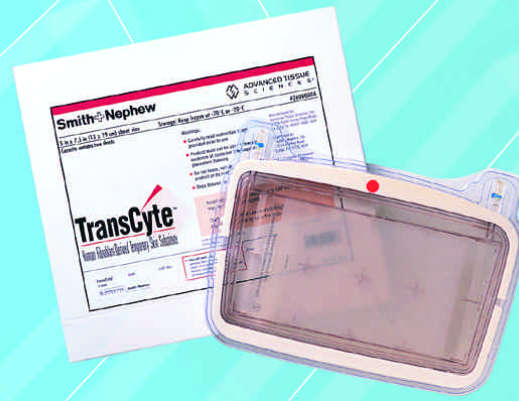


**Optimal viewing for this document is 125%  
(click on magnifying glass to zoom in)**



10933 NORTH TORREY PINES ROAD  
LA JOLLA, CA 92037-1005



What's Next?

Advanced Tissue Sciences is a leader in tissue engineering. The Company is using innovative core technology to develop a broad range of human-based products for the repair or replacement of damaged and destroyed tissue. The Company believes that its human-based tissue may offer significant advantages over alternative treatments, such as cadaveric or bovine-based products, for both the patient and the health care system. Research has clearly shown that human cells respond to their surrounding environment, and this response affects the proteins and growth factors they produce. A metabolically active tissue with a matrix produced by human cells more closely resembles the tissue it is designed to replace.

# Multiplying Our Products

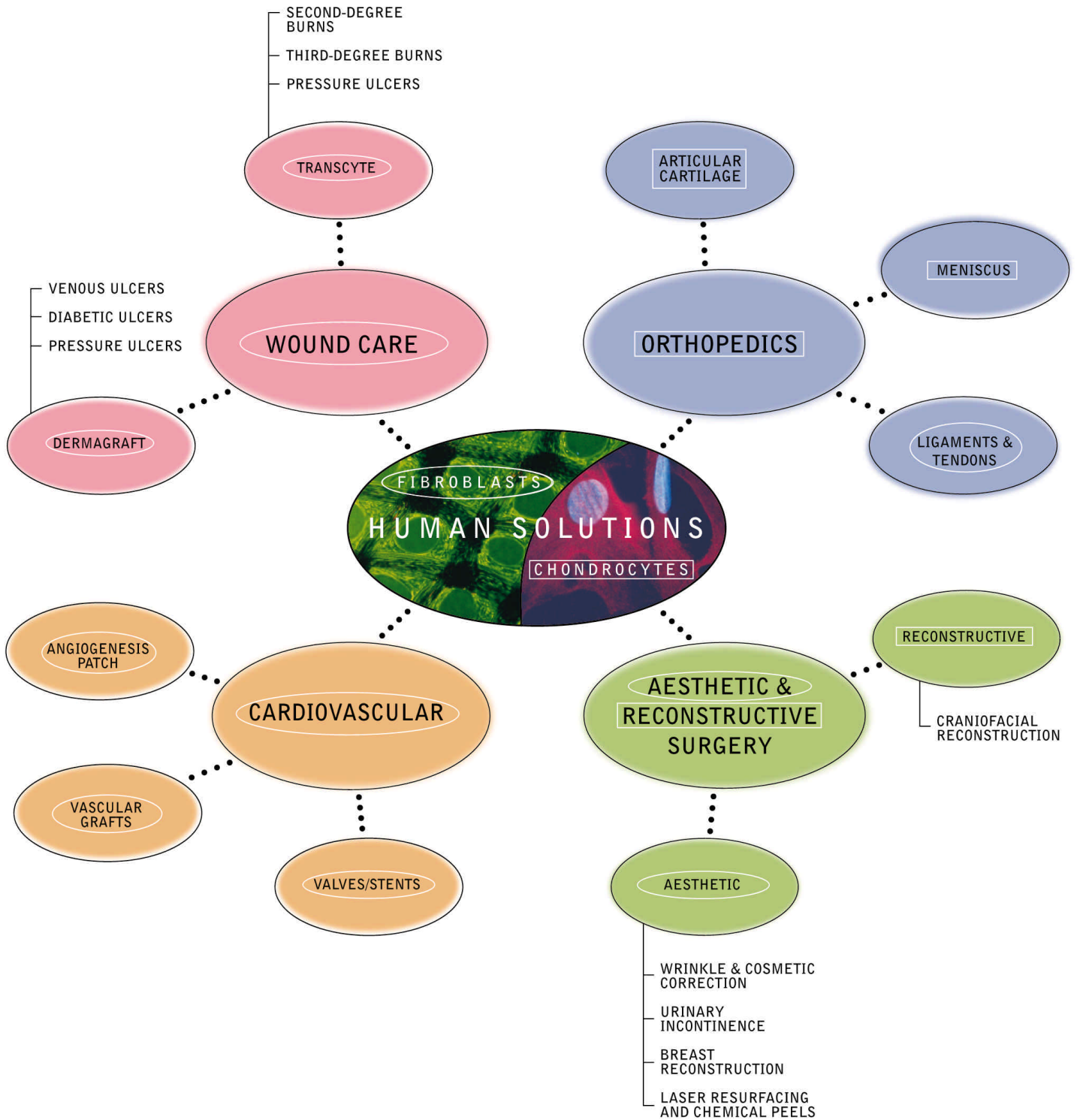
To date, Advanced Tissue Sciences has commercialized two products based on its proprietary tissue engineering technology — TransCyte™, a temporary wound covering for the treatment of burns, and Dermagraft®, a human dermal replacement designed as a treatment for skin ulcers.

