E. R. ZUMWALT, JR.
ADMIRAL, U.S. NAVY (RET.)

June 28, 1999

Vice Admiral Richard A. Nelson
Surgeon General of the Navy

Washington, DC

Dear Dick:

I attach a letter from James Burns, Chief Executive Officer of Osiris Therapeutics, Inc., which I requested he write me after having followed his company for several years and because I am so impressed with his progress with DARPA.

I believe it is time for operational medicine to become aware of the dramatic opportunities that Osiris can bring to bear. I strongly recommend as one who remains deeply concerned about our capabilities that you take time from your busy calendar to meet and be briefed by him.

I have no financial relationship with this corporation.

Sincerely,

E. R. Zumwalt, Jr.
Admiral, USN (Ret.)

1000 Wilson Boulevard, Suite 3105
Arlington, VA 22209-3909

Tel: (703) 527-5380
Fax: (703) 528-5795

Enclosure

E. R. ZUMWALT, JR.
ADMIRAL, U.S. NAVY (RET.)

June 28, 1999

Lieutenant General Ronald R. Blanck
Surgeon General, U.S. Army

Falls Church, VA

Dear Ron:

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Enclosure

E. R. ZUMWALT, JR.
ADMIRAL, U.S. NAVY (RET.)

June 28, 1999

Lieutenant General Charles H. Roadman II
Air Force Surgeon General
Bolling AFB, DC

Dear General Roadman:

I attach a letter from James Burns, Chief Executive Officer of Osiris Therapeutics, Inc., which I requested he write me after having followed his company for several years and because I am so impressed with his progress with DARPA.

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Enclosure

OSIRIS THERAPEUTICS, INC.

Regenerative Tissue Therapy

June 17, 1999

E. R. Zumwalt, Jr.
Admiral, USN (Ret.)
1000 Wilson Boulevard
Suite 3105
Arlington, VA 22209

Dear Admiral Zumwalt:

As we discussed during our recent luncheon, Osiris has made substantial progress in developing cellular therapeutics for the regeneration and functional restoration of damaged or diseased tissue. The Company's technology is based on the use of adult stem cells, referred to as mesenchymal stem cells or MSCs, that are responsible for the normal replacement and regeneration of human connective tissues, including bone marrow stroma, bone, cartilage, muscle, tendon, ligament and fat.

Regenerative Medicine

Adult stem cells are maintained throughout life and form normal tissue through a process similar to prenatal tissue formation. Osiris has developed proprietary technology to isolate and greatly expand these human stem cells for the regeneration of tissues damaged through injury, aging or degenerative disease. Osiris is a pioneer in the development of this technology, owns the key patents, and is the first to commercialize products from adult stem cells for the emerging field of *Regenerative Medicine*™.

The implications of this technology are quite profound. For example, regenerating bone marrow stroma following cancer chemotherapy could decrease the length of hospital stays and improve patient tolerance to higher or more frequent doses of cancer chemotherapy. Regenerating bone in spinal fusion could eliminate the need for harvesting normal bone tissue from the patient or donors. Regenerating joint cartilage could postpone or obviate the need for joint replacements to treat osteoarthritis. Regenerating cardiac muscle could save the lives of many patients with congestive heart failure or following a heart attack. MSCs to regenerate bone, fat and muscle could be implanted during reconstructive surgery without the need for harvesting the patient's normal tissue. Muscle, fat and dermis could be regenerated simultaneously in deep tissue wounds.

Adult stem cells are responsible for the formation of tissues that comprise nearly 90% of the body's structure. The ability to regenerate damaged tissue directly will alter the face of medicine over the next 5-10 years. The emerging field of Regenerative Medicine™ will profoundly affect treatment of aging disorders and will improve the quality of life as a result.

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In April, a research team from Osiris reported results in the journal *Science* from studies that confirm the existence and capability of human adult stem cells to form structural and connective tissues. The Osiris team, led by Dr. Mark F. Pittenger, demonstrated that adult stem cells can undergo substantial expansion starting from a single stem cell, and that the resulting expanded cell population can be maintained as stem cells in culture or induced selectively to form bone, cartilage and fat. These findings confirm what developmental biologists have long maintained: that tissue regeneration recapitulates the normal pattern of development. Over 700 newspaper and magazine articles in the U.S. and Europe covered the story.

"Off-the-Shelf" Tissue Regeneration

The Company's strategy is to develop Regenerative Medicine™ human MSC (hMSC) products based on the use of universal donor (allogeneic) stem cells obtained from a single donor or from several donor pools. The goal is to regenerate damaged tissue on demand without the delays and cost required to process patient-derived (autologous) stem cells. If successful, allogeneic stem cell products would revolutionize the treatment of connective tissue disorders and bring Regenerative Medicine™ within the cost and margin structure of traditional pharmaceuticals. The Company has evidence from both *in vitro* and *in vivo* animal studies that this goal is feasible.

The Company's first donor-derived human MSC product is targeted to improving engraftment and reducing graft-versus-host disease (GVHD) in allogeneic bone marrow transplants. A Phase I safety and dose escalation trial has commenced for Allogen™, a donor-derived hMSC product being tested in leukemia and lymphoma patients. Human MSCs are isolated from a small sample of bone marrow obtained from a matched relative of the patient and expanded until the number of hMSCs has increased over 3000 fold. We anticipate that Allogen™ donor-derived hMSCs will enhance marrow engraftment and reduce GVHD following their infusion into the patient. MSCs also support blood cell formation in cancer and trauma situations. The Allogen™ clinical trial is being conducted in seven U.S. and European cancer centers. Further trials are being planned for bone, cartilage and tendon regeneration.

Implications for Armed Forces Medicine

MSCs can regenerate new tissue directly. When implanted in a critical size bone defect, MSCs will form bone. When implanted in an osteochondral defect, MSCs can regenerate both the articular joint cartilage and the subchondral bone. Local biochemical cues direct the adult stem cells to undergo programmed differentiation and regenerate the proper tissue. Furthermore, Osiris has shown that MSCs are not immunogenic and that donor MSCs will form the appropriate tissue without rejection.

We believe that the implications for off-the-shelf tissue regeneration in military applications are substantial. The ability to initiate tissue regeneration at the first medical intervention for tissue trauma using a common stem cell product means that: 1) fewer soldiers should sustain permanent or disabling injuries, 2) normal tissue function could be restored where current therapies fail, 3) accelerated healing could return wounded soldiers to active duty sooner, and 4) tissue regeneration should cut the cost of rehabilitation and long term nursing care.

We are well along in our efforts at proving efficacy in small and large animal models. We are accumulating patient safety data in our human clinical trials and we are well along in proving that our technology works for donor stem cell therapy. As you know, we are also working with DARPA to use MSCs as a platform for delivering multiple vaccines against lethal pathogens as part of the Unconventional Pathogen Countermeasures Program. We have already demonstrated feasibility in this program.

Linking Osiris Technology with DOD Need

Bud, our ability to regenerate damaged connective tissues has progressed to the point where our products should be of direct interest to the Surgeon General of each Service. The ability to regenerate tissue with stem cell products represents a major advance in trauma and rehabilitation medicine. We would like the opportunity to present our technology to the Department of Defense, with an eye toward developing products specifically for military application. Any help that you could provide in getting us in contact with the appropriate DOD groups would be most helpful. Thank you for your help and your continued interest in our Regenerative Medicine™ products.

Best regards.

Sincerely,

James S. Burns
President & Chief Executive Officer