World Sole Manufacturer Of Stem Cell Xenotransplants Chooses Malaysia As Its Global Hub

Bio-Cellular Research Organization LLC (BCRO), with the world's foremost research expertise on stem cell transplantation of almost 3 decades standing, is choosing to site its main manufacturing plant in Malaysia. This facility will produce various stem cells for transplantation to meet worldwide demand. BCRO Stem Cell Transplantation (BCRO SCT) Sdn. Bhd. has been registered for this purpose. Spearheading this team will be Dr. E. Michael Molnar one of the world's foremost experts on stem cell transplantation, both in clinical and manufacturing aspects of the project.

Headquatered in USA, BCRO is currently the largest manufacturer of stem cells in the world with its manufacturing plant sited in Slovakia, European Union (EU). BCRO is projecting an estimated investment of about USD 80 million (approximately RM 280 million) over a 3 year period through its Malaysian counterpart BCRO SCT Sdn. Bhd. in order to transfer its cutting edge technical know how by its scientists from USA & EU. BCRO is optimistic, hoping to gain strong support and easy passage to establish its manufacturing plant in Malaysia.

BCRO currently supplies stem cell transplants to trained doctors and hospitals in North and South America, Europe, Africa, Asia and Australia. Its treatment expertise has been extended by a total of about 200 patients in S.E Asia, Hong Kong and Australia, including about 100 cases in Malaysia alone over the last 2.5 years with best results seen among Down Syndrome and brain-injured children, and adult patients with neurodegenerative diseases and complications of diabetes mellitus.

BCRO recently cemented a collaborative project with the Chinese government via the Science and Technology Development and Exchange Centre to further clinical research and development (fully funded by the Chinese government) with some of China's top stem cells experts from Fudan University and Shanghai University Hospital.

Media coverage on stem cell treatment is healthy. But some significant confusion has emerged arising from less than succinct definition of claims made by proponents of cell therapy, cord blood stem cells, autologous stem cells, and bone marrow transplants, among others. None of these can come close to BCRO stem cell transplantation. Please, read 'Glossary of Terms' at the end of this announcement to elucidate the confusion about what is what.

BCRO stem cell transplantation has been carried out without any immunosuppression whatsoever(!) for 16 years, with a negligible pain, and rare local infection as the only side effect. This qualifies this method as a cutting edge technology for therapy of a whole variety of indications such as:-

(1) Diabetes Mellitus, types 1 and mixed 1/2, particularly when complications have already developed, such as:

- Diabetic Retinopathy
- Diabetic Nephropathy
- Diabetic Polyneuropathy
- Diabetic Lower Extremity Arterial Disease, as well as Brittle Diabetes Mellitus in children, and Diabetes Mellitus in pregnancy or diabetes mellitus as a cause of female infertility and habitual pregnancy loss.

(2) Other hormone deficiency disorders, where hormone replacement therapy could not re-establish a normal hormonal balance;

(3) Early menopause, and some other serious gynecological diseases, where state-of-art treatment has failed;

(4) Male and female infertility, where usual treatment has failed;

(5) Immune deficiency disorders, such as chronic weakness syndrome, AIDS, cancer, etc., as well as autoimmune illnesses;

(6) Aging disease, including menopause, im potence, depression, etc.

"**Aging** has no known treatment" has been a slogan perpetuated by drug regulatory agencies for decades. But 4 million (80%) out of 5 million patients treated by **stem cell therapy (SCT)** worldwide during the last 70 years have done so because they suffered from '**aging disease**'. Their decision was based on their instincts and intuition, and in total disregard of official statements about a lack of acceptable research protocols to prove the value of any therapy in slowing down the aging process. Because the issue has always been **'not to add years to life, but life to years'.** One cannot treat aging related diseases, or for that matter many diseases in an aging individual, without **anti-aging treatment.** There is hardly a 40+ years old individual in the civilized world that is perfectly healthy physically, mentally and spiritually, and thus does not require treatment of 'aging disease'.

(7) Spinal cord injury, old or recent, Parkinson's and other degenerative diseases of the central nervous system;

(8) Many genetic and chromosomal diseases of children, such as Down syndrome, as well as failure to thrive, mental retardation, frequent illnesses, etc., due to various prenatal, natal or postnatal causes have been treated by stem cell transplantation**(SCT)** in clinical practice for 70+ years. Standard medical textbooks state that genetic and chromosomal diseases have no known treatment, with rare exceptions. In reality there have been many publications from the university hospitals of Germany, France, U.S.S.R./ Russia, Spain, etc. that report on the success in the *treatment of many genetic and chromosomal diseases by stem cell transplantation*, so that **therapeutic nihilism is not justified whatsoever.**

There are ~2,000 genetic diseases, and many variants thereof, and only a few of them have any known treatment. Some of them have been treated with stem cell transplantation with success, but many others, particularly the rare ones, not yet, because no one has attempted to do it. Or at least no medical report has been written about it.

There is a clinical experience with stem cell transplantation in thousands of patients suffering also from variety of incurable pediatric diseases: mental retardation, cerebral palsy, cardiomyopathy, Gaucher's disease, Fanconi's syndrome, immune deficiencies, autoimmune diseases, hypothyroidism, certain muscular dystrophies, etc.

Since stem cell transplantation is indeed safe, safer than taking aspirin, there is no harm to try to use it to treat an infant with a newly diagnosed genetic disease. There are only two possible outcomes: either there will be an improvement, or there will be no change in the condition of patient. Unfortunately a **physician can learn about the benefit of stem cell transplantation for the treatment of that specific child with a rare genetic disease only by trial and error.** Animal experimentation is of no predictive value, and animal models of many diseases do not exist.

There is no harm in trying SCT in such case. If parents would make a decision to treat their child, then stem cell transplantation should be carried out without delay.

(9) Degenerative diseases of liver, gastrointestinal tract, cardiovascular system, and other organ systems have been treated with SCT with good results.There is clinical experience with stem cell transplantation in thousands of patients suffering from liver cirrhosis, chronic hepatitis, chronic pancreatitis, ulcerative colitis, Crohn's disease, etc.

C**irhosis of the liver** and **chronic hepatitis** have been treated by **stem cell transplantation (SCT)** with success for the last four decades. There are many German publications to confirm value of stem cell therapy in the treatment of incurable liver diseases. **Cirrhosis of liver and chronic hepatitis** were very common in Germany in 40 - 50 - 60 -ies. This was a result of severe epidemic of viral hepatitis in Germany during WW2 and thereafter. Since even

today there is no effective therapy for damaged liver, **stem cell therapy became a treatment of choice** for such serious liver diseases

The same applies to a congestive heart failure.

Besides the above groups of diseases physicians have utilized stem cell transplantation x as **treatment of many other ailments**, whenever they recognized that their patient needs a *direct stimulation of regeneration (i.e. repair)* of the damaged cells & tissues of various organs, or an *outright transplantation of fetal cells* to replace the dead or non-functioning cells.

BCRO has not discovered a procedure of (stem) cell transplantation, it found a method to prepare (stem) cell transplants of any of the ~200 kinds of cells for clinical use, that can be implanted with 'state-of-art' safety, and without immunosuppression.

The proof of effectiveness of stem cell transplantation is in medical references (including that of BCRO collaborators) of the past 15 years that can be easily found on PUBMED, a medical data base of MEDLINE, the U.S. National Library of Medicine, where more than 250,000 summaries about stem cell transplantation can be studied. This proves that the use of stem cell transplantation in clinical practice is not a rarity.

Stem cell transplantation was introduced into clinical practice in 1931 and has historically preceded organ transplantation by several decades. It will apparently dominate the medicine of 21st century. The main reasons for such statements are:

minor procedure for a patient, and for that reason it can be, and should be, used in the earlier stages of those diseases that current medicine cannot cure, or even treat. It means that there is no logical reason to wait until the end-stage, as is the case with organ transplantation.

2. One of the reasons why stem cell transplantation is such a simple procedure for a patient to go through is the principle of 'homing'.

'Homing' means that the respective stem cells do not have to be implanted into a damaged organ, (e.g. liver stem cells into liver), they can be implanted into more accessible superficial tissues, (e.g. under the aponeurosis of rectus abdominis muscle), because they will find their way into the damaged organ, as if 'attracted' by it. (Implanted stem cells are not attracted by healthy organ, tissue or cells.)

3. Every diseased organ can be treated by stem cell transplantation.

Transplanted cells bring back to life (or repair) those cells of such organ that actually have not died, just stopped functioning as a result of the disease, besides serving as a replacement for dead cells of a diseased organ. In other words, besides transplanting new stem cells there is another mechanism of action of stem cell transplantation: a 'direct stimulation of regeneration (or repair)', much more important for treatment of a disease than the replacement of dead cells.

4. If stem cells are properly prepared, such as by BCRO method, they can be implanted without immunosuppression, and thereby avoid all complications caused by such medications.

Manufacture Of BCRO Individually-For-Each-Patient Prepared Stem Cell Transplants

BCRO has always manufactured stem cell transplants from rabbit fetuses. Due to a panic about the 'Mad Cow Disease', we stress that according to the world's medical literature, no transmission of any viral disease has been known to occur from rabbit to man.

The natural barrier that has always existed in "Nature" has largely prevented a transmission of infections between species. The more distant the species are, the stronger this barrier has been; this is the case between rabbit and man.

Coming from a closed colony in existence for nearly 30 years, with documented lineages, having been bred and raised in captivity with a minimal exposure to vectors of infectious agents, the rabbit fetuses used by BCRO have been remarkably free of any disease. Besides that, rabbits are the sole laboratory animal in which no retroviruses have been identified yet.

BCRO method of manufacturing of **individually for each patient prepared stem cell transplants** incorporates all pertinent requirements of

PHS Guidelines on Infectious Disease Issues in Xenotransplantation" of January 19, 2001 (Federal Register, Volume 66, Number 19, pages 8120–1

that is the final version of the same regulation issued initially as a "Draft" on September 23, 1996 (available from Federal Register under 61FR49920).

On February 16, 2000, by its favorable ruling in the case of BvR 420/97, the German Supreme Court ('Bundesverfassungsgericht') re-affirmed that this type of treatment, **in medical practice in Germany since early 50-ies,** had continued to be permitted, whereby Germany had re-established its leadership in this field.

This decision of German Supreme Court, with a power of law, applies to all Member States of the European Union.

Legally it is related to *certain* chapters of the **2001/83/EC European Community Council Directive**, that in turn had become incorporated in national laws of all Member States of European Union, as mandated by Maastricht Treaty.

Our manufacture of stem cell transplants is in full compliance

- with the decision of the German Supreme Court in case of 1 BvR420/97,
- with EC Directives, as well as
- national laws of all Member States of European Union.

GLOSSARY of TERMS

STEM CELL is a cell from the embryo, fetus, or adult, that has the ability to reproduce itself for life or indefinitely. It can give rise to specialized cells that make up the tissues and organs of the body.

EMBRYONIC STEM CELL is derived from the blastocyst of an embryo, or from fetal tissue destined to become part of the gonads. In the laboratory, and only under such conditions(!), this type of stem cell can proliferate indefinitely. It is pluripotent, which means that it has an ability to give rise to all types of cells, which develop from any of the three germ layers, from which all the cells of the body arise. But with equal ease it can give rise to a cancer cell. It remains in such uncommitted state until it receives a signal to develop into one of ~200 known specialized cell types. When maintained as a cell line, embryonic stem cells change, lose their normal appearance. In cell lines, as a result of prolonged living in artificial conditions of cell culture, cells have abnormal number of chromosomes, double, triple, quadruple, and chromosomal structure is abnormal, as a result of which cells cannot be recognized as to their origin, as the histotypical differentiation lacks as well. In cell lines, sex chromatin disappears, the cell division runs without any control, as in cancer cells, cell membranes are defective. Cells from cell lines have lowered resistance against viral infections, a real problem of laboratory medicine.

For this reason the idea of manufacturing embryonic stem cells from cell lines in factories is beyond comprehension. No physician has ever used embryonic stem cells for transplantation as a therapy in 75 years long history of this medical field: why to use cells that clearly look abnormal, like cancer cells, and behave like cancer cells, and go against Hippocrates Oath: "Primum non nocere", i.e. "First of all, do not harm". Fear of oncogenicity has kept medical profession from transplantation of embryonic stem cells for 75 years.

FETAL STEM CELL is an undifferentiated cell that occurs within a differentiated tissue of the fetus, renews itself for the lifetime of the organism, and differentiates into all of the specialized cell types of the tissue from which it originated.x

PRECURSOR (PROGENITOR) STEM CELL occurs in fetal tissues, rarely in adult tissues, and is partially differentiated. It divides and gives rise to a specialized cell of the tissue to which it belongs(!). It regenerates damaged xcells, and thus maintains the integrity and function of the tissue of origin. It 'homes' to the tissue it comes from. Precursor stem cells have a limited life span, the same as the donor. In tissue culture these cells look normal, their chromosomal count and shape remains normal, their appearance, structure and biochemistry, is the same as in the organ or tissue they originate from. These cells grow in practically the same environment as when they were a part of organism from which they were taken.

These are the only stem cells that can be safely used for treatment. BCRO stem cells are 'precursor stem cells'. They are prepared by a primary tissue culture of 11 days.

DIFFERENTIATION is the process by which an unspecialized cell (such as stem cell) becomes specialized into one of ~200 cell types that make up the body.

HOMING is a process whereby a transplanted cell is attracted by and travels to the injury site within the tissue it originates from.

BLASTOCYST is a pre-implantation embryo of 30 – 150 cells.

IMMUNOGENICITY means producing an immune response.

ALLOTRANSPLANTATION is implantation of cells, tissues or organs within species, e.g. from man to another man, or from dog to another dog, etc.

Umbilical Cord Blood Stem Cell Transplantation or Peripheral Blood Stem Cell Transplantation are types of allotransplantation. Umbilical cord blood or peripheral cord blood contain only stem cells of hematopoietic and immune systems and thereby are usable only for the treatment of blood diseases, and immune system deficiencies. Claims that these two therapeutic methods can be used for treatment of any & all diseases of man are false.

XENOTRANSPLANTATION is an implantation of cells, tissues or organs between species, e.g. from animal to man, from dog to cat, etc.

AUTOLOGOUS STEM CELL TRANSPLANTATION means taking stem cells from the patient and re-implanting them back into the body of the same patient. Stem cells of an adult are as old as the adult patient and thereby their therapeutic effectiveness is markedly lower that those of stem cells from a fetus. In order to get autologous stem cells you have to obtain a sample of an organ that you want to treat, i.e. a sample of patient's brain tissue, heart muscle, pancreas, etc. if you wish to treat a patient with disease of brain, or heart, or diabetes mellitus, and that is too risky. Claims that autologous stem cell transplants could be used for treatment of brain diseases, heart diseases, or diabetes mellitus, when the samples for their preparation were obtained from patient's blood, subcutaneous fat, peripheral muscle, are false.

More information on stem cell transplantation can be found at: www.bcro-stemcells.com and www.bcro-asia.com