Our business strategy is to efficiently and cost-effectively expand the number of potential products that can be derived from our core proprietary technology, and to fund

development of those products through strategic alliances and research grants. Currently, the Company is developing additional wound care products as well as products for orthopedic, cardiovascular, aesthetic and reconstructive applications.

Of the 200-plus cell types found in the human body, Advanced Tissue Sciences is presently focusing on developing multiple therapeutic products from two: fibroblasts (connective tissue cells) and chon-

drocytes (cartilage cells). We believe we can ultimately use many other human cell types with our tissue engineering technology to develop additional therapeutic products.



# LETTER TO OUR SHAREHOLDERS

## The Company's Value Creation Model

Spread the cost of developing and manufacturing products across a wide variety of indications and payers, while maximizing the adoption of the technology.

- Establish a "human-based" approach as the preferred choice among physicians and their patients.
- Multiply product extensions from individual cell types, (i.e., develop new products from the same cell type for new indications.)
- Use strategic partners to gain relevant technical expertise, market access and financial resources, and to achieve optimal product adoption.
- Accomplish cost-effective commercialization through high-volume manufacturing utilizing common processes, know-how and capital investments for multiple products derived from a common cell type.
- Develop products that can be used "off-the-shelf" and that can be thoroughly tested prior to distribution.

We are very pleased with the progress the Company has made over the past year. We have continued to generate additional clinical data on Dermagraft® to support our application for marketing approval by the U.S. Food and Drug Administration (FDA). We have also continued to expand the value of our proprietary core technology through the development of new products and new indications.

With TransCyte™ being marketed in the U.S. and several other countries for the treatment of burns, and with Dermagraft being marketed internationally for the treatment of diabetic foot ulcers, we are well-positioned to extend our technology to new wound care applications as well as to the orthopedic, cardiovascular, aesthetic and reconstructive markets. We are leveraging our technical expertise in tissue engineering and our operational capabilities to develop new products and indications in a cost-effective manner. To advance this process, we have also formed strategic alliances with partners who offer relevant technical expertise, established market access and greater financial resources.

## WOUND CARE PROGRAM

### *Dermagraft*

Dermagraft, a living, human dermal replacement, is designed to treat conditions where the skin has been injured or destroyed. In 1998, the FDA advised us that before it could approve our marketing application for Dermagraft in the treatment of diabetic foot ulcers, it would need confirmatory data from an additional controlled clinical trial. One of our top priorities throughout 1999 was to generate these additional clinical data. We conducted a planned interim analysis of the data at the end of the year. Although the study results did not achieve statistical significance, they showed that among all patients, Dermagraft was healing more ulcers at 12 weeks than the control treatment; and among patients whose diabetic foot ulcers had persisted for more than six weeks, Dermagraft was healing approximately twice as many ulcers at 12 weeks as the control treatment.

In early 2000, the FDA approved an amendment to the study plan for the ongoing clinical trial to revise the enrollment criteria and the statistical plan for data analysis. The amendment allows us to limit our future enrollment in this trial to patients with ulcers of greater than six weeks duration. In addition, the amended statistical plan allows us to integrate the data from the interim analysis with additional data generated since that time. If these additional data confirm the treatment benefit that was seen in the interim analysis for patients with ulcers lasting more than six weeks, we believe we could submit an amended application for marketing approval of Dermagraft to the FDA as early as mid-year.

Dermagraft is being marketed internationally for diabetic foot ulcers in the United Kingdom and several other European countries, and in Canada, Australia and New Zealand. Marketing activities are being carried out by our joint venture partner, Smith & Nephew plc—the leader in sales to the global wound management market.

We have enjoyed a long-term relationship with Smith & Nephew, establishing the Dermagraft Joint Venture in 1996 for diabetic foot ulcers, and expanding it in 1998 to include venous and pressure ulcers as well as the marketing of TransCyte. The joint venture was recently restructured, and it is our belief that the restructuring was in the best interest of both partners. We and Smith & Nephew are encouraged by the product's clinical performance, and we both remain committed to continuing the partnership and obtaining long-term shareholder value for our respective shareholders.

### *TransCyte*

TransCyte was the first human-based, fibroblast-derived temporary skin substitute to receive FDA approval. Approved for use as a temporary wound covering for second and third-degree burns, TransCyte has been shown by physician groups to reduce the length of hospital stay and decrease hospital costs when compared to the standard treatment for second-degree burns. Such cost savings—together with the reduced pain and faster return to normal activities reported by TransCyte patients—support our belief in the product's potential to improve the quality of life of many burn victims.

## AESTHETIC AND RECONSTRUCTIVE PROGRAM

Our alliance with Inamed Corporation, established in May 1999, is an excellent example of our strategy to maximize the value of our existing products and technology platform by adding new product indications. Inamed licensed rights to further develop, manufacture and sell certain fibroblast-based products for a wide range of indications. These applications include the correction of cosmetic problems (includ-

ing wrinkles), treatment of urinary incontinence, breast reconstruction following lumpectomy, and skin treatment following resurfacing procedures. Inamed also licensed rights to certain of our chondrocyte-based products for craniofacial reconstruction.

The cosmetic and incontinence products will be based on injectable human collagen, which is being derived from our proprietary tissue engineering technology. LaserDerm™, a product for treating the skin following chemical peels and laser resurfacing, represents a potential new application for our TransCyte technology. The work in both these areas demonstrates how we are developing new product applications from our existing technology using common cell sourcing and processes.

#### **ORTHOPEDIC PROGRAM**

Through our joint venture partnership with Smith & Nephew, we are developing NeoCyte™, a human, tissue-engineered cartilage for orthopedic applications such as the repair of articular cartilage and the repair or replacement of the meniscus in knee joints. Preclinical studies with NeoCyte in a small animal model have generated favorable results with respect to healing, scarring and integration of the tissue. Preclinical trials focusing on surgical technique and fixation in a large animal model are continuing. With successful preclinical trials, pilot clinical studies could begin in 2000, subject to FDA approval.

#### **CARDIOVASCULAR PROGRAM**

Our collaborative program with the University of California, San Diego, conducted under a multi-year \$2 million grant from the National Institute of Standards and Technology, made good progress in the development and evaluation of tissue-engineered vascular grafts. During 1999, we reported positive data from our work on tissue-engineered small-diameter blood vessels having certain functional properties similar to those of normal blood vessels.

In addition to our research on vascular grafts, we are also evaluating Dermagraft as a patch to be used to stimulate angiogenesis (formation and growth of new blood vessels) in the heart following coronary occlusion or ischemia (inadequate blood supply). Restoring blood flow is the most common method to relieve painful ischemic symptoms and to reduce the long-term risk of a heart attack. Data from preclinical studies presented in March 2000 demonstrated the ability of metabolically active Dermagraft to induce blood vessel formation and improve cardiac function. These data are consistent with results showing increased blood flow and blood vessel formation in diabetic ulcer patients, and indicate Dermagraft's potential as an angiogenesis-promoting product for multiple surgical applications, which could benefit tens of millions of patients.

#### **THE HUMAN ADVANTAGE**

Advanced Tissue Sciences is a tissue engineering company offering a human-based tissue, and we believe "human is better." In our proprietary systems, human cells are seeded onto a scaffold where they attach, divide and secrete human extracellular matrix proteins and growth factors. We believe that human-based products may better respond to their environment physiologically, and more closely resemble the tissue they are designed to replace, providing significant advantages to the patient.

#### **FOUNDATION FOR VALUE CREATION IN PLACE**

We have developed what we believe is a winning business strategy for creating shareholder value. In executing this strategy, we believe we have put in place the technological assets and core competencies necessary for us to succeed. In addition, our strong management team is continually managing the financial resources that will enable us to achieve our goals and provide a solid return to our shareholders.

On balance, we can say that 1999 was a year of considerable progress for our company. While we were faced with several challenges during the year, our people successfully addressed them and in the process strengthened the fundamentals of the Company. For the coming year, our goals include obtaining FDA approval and launching Dermagraft for diabetic foot ulcers in the U.S.; continuing the development of products through our alliance with Inamed; advancing our development programs on cartilage and an angiogenesis patch for the heart; and establishing a partnership for our cardiovascular program.

We are very proud of our people, their accomplishments and their commitment to our mission. With so many opportunities ahead for our technology, and with a staff as talented and committed as ours, we remain strongly optimistic about the future.

Sincerely yours,



ARTHUR J. BENVENUTO  
Chairman & Chief Executive Officer

GAIL K. NAUGHTON, PH.D.  
President & Chief Operating Officer

## Wound Care

Through its Dermagraft Joint Venture with **Smith+Nephew** Advanced Tissue Sciences is commercializing human-based tissue products for the treatment of burns and skin ulcers. Each year in the U.S., 30,000 to 40,000 patients suffer from second-degree burns. Another 13,000 patients suffer from third-degree burns, 1,500 of whom require extensive skin grafts. In addition, each year there are 300,000 to 400,000 diabetic patients with difficult-to-heal foot ulcers, as well as another 700,000 patients with venous ulcers and 1.5 million with pressure ulcers.

### OUR WOUND CARE TEAM (left to right)

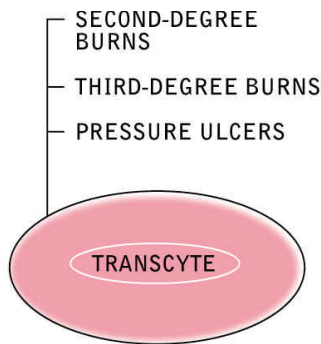
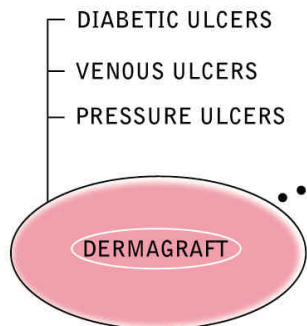
Rob Sorensen	Senior Director, Manufacturing Operations
Karen Garcia	Director, Sales Logistics, Dermagraft Joint Venture
Lynda Cazares	Quality Control Manager
Kathy McGee	Manufacturing Manager
Sharron Starkey	Director, Quality Assurance
Chito Hernandez, Ph.D.	Director, Biostatistics & Clinical Data





**Dermagraft®**

Dermagraft is a human, living dermal replacement designed for treating skin ulcers and other conditions where the skin has been injured or destroyed. As a living, metabolically active human tissue, Dermagraft is capable of interacting with the wound bed to promote healing. Dermagraft is currently being marketed by Smith & Nephew in several countries internationally for the treatment of diabetic foot ulcers, while it is in ongoing clinical trials in the U.S. for that indication. Dermagraft is also being studied in the treatment of venous and pressure ulcers.



**TransCyte™**

TransCyte is the first human-based, bioengineered temporary skin covering for the treatment of burns to be approved by the FDA. It is marketed in the U.S. and in certain countries internationally by Smith & Nephew. TransCyte consists of human dermal tissue (the lower layer of skin) combined with a synthetic epidermal layer (the upper layer of skin). This product is also being studied as a treatment for pressure ulcers.

## Orthopedic

Advanced Tissue Sciences is working with **Smith+Nephew** through their NeoCyte Joint Venture to develop human cartilage tissue derived from chondrocytes (cartilage cells.) The joint venture is initially focusing on developing cartilage products for the repair of damage in the knee, especially damage to articular cartilage. With 418,000 knee arthroscopies for articular cartilage performed in the U.S. each year, the clinical need is significant.

### OUR ORTHOPEDIC TEAM (left to right)

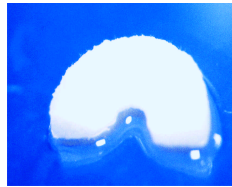
Mark Applegate, Ph.D	Director, Bioengineering
Twana Davisson	BioProcess Engineer II
Jerry Yaddgo	Project Engineer
Sharon Stevenson, D.V.M., Ph.D.	Executive Director, NeoCyte Joint Venture
Noushin Dunkelman	Associate Research Scientist





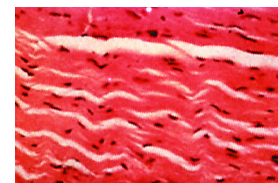
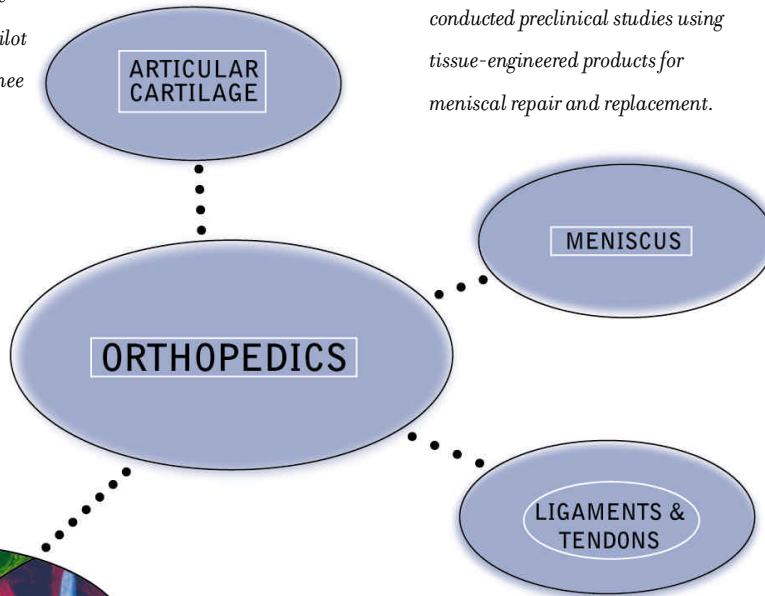
*Articular Cartilage*

*Articular cartilage covers the opposing surfaces of all moving joints in the body. Defects in the cartilage can cause pain and limit motion and can lead to longer term chronic conditions such as arthritis. Pilot clinical studies for articular knee cartilage could begin in 2000, subject to FDA approval.*



*Meniscus*

*The meniscus acts as a cushion or shock absorber in the knee. The meniscus is often damaged in sports injuries, and long-term repair is difficult to achieve. The Company has conducted preclinical studies using tissue-engineered products for meniscal repair and replacement.*



*Ligament and Tendon*

*Frequently, sports injuries involve damage to ligaments and tendons, particularly the anterior cruciate ligament in the leg. Degradable polymers shaped into tendon-like structures combined with fibroblasts have been used by Advanced Tissue Sciences to engineer a living ligament.*

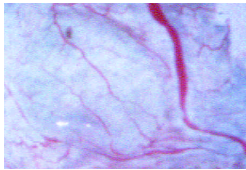
## Cardiovascular

Advanced Tissue Sciences is exploring a variety of tissue-engineered products including small-diameter vascular grafts, stents and heart valves. These applications could represent potentially significant market opportunities, since over 600,000 coronary artery bypass procedures, 695,000 stent procedures and more than 70,000 heart valve replacement procedures are performed in the U.S. each year. In addition, preclinical studies have shown that Dermagraft<sup>®</sup> has the potential to promote the development of new blood vessels, or angiogenesis, which is critical to the regeneration of damaged or diseased tissue in the heart.

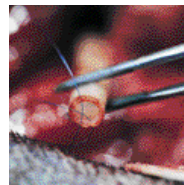
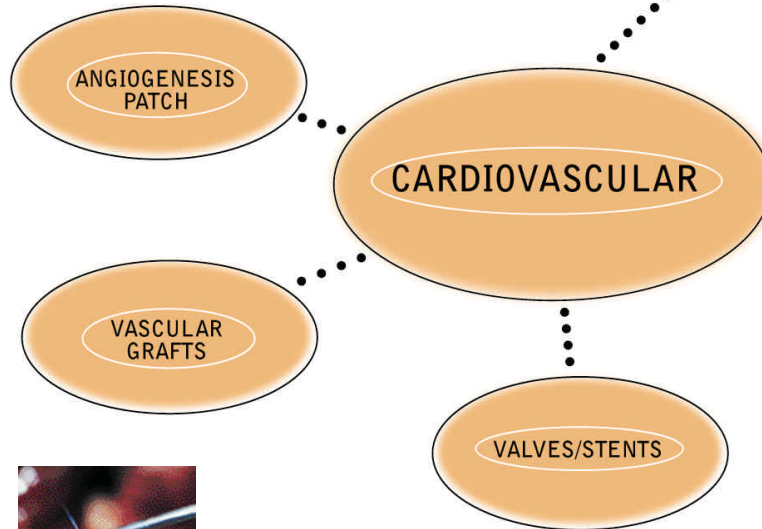
### OUR CARDIOVASCULAR TEAM (left to right)

Linette Edison	Director, Research Planning & Sponsored Research
Andreas Kern, Ph.D.	Senior Research Scientist
Lee Landeen	Research Scientist/Research Project Manager
Arnie Garcia	Associate Research Scientist
Jonathan Mansbridge, Ph.D.	Senior Principal Scientist



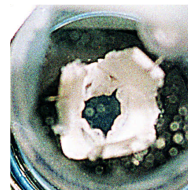


*Epicardial Angiogenesis Patch  
Dermagraft was used in preclinical studies to provide a sustained supply of angiogenic growth factors, including vascular endothelial growth factor (VEGF), to stimulate the formation and growth of new blood vessels following damage to the heart.*



*Peripheral and Coronary  
Vascular Grafts*

*There has been steady progress in Advanced Tissue Sciences' program to develop tissue-engineered blood vessels for small-diameter vascular grafts. The availability of tissue-engineered vascular grafts could be beneficial to bypass surgery patients, since no satisfactory alternative to the use of native blood vessels for vascular grafts currently exists.*



*Heart Valves*

*Advanced Tissue Sciences believes that the potential benefits of heart valves developed with its human-based tissue engineering technology may include increased durability, a reduced need for anticoagulant therapy and an ability to grow with the patient over time.*

*Stents*

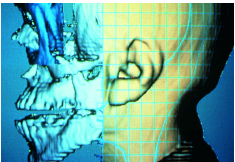
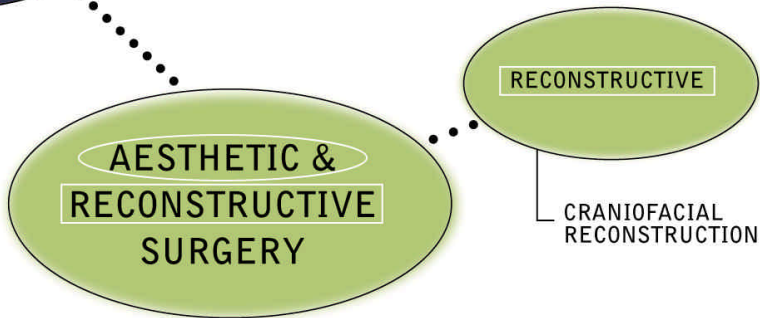
*Advanced Tissue Sciences envisions developing living, bioengineered stents and/or coating stents with human matrix to reduce restenosis, or recurrence of narrowing, in blood vessels opened by angioplasty.*

## Aesthetic & Reconstructive

Through our alliance with **INAMED**, Advanced Tissue Sciences is using its core technology to develop products for aesthetic and reconstructive surgery applications. This alliance is an excellent example of our strategy to maximize the value of our existing products by developing new products based on our TransCyte and human dermal tissue technology. Each year in the U.S., approximately 1.1 million skin-restoration procedures are performed using laser resurfacing or chemical peels. There are also approximately 250,000 collagen injection procedures for wrinkle and other cosmetic correction, and 80,000 incontinence treatments performed annually.

**OUR AESTHETIC & RECONSTRUCTIVE TEAM (left to right)**  
Frank Ziegler      Research Project Manager  
Dave Bagley      Senior Director, Manufacturing  
                                 Process & Support  
Mark Baumgartner      Senior Process Development  
                                 Engineer  
Stephen Kemmerrer      Engineering Manager  
Uyen Nguyen      Biochemical Engineer  
Chuck Bankert      Manager, Manufacturing  
                                 Engineering





CRANIOFACIAL RECONSTRUCTION

*Reconstructive Cartilage*  
 Tissue-engineered cartilage products in development could potentially be used in cosmetic surgery, in craniofacial reconstruction and for repair of the temporomandibular joint (in the lower jaw).



- WRINKLE & COSMETIC CORRECTION
- URINARY INCONTINENCE
- BREAST RECONSTRUCTION
- LASER RESURFACING AND CHEMICAL PEELS



*LaserDerm™*  
 LaserDerm, based on Advanced Tissue Sciences' TransCyte™ technology, is in clinical development as a temporary skin covering to promote healing, reduce pain and improve outcomes following laser resurfacing and chemical peel cosmetic procedures.



*Human Injectable Collagen*  
 Advanced Tissue Sciences' ability to create, from a single cell type, new products for new applications is demonstrated by its development of human collagen for cosmetic applications and for use as a bulking agent in urinary incontinence.

## Our Competitive Advantage

Our extensive patents serve to protect and support our efforts to develop human-based tissue-engineered products to improve the quality of patients' lives around the world. Advanced Tissue Sciences has established a broad intellectual property position consisting of more than 100 U.S. and foreign patents directly owned by or licensed to the Company. These patents strengthen our technological advantage and maintain our competitive position.



*Cryopreservation, prolonged shelf life.*



*Innovative manufacturing facility.*



*Automated, multiple unit production*



*High volume growth system.*



*Complete testing prior to release.*



*Proprietary bioreactor design – growth, shipping, storage.*





10933 NORTH TORREY PINES ROAD  
LA JOLLA, CA 92037-1005