion/chorion membrane, in conjunction with comprehensive wound care protocols.²⁵ In this study, the average patient age was 66.7 years, and each patient had 3.8 comorbidities on average.



Closure rate with Grafix was significantly higher



Wounds closed with Grafix were 4x larger

The odds ratio for complete closure for a Grafix-managed wound compared with EpiFix was 7.50 (95% CI 2.84 – 21.30).

CASE EXAMPLES

IMMINENT HARDWARE EXPOSURE

PATIENT INFORMATION

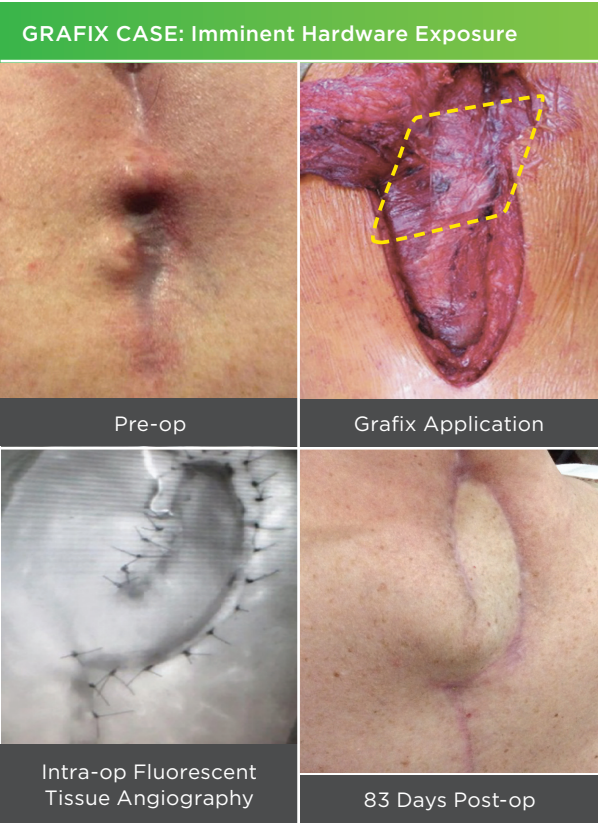
A 56 year-old female presented with hardware nearly exposed from a prior posterior cervical fixation, required after an initial anterior cervical discectomy with esophageal perforation. The patient had a medical history of hypertension, hypothyroidism, degenerative joint disease, rheumatoid arthritis, and migraines, and past surgical history including thyroidectomy with recurrent laryngeal nerve injuries.

PROCEDURE

All hardware was surgically removed and a rotational trapezius flap was performed. Graftix CORE 5 cm x 5 cm was laid over the hardware removal site prior to flap closure.

OUTCOME

The flap site remained closed with no sign of surgical infection or dehiscence.



Images provided by Christopher Dress, M.D., F.A.C.S., Fort Walton Beach Plastic Surgeon, Fort Walton Beach, FL

HIDRADENITIS SUPPURATIVA

PATIENT INFORMATION

A 38-year-old female with a 10 year history of bilateral axillary hidradenitis suppurativa who had undergone incision and drainage in both axillae 1 month prior still had pain and drainage of malodorous fluid. The right side was more symptomatic, so the decision was made to treat it surgically.

PROCEDURE

The right axillary skin was excised resulting in an 8 cm x 14 cm wound that was partially closed with sutures. The remaining 8 cm x 3 cm wound that could not be closed with sutures was covered with Stravix. Xeroform gauze and dry sterile gauze were placed over Stravix. The patient changed the dry sterile gauze every day and Xeroform gauze 2 times a week, starting 3 days post-op. The patient was on antibiotics (PO Bactrim) for 2 weeks prior to and for 1 month after the procedure for hidradenitis suppression.

OUTCOME

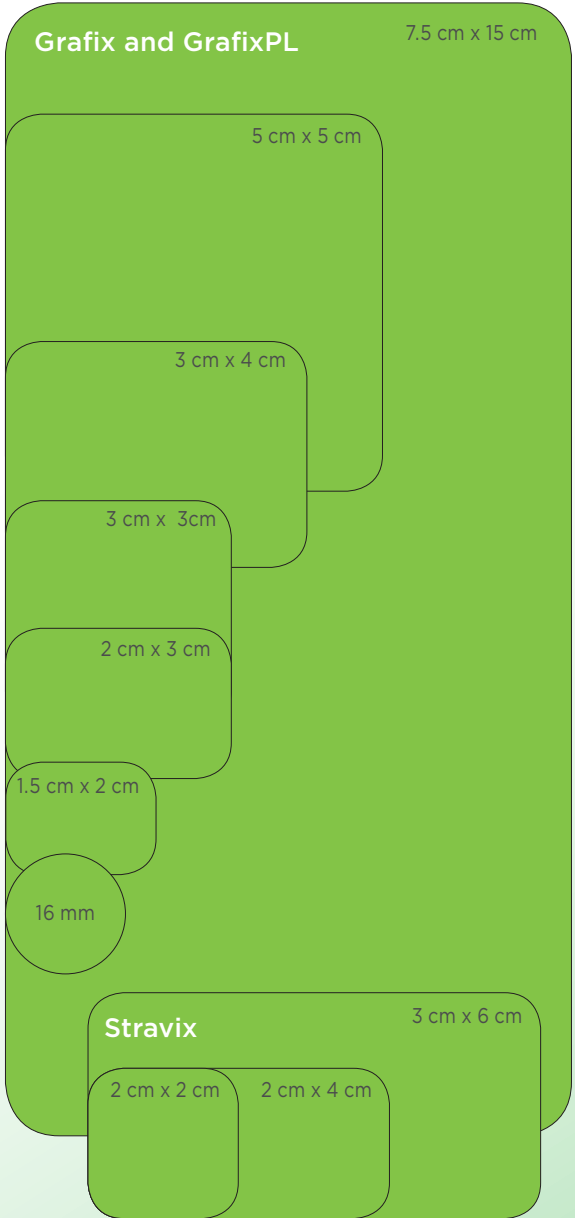
The wound completely closed by 6.5 weeks post-op. There was significant improvement in the cosmetic appearance and complete resolution of pain, drainage, and intermittent fevers.



Images provided by Kelly Harris, M.D., The Jackson Clinic, Jackson, TN

GRAFIX, GRAFIXPL, AND STRAVIX

Multiple Sizes for Optimal Coverage as Wound Covers, Barriers, or Wraps



Actual sizes shown

PLACENTAL TISSUE SOURCE	PRODUCT DESCRIPTION	PART #
Cryopreserved Amniotic Membrane	Graftix PRIME 16 mm Disc (2 cm²)	PS60013
	Graftix PRIME 1.5 cm x 2 cm (3 cm²)	PS11015
	Graftix PRIME 2 cm x 3 cm (6 cm²)	PS11023
	Graftix PRIME 3 cm x 4 cm (12 cm²)	PS11034
	Graftix PRIME 5 cm x 5 cm (25 cm²)	PS11055
	Graftix XC 7.5 cm x 15 cm (113 cm²)	PS24075
Lyopreserved Amniotic Membrane	GraftixPL PRIME 16 mm Disc (2 cm²)	PS13016
	GraftixPL PRIME 1.5 cm x 2 cm (3 cm²)	PS13015
	GraftixPL PRIME 2 cm x 3 cm (6 cm²)	PS13023
	GraftixPL PRIME 3 cm x 3 cm (9 cm²)	PS13033
	GraftixPL PRIME 3 cm x 4 cm (12 cm²)	PS13034
	GraftixPL PRIME 5 cm x 5 cm (25 cm²)	PS13055
Cryopreserved Chorionic Membrane	Graftix CORE 3 cm x 4 cm (12 cm²)	PS12034
	Graftix CORE 5 cm x 5 cm (25 cm²)	PS12055
Cryopreserved Umbilical Amnion and Wharton's Jelly	Stravix 2 cm x 2 cm (4 cm²)	PS60006
	Stravix 2 cm x 4 cm (8 cm²)	PS60005
	Stravix 3 cm x 6 cm (18 cm²)	PS60008

REFERENCES: **1.** Woo KY, Support Surfaces for Skin Grafts and Flaps: A Scoping Review. *Woundsourc* (White Paper) 2014. **2.** Inui T, Bandyk DF. Vascular surgical site infection: risk factors and preventive measures. *Semin Vasc Surg.* 2015; 28(3-4): 201-7. **3.** Ahmad G, O'Flynn H, Hindocha A, et al. Barrier agents for adhesion prevention after gynaecological surgery. *Cochrane Database Syst Rev.* 2015; (4): CD000475. **4.** Krueger EA, Wilkins EG, Strawderman M, et al. Complications and patient satisfaction following expander/implant breast reconstruction with and without radiotherapy. *Int J Radiat Oncol Biol Phys.* 2001; 49(3): 713-21. **5.** Giles KA, Hamdan AD, Pomposelli FB, et al. Body mass index: surgical site infections and mortality after lower extremity bypass from the National Surgical Quality Improvement Program 2005-2007. *Ann Vasc Surg.* 2010; 24(1): 48-56. **6.** Rasouli MR, Restrepo C, Maltenfort MG, et al. Risk factors for surgical site infection following total joint arthroplasty. *J Bone Joint Surg Am.* 2014; 96(18): e158. **7.** Breyer BN, McAninch JW, Whitson JM, et al. Multivariate analysis of risk factors for long-term urethroplasty outcome. *J Urol.* 2010; 183(2): 613-7. **8.** Sayles M, Grant DG. Preventing pharyngo-cutaneous fistula in total laryngectomy: a systematic review and meta-analysis. *Laryngoscope.* 2014; 124(5): 1150-63. **9.** Korol E, Johnston K, Waser N, et al. A systematic review of risk factors associated with surgical site infections among surgical patients. *PLoS One.* 2013; 8(12): e83743. **10.** Pinkney TD, Calvert M, Bartlett DC, et al. Impact of wound edge protection devices on surgical site infection after laparotomy: multicentre randomised controlled trial (ROSSINI Trial). *BMJ.* 2013; 347: f4305. **11.** Niknejad H, Peirovi H, Jorjani M, et al. Properties of the amniotic membrane for potential use in tissue engineering. *Eur Cells Mater.* 2008; 15: 88-99. **12.** Mamede AC, Carvalho MJ, Abrantes AM, et al. Amniotic membrane: from structure and functions to clinical applications. *Cell Tissue Res.* 2012; 349(2): 447-458. **13.** Faulk WP, Matthews R, Stevens PJ, et al. Human amnion as an adjunct in wound healing. *Lancet.* 1980; 1(8179): 1156-8. **14.** Mao Y, Hoffman T, Johnson A, et al. Human cryopreserved viable amniotic membrane inhibits the growth of bacteria associated with chronic wounds. *J Diabetic Foot Complications.* 2016; 8(2): 23-30. **15.** Dhall S, Coksaygan T, Hoffman T, et al. Viable cryopreserved umbilical tissue (vCUT) reduces post-operative adhesions in a rabbit abdominal adhesion model. *Bioact Mater.* 2018; 4(1): 97-106. **16.** Dhall S, Sathyaamoorthy M, Kuang JQ, et al. Properties of viable lyopreserved amnion are equivalent to viable cryopreserved amnion with the convenience of ambient storage. *PLoS One.* 2018 Oct 2;13(10):e0204060. **17.** Brantley JN, Verla TD. Use of Placental Membranes for the Treatment of Chronic Diabetic Foot Ulcers. *Adv Wound Care (New Rochelle).* 2015 Sep 1;4(9):545-559. **18.** Frykberg RG, Gibbons GW, Walters JL, et al. A prospective, multicentre, open-label, single-arm clinical trial for treatment of chronic complex diabetic foot wounds with exposed tendon and/or bone: positive clinical outcomes of viable cryopreserved human placental membrane. *Int Wound J.* 2016; doi: 10.1111/iwj.12649. **19.** McGinness K, Kurtz Phelan DH. Use of Viable Cryopreserved Umbilical Tissue for Soft Tissue Defects in Patients With Gas Gangrene: A Case Series. *Wounds.* 2018; (4): 90-95. **20.** Fincke BG, Miller DR, Turpin R. A classification of diabetic foot infections using ICD-9-CM codes: application to a large computerized medical database. *BMC Health Serv Res.* 2010; 10: 192. **21.** Nichols F, Overly A. Novel approach for enterocutaneous fistula treatment with the use of viable cryopreserved placental membrane. *Case Rep in Surg.* 2016; 879691; 4. **22.** Rodriguez-Collazo E, Tamir Y. Open surgical implantation of a viable cryopreserved placental membrane after decompression and neurolysis of common peroneal nerve: a case series. *J Orthop Surg Res.* 2017; 12(1): 88. **23.** Lavery LA, Fulmer J, Shebetka KA, et al. The efficacy and safety of Graftix® for the treatment of chronic diabetic foot ulcers: results of a multi-centre, controlled, randomised, blinded, clinical trial. *Int Wound J.* 2014; 11(5): 554-560. **24.** Nuccio EJ, Lavery LA, Min SJ. Innovative Treatment of Chronic Diabetic Foot Ulcer in a Controlled Randomized Clinical Trial Produces Fewer Adverse Events, Faster Wound Closure, and Lower Costs. *Diabetes Manag.* 2016; 6(4): 76-81. **25.** Johnson E, Marshall J, Michael G. A comparative outcomes analysis evaluating clinical effectiveness in two different human placental membrane products for wound management. *Wound Repair Regen.* 2016; doi: 10.1111/wrr.12503.

VERSATILE LIVING TISSUES TO AUGMENT SURGICAL PROCEDURES ACROSS MULTIPLE SPECIALTIES, INCLUDING BUT NOT LIMITED TO:

GENERAL, VASCULAR, AND PLASTIC RECONSTRUCTIVE SURGERY

- Flap reconstructions
- Split- and full-thickness grafts
- Vascular bypass graft sites
- Pilonidal cyst removal
- Burns and radiation wounds
- Complex ventral hernia repairs
- Breast reconstructions
- Hidradenitis suppurativa excision

ORTHOPAEDICS AND SPORTS MEDICINE

- Total joint replacements and arthrofibroses
- Exposed hardware and removal of hardware
- Cervical and lumbar laminectomies
- Tendon and ligament repairs
- Nerve transpositions and decompressions

UROLOGY AND GYNECOLOGY

- Nerve-sparing robot-assisted prostatectomies
- Ureteral and urethral reconstructions
- Nephron-sparing partial nephrectomies
- Hysterectomies, endometrioses, and uterine fibroids

ORAL MAXILLOFACIAL SURGERY

- Osteoradionecrosis mucosal defects
- Mandible/maxilla reconstructions
- Sinus and soft palate reconstructions

EAR, NOSE, AND THROAT SURGERY

- Oral cutaneous and pharyngocutaneous fistulae
- Intranasal and septal repairs
- Free flaps of the face and scalp
- Parotidectomy

COLORECTAL SURGERY

- Colon anastomoses
- Rectovaginal and perianal fistulae

DERMATOLOGY

- Keloid removal
- Moh's surgery

FOOT & ANKLE SURGERY

- Limb salvage
- Tunneling/undermining wounds
- Tendon and ligament repairs
- Nerve wraps

Osiris Therapeutics, Inc. researches, develops, manufactures and commercializes regenerative medicine products intended to improve the health and lives of patients and lower overall healthcare costs.