HOPE Program (HOPE I + HOPE II) Project Plan

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Contents

1. Introduction

1.1 HOPE Program (HOPE I + HOPE II) Rationale

Ossium's mission is to improve human health, vitality, and longevity through bioengineering. To achieve our mission, Ossium is developing stem cell-based therapies to improve treatment for patients suffering from hematologic diseases, organ transplant rejection, and diseases of inflammation.

Although the U.S. Food and Drug Administration (FDA) has determined that HPC, Marrow does not require their oversight when indicated for hematopoietic and immunologic reconstitution, Ossium is conducting the PRESERVE I & II clinical trials to characterize the safety and effectiveness of HPC, Marrow. The key endpoints of the PRESERVE study are engraftment success, GVHD incidence rate, and one-year overall survival rate.

We recognize that not all patients who could benefit from Ossium's HPC, Marrow can access the PRESERVE trial for logistical or eligibility reasons. In pursuit of Ossium's mission to improve human health, we've created the HOPE, *HPC Offered for PRESERVE Expansion* Program comprising of 2 separate cohorts HOPE-P and New HOPE.

1.2 Regulatory landscape for HOPE Program (HOPE I + HOPE II)

1.2.1 Background

The Federal Policy for the Protection of Human Subjects (45 CFR 46) requires all federally-supported research involving human subjects to be reviewed and approved by an IRB. *Human subject* is defined as a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens (45 CFR 46.102(e)). *Research* is defined as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102(l)). This policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency (45 CFR 46.101(a)). In accordance with this regulation, clinical investigations that support FDA submissions may not be initiated unless that investigation has been reviewed and approved by an IRB.

The Office for Human Research Protection (OHRP) also provides recommendations for IRB review for section regarding recommendations for Deceased Donor Intervention Research (DDIR) in its publication titled "Issues Surrounding Deceased Donor Interventions under 45 CFR Part 46" (Attachment B -Deceased Donor Intervention Research 45 CFR part 46), which refers to a consensus study report from the National Academy of Medicine (NAM) (Opportunities for Organ Donor Intervention Research: Saving Lives by Improving the Quality and Quantity of Organs for Transplantation | The National Academies Press). These recommendations address protections for recipients of vascularized organs that have been subjected to research interventions, and in whom transplanted organs are now being studied for their function, efficacy, and safety, should be treated as research subjects. The purpose of DDIR is to improve the quality and quantity of organs for transplantation to combat the solid organ shortage and growing transplant waiting list in the US. Interventions include medications, devices, and donor management protocols to maintain or improve organ quality prior to, during, and following transplantation, either while the organ is still in the deceased donor or after it is recovered from the donor but before it is transplanted into a

recipient. Protocols for DDIR are designed to maintain the organs in the best possible condition by minimizing the organ stress, damage, and dysfunction until the organs are recovered.

21 CFR 1271.3(d)(4) states that minimally manipulated bone marrow for homologous use and not combined with another article (except for water, crystalloids, or a sterilizing, preserving, or storage agent, if the addition of the agent does not raise new clinical safety concerns with respect to the bone marrow) is not considered a human cells, or cellular and tissue-based product (HCT/P) and is therefore not regulated by the FDA. FDA confirmed that this product does not require FDA oversight in a 2017 email and confirmed the classification in a 2020 email.

1.2.2 HOPE Program (HOPE I + HOPE II) Regulatory landscape

The HOPE Program meets the definition of research involving human subjects because participants are human subjects and participants' transplant outcomes will contribute to generalizable knowledge; however, this program is not subject to the Federal Policy for the Protection of Human Subjects (45 CFR 46) because it is not federally-supported and not intended to support a submission to the FDA.

Furthermore, the OHRP policies and recommendations regarding DDIR do not apply to the HOPE Program because Ossium Health's deceased donor-derived bone marrow:

1. Is not not subject to research interventions, and
2. Is not a vascularized organ

Ossium Health's bone marrow donors do not undergo research interventions. Organ donors' vertebral bodies are recovered by OPOs following standard organ recovery protocols and shipped to Ossium Health. Processing by Ossium Health meets the FDA definition of "minimal manipulation" (Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use). Ossium Health's deceased donor-derived bone marrow is equivalent to living donor-derived bone marrow, and its use for hematological reconstitution is considered standard medical practice.

Footnote 3 in the OHRP recommendations on DDIR (Attachment B) clarifies that "organs" refers to vascularized human organs regulated by HRSA and the OPTN in accordance with the definition of organ set forth in 42 CFR 121.2, and not to human tissues or human cells, or cellular and tissue-based products (HCT/Ps) regulated by the FDA. As Ossium's bone marrow is not a vascularized organ, this section does not apply.

1.2.3 Summary and Conclusion

The HOPE Program (HOPE I + HOPE II) is outside the scope of research requiring IND opening with FDA or IRB review and the OHRP recommendations on DDIR. Although this program does include limited data collection, it is not intended to support a submission to the FDA and is not funded by the federal government. Furthermore, the HOPE Program does not qualify as Deceased Donor Intervention Research (DDIR) and recommendations regarding DDIR are not applicable to the program.

All links are also available in Appendix 1.

1.3 Background

1.3.1. Unmet Need

Allogeneic HCT is a potentially curative therapy for a variety of hematologic diseases, including the acute and chronic leukemias, myelodysplasia, lymphoma, and multiple myeloma as well as many non-malignant blood disorders. Clinical data now confirm that T-cells contained within the donor graft exert a "graft-versus-malignancy" effect (Horowitz et al., 1990). However, successful application of allogeneic HCT for patients with hematologic diseases is limited by the toxicity related to the allogeneic donor cells which result in graft versus host disease (GVHD), a life-threatening complication. Development of GVHD is associated with lower overall survival (OS) and thus the prevention of GVHD is a cornerstone of allogeneic HCT therapy (Choi & Reddy, 2014).

The current standard human leukocyte antigen (HLA) match for optimal outcomes in unrelated donor hematopoietic cell transplantation HCT is an HLA-A, B, C and DRB1 matched donor (8/8 match) (Dehn et al, 2019). However, availability of 8/8 HLA-matched donors varies by the patient race/ethnicity (e.g., 29% for African Americans vs. 79% for non-Hispanic White for the National Marrow Donor Program (NMDP) donor registry) (Gragert et al, 2014; NMDP 2022). In addition, the ethnic diversity of the U.S. population is increasing according to the 2020 U.S. Census Bureau (US Census Bureau, 2020). Lower 8/8 HLA-matched donor availability is associated with less donor choice and difficulty identifying a donor with favorable characteristics, such as younger age, which has shown to be robustly associated with improved transplant outcomes (Shaw et al, 2018; Kollman et al, 2016).

Use of HLA-mismatched unrelated donors (MMUD) would greatly increase treatment options for all patients, but particularly for those who are ethnically diverse. For instance, 7/8 donors are more frequently available for patients for whom an 8/8 donor is not identified. The 7/8 match rate ranges from 99% in patients of White European ancestry to 72% in patients of African ancestry (Gragert et al, 2014). However, HCT using HLA-mismatched donors has historically been associated with reduced survival and increased GVHD which is a leading cause of post-transplant mortality. Multiple retrospective studies have shown that HLA mismatches result in an approximately 10% decrease in survival with each single mismatch at HLA-A, B, C, DRB1 using conventional calcineurin-based GVHD prophylaxis strategies (Lee et al, 2007; Pidala et al, 2014; Furst et al, 2013).

Crossing the HLA barrier of HLA-mismatched unrelated donors seemed previously insurmountable due to high rates of GVHD and subsequent transplant mortality. However, recent improvements in transplant outcomes have been observed using mismatched haploidentical related donors (haploidentical) with the incorporation of post-transplant cyclophosphamide (PTCy) for GVHD prophylaxis (Luznik et al, 2008). Wide adoption of the PTCy GVHD prophylaxis strategy has increased utilization of haploidentical donors dramatically in recent years due to favorable outcomes and donor availability (all biological parents, children and 50% of siblings are haploidentical to the patient). However, even related haploidentical donors are still not available for all patients in need of transplant (Kosuri et al, 2017).

The NMDP recently completed the 15-MMUD study, a multi-center phase II clinical trial using MMUD bone marrow in patients with hematologic malignant diseases who received PTCy, sirolimus and MMF as GVHD prophylaxis (Shaw et al., 2021). The study had two non-randomized conditioning intensity strata, either myeloablative regimen (MAC) or reduced-intensity regimen (RIC), with the strata selected at the transplant center's (TC) discretion. TCs selected among three FIC regimens: cyclophosphamide and total body irradiation (TBI); busulfan and cyclophosphamide; or fludarabine and busulfan. One RIC regimen was used; fludarabine, cyclophosphamide, and low-dose TBI. Thereafter, patients received a fresh BM graft on

day 0, PTCy on Days 3, 4, and sirolimus and mycophenolate mofetil starting on Day 5. Supportive care was per TC policy. The primary objective was to assess 1-year overall survival (OS) (Table 1).

Table 1 Results from NMDP Phase II, Multi-Center Study of HLA-MMUD BMT using PTCy

	MAC	RIC	Total
Number of patients, n	40	40	80
Median Age at HCT (min – max), years	48.5 (18-66)	59.5 (23-70)	51.5 (18-70)
Median Donor Age (min – max), years	27 (18-56)	29 (21-44)	29 (18-56)
1-year OS, %	72	79	76
aGVHD at Day 100, %			
Grade II-IV	42.5 (29.8-55.7)	32.5 (20.9-45.3)	NA
Grade III-IV	17.5 (8.7-28.5)	0	NA
cGVHD at 1 year, %	35.5 (23.3-48.7)	17.5 (8.7-28.5)	NA
1-year cumulative incidence of NRM, %	7.5 (2.1-15.8)	10 3.6-19.2)	NA
1-year cumulative incidence of relapse, %	30.4 (18.9-43.2)	22.5 (12.6-34.3)	NA

Study results showed a 1-year overall survival of 76% similar to a real-life comparator dataset of patients receiving haploidentical transplant with PTCy and meeting all main study eligibility criteria (Shaw et al, 2021). In addition, the MMUD platform enabled 48% of ethnically diverse patients to receive a life- saving transplant (Shaw et al, 2021). One-year GVHD-free, relapse-free survival (GRFS) rate was 54%, three-times greater than a historical cohort patient population receiving another form of GVHD prophylaxis, anti-thymocyte globulin (ATG) (Jimenez et al, 2022). The result of the study clearly shows that MMUD transplants are feasible, safe, and effective. Important factors favoring mismatched donor include the ability to select a younger donor, or a donor better matched with respect to virologic serostatus and ABO blood type. Selection of younger donors was associated with significantly better OS, as well as several other end points. Donor specific antibodies, a significant issue in the mismatched related setting (associated with increased graft failure), can be completely avoided in the MMUD setting.
In addition to addressing the HLA barrier, optimizing graft provision for all patients in need would include providing the timely infusion of a graft with an adequate cell dose. Rapid identification of an unrelated donor improves survival after allogeneic HCT, especially for those patients with high-risk malignant disease (Pagel et al, 2020). Achieving disease remission without further chemotherapy or immunotherapy would enable patients to proceed to allogeneic HCT faster and decrease risk organ toxicity associated with additional therapies to maintain disease remission. In addition, reducing logistics associated with donor graft collection, including obtaining optimal cell dose (Dominietto et al, 2002; Gaunter et al, 2022) would be ideal. As securing an allograft from a domestic and international unrelated donor from the time of formal donor search to infusion can take on average 92 and 114 days, respectively (Auletta et al, 2021).

Additionally, the MMUD platform, study results showed 75% overall survival rate after 1 year with over 90% engraftment and there was 11% rate of aGVHD III-IV at 100 days. The post-transplant outcomes were not significantly different between 7/8 and 4-6/8 matched patients. The study also showed no statistical

difference in overall survival at 3 years based on HLA Match as shown in Table 2 (Shaw et al, 2021).

Figure 1:

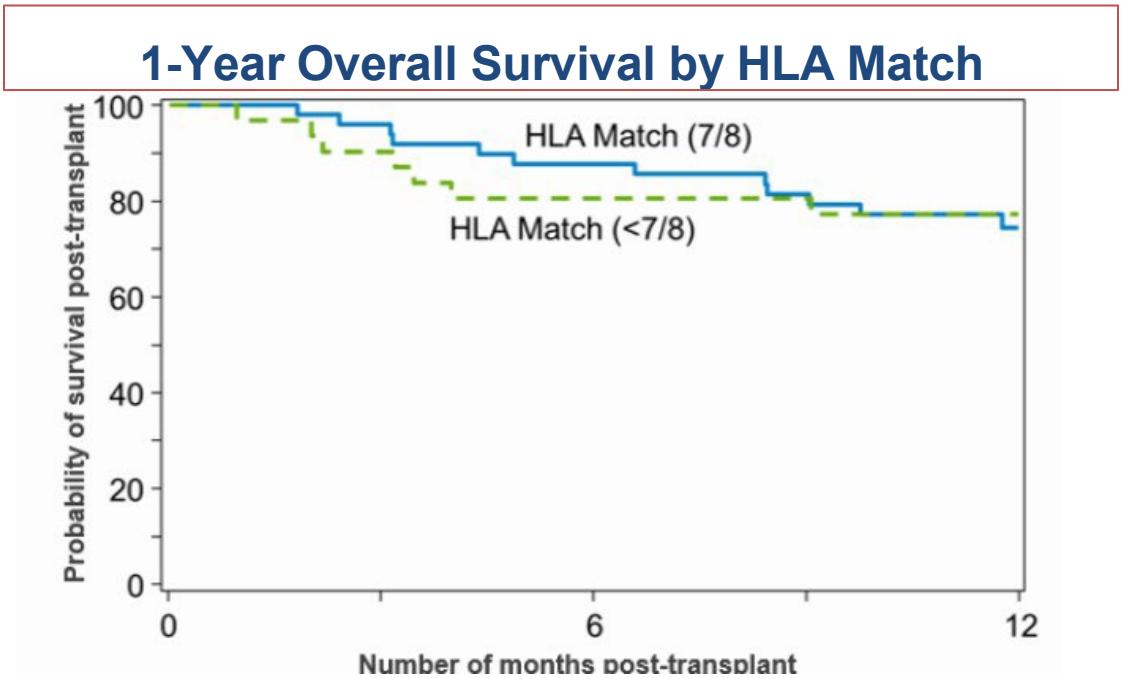

Table 2:

HLA Match	1-Year OS	3-Year OS	Chronic GVHD	Relapse Rate
7/8	75%	63%	37%	44%
4-6/8	77%	71%	16%	33%

The interim results from the ACCESS study show that the rate of GVHD and other complications are similar to HLA-matched donor recipients (Al Malki et al, 2024).

1.3.2 Ossium Solution To Unmet Need

Ossium produces cryopreserved hematopoietic progenitor cell bone marrow (HPC, Marrow (Cryopreserved)) recovered from deceased organ donors using good manufacturing practice (GMP) processing, Ossium's HPC, Marrow (Cryopreserved) is supplied in units suitable for transplantation by infusion, the same procedure used for transplantation of other sources of HPCs, such as live donor BM aspirates, live donor apheresis products, or cord blood. Thus, no changes to existing HPC transplantation protocols are required to use Ossium product in adult and pediatric populations.

The conventional medical uses of HPC transplants are to treat blood cancers, blood disorders, and bone marrow failure by providing hematologic and immunologic reconstitution. Medical use of HPCs to induce immune tolerance in recipients of same-donor solid organ transplants is an additional emerging use that promises to eliminate the need for post-transplant, lifelong immunosuppression and greatly expand the accessibility and success of solid organ transplants.

Ossium's HPC, Marrow (Cryopreserved) provides an "on-demand", ready to use source of hematopoietic cell graft and enable a rapid treatment for patients without available living donors. HPC, Marrow (Cryopreserved) will expand access to life saving hematopoietic cell transplantation to individuals comprising the expanding racially and ethnically diverse populations in the USA. Furthermore, the Ossium HPC, Marrow (Cryopreserved) bank would reduce the interval between diagnosis and time to transplant, which is a critical factor for post-transplant outcomes.

1.3.3 Cryopreserved Bone Marrow (BM) from Deceased Donors

It was recognized over 60 years ago that BM recovered from deceased organ donors was a potentially useful source of HPC for transplantation (Ferrebee et al., 1959, Thomas et al., 1957). Recovery of functional BM from deceased donors is conceptually similar to the procurement of organs and tissues, which is robust and well established in the US. And as the FDA does not regulate bone marrow transplants from living donors per 21 CFR 1271.3(d)(4), the FDA has deemed Ossium's HPC, Marrow (Cryopreserved) product equivalent to live donor aspirated HPC, Marrow and not requiring a Biologics License Application (BLA) for use.

1.3.4 Acquisition Technique

Potential donors can either sign up themselves or families can elect to donate their loved one's organs or tissues at the time of death. A network of 57 Organ Procurement Organizations (OPOs) are tasked by the government with this process, and Ossium works with these organizations to recover spines for bone marrow processing.

When a potential donor is identified, the local OPO speaks with the family to obtain or confirm consent and complete authorization documents. The next of kin completes the Uniform Donor Risk Assessment Interview (UDRAI) to highlight any high-risk behavior or areas of concern. The OPO then works with the hospital to complete all required serological testing, and at this point, the OPO contacts Ossium to review the donor's record and determine if they are acceptable bone marrow donors. If a donor is accepted, following Ossium's donor acceptance SOPs (cause of death, risk factors, serology results, and medical history), a highly trained OPO staff recover the spinal column and ship it to Ossium via special logistics companies who handle human tissue through their courier systems.

Ossium provides the necessary training and supplies for the procurement of vertebral bodies by the local organ recovery team including recovery kits and shipping supplies (e.g., Recovery Pack, labels, and insulated shipping containers). Vertebral bodies are carefully recovered via aseptic technique and are transported to Ossium on ice by Quick Courier Service. Materials are processed within 72 hours of the VBs being placed on ice.

At Ossium, the tissue is received in a dedicated room and reviewed for eligibility for processing. Bone marrow is recovered from the tissue in a dedicated recovery suite, and then goes on to processing in separate processing suites. Donor serology testing is performed as part of organ donation through CLIA certified laboratories and reported to Ossium Health as part of donor screening. Additional tests required by Ossium based on blood donor regulations (e.g., HTLV, Chagas, etc.) are performed as part of this process. Cell counts and viability assessments (pre-freeze and post-thaw) are performed in house through the Ossium Health CLIA-certified testing laboratory (CLIA ID: 15D2155085). Final product sterility assessment utilizing validated methods is performed by a contract CLIA-certified microbiology lab (VRL Eurofins; CLIA ID:06D0717586). Confirmatory HLA typing is performed by a contract CLIA- certified testing laboratory (Histogenetics).

Vertebral segments are incised and separated by cutting through the discs using sterilized osteotomes, mallets, knives, scissors, and scalpels. As much of the spinal cord and soft tissue are removed as possible. Pedicles and spinous process are removed from VBs using a bone saw. Identification of any visible anatomical pathologies present is performed, including bone spurs, degenerative discs, herniated discs, and atrophic bone marrow.

All the vertebral bodies from the same donor are then cut into small pieces and ground with a bone grinder in media containing Plasma-Lyte A Injection pH 7.4 (Multiple Electrolytes Solution, Type 1, USP), human serum albumin (I, 25%, USP; diluted to 2.5% for the rinse media), Heparin, and Benzonase. The bone grindings then go through a series of rinsing, filtration, and centrifugation steps to remove fat and concentrate the bone marrow using sterile, disposable Bone Marrow Collection Kit. The resulting product is minimally manipulated, plasma and red blood cell reduced (pre-freeze HCT ~5%) human bone marrow, with multiple bags available from an individual donor. Each bag contains 65±5mL at ~$1.4x10^8$ nucleated cells/mL. Packaging volume is designed for allocating a single bag for a 35kg patient, with 2 bags utilized for a 70kg patient, at the physician's discretion. Samples are tested for sterility, viability (for CD34+, CD45+ and CD3+ cells), potency (colony-forming unit; CFU), and residual Benzonase.

After processing, bone marrow is packaged in volumes of 65-70mL with a cell concentration of 140M nucleated cells/mL in cryopreservation bags with Information Standard for Blood and Transplant (ISBT 128 Donation Identification Number (DIN)) and product code.
Integral test segments are included for HLA confirmatory typing and additional vials are prepared for post-thaw QC assessment. Bags and vials are cryopreserved utilizing passive cooling in a dedicated static temperature chamber using a validated system which includes dimethyl sulfoxide (DMSO) as a cryoprotectant. Following cryopreservation, units are held in quarantine tanks until serology and sterility tests are complete and then relocated to conditionally released tanks. A rigorous quality process is followed from beginning to end to ensure proper authorization, testing, screening, and tracking. Ossium's Quality unit along with the Medical Director performs a final document review before units can be released for transplant. Infectious disease marker testing, donor demographics, and other information are available as physicians make transplant decisions, ensuring that each patient gets a safe

transplant that is optimal for their situation.

Ossium HPC, Marrow is cryopreserved in a validated cryo-storage bag, utilizing a blood-bag closure system that is hermetically sealed using a Radio Frequency (RF) welder. The 250 mL capacity cryobags will be filled with 65-70 mL of final Ossium HPC, Marrow product.

1.3.4.1 Freezing is performed as follows:

The final cell product is centrifuged and pelleted; supernatant is aspirated. Freeze media which includes 100% dimethyl sulfoxide (DMSO) and components of the rinse media (Plasma-Lyte A aIHSA) is then added to concentrated bone marrow. Final product is bone marrow cells suspended in Plasma Lyte, 2.5% HSA and 5% or 10% DMSO and packaged in 250 mL cryobags. Each bag contains a cell concentration of ~1.4 x 10^8 nucleated cells/mL. Final absolute CD34+ counts are determined for each donor lot and are reported. The final volume in each bag is 65-70 mL. Cryobags are labeled and passively cooled at ~1˚C/min in a -86°C freezer dedicated to and validated for cryopreservation processing. Bags are transferred to liquid nitrogen (LN2) vapor after 24 hours into a designated, continually monitored LN2 vapor tank with a storage temperature of <-150°˚C.

1.3.5 HPC Comparison of Live vs. Deceased Donors

Previously published studies have confirmed that stem and progenitor cells within deceased organ donor BM are highly viable and comparable to living donor cells (Fig 1) (Kenyon et al., 1995; Rybka et al., 1995; Ahrens et al., 2004; Baumert et al., 2012; Blazar et al., 1986; Soderdahl et al., 1998). Ossium's current processing methodology which was developed to meet GTP considerations builds on this historic data and yields high recoveries of functionally viable cells. All the infectious disease marker panels are included in the Certificate of Analysis and the Donor Infectious Disease Markers forms as seen in Appendix 2.

A comparison of HPC, Marrow obtained from deceased organ donor vertebral bodies (OD-VB) produced using Ossium's methods and living donor BM established compositional similarity between the two sources. Living donor iliac crest (LD-IC) BM was aspirated from young healthy donors and shipped to Ossium with environmental control to maintain temperature at approximately 20°C. Deceased OD-VB HPC, Marrow was processed from vertebrae received on ice. Samples of freshly isolated whole BM were analyzed prior to immunomagnetic selection of CD34+ cells which were then analyzed after cryopreservation. There was no difference in viability of CD45+ WBC, CD34+ HSPC or CD3+ T lymphocytes (Fig 1A-C). The percentage of CD34+ HSPC in the WBC of HPC, Marrow (1.2±0.27%, mean and SD) was not different than in LD-IC (0.89±0.24%) (Fig 1D). There were significantly less T cells in OD-VB BM (6.8±2.3%) compared to LD-IC BM (18.4±3.9%) (Fig 1E). The GM-CFU potential was the same for both sources (Fig 1F); however, total CFUs were higher in OD-VB BM (Fig 1G).

CD34 and CFU

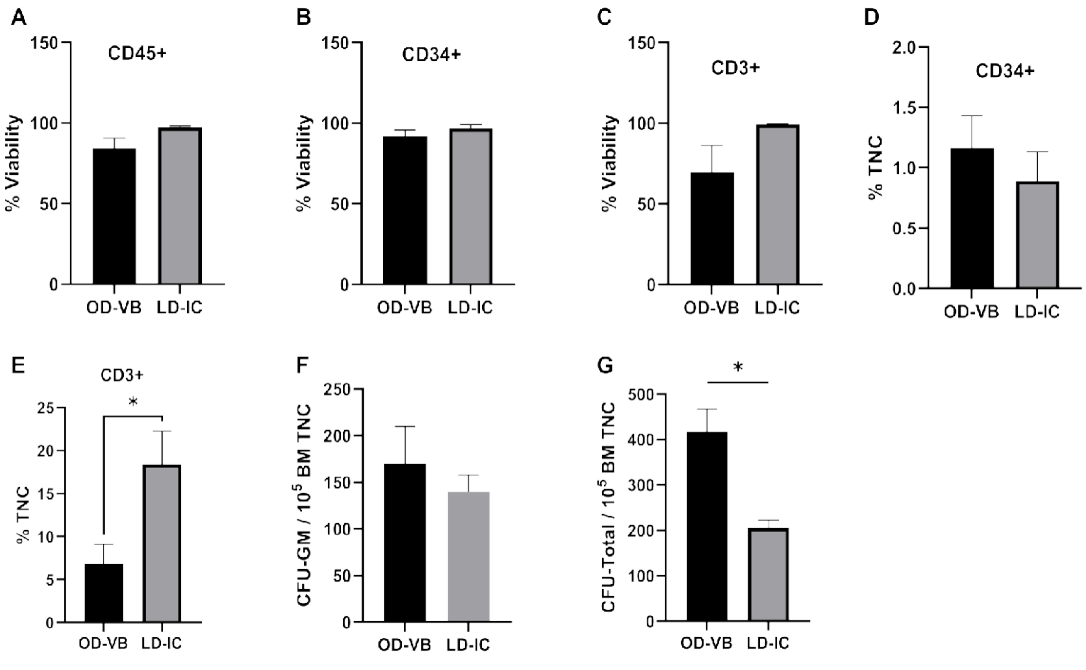

Figure 1. Comparison of Ossium produced HPC, Marrow from deceased organ donors (OD-VB) to living donor (LD-IC) BM.

A characterization study of Ossium produced HPC, Marrow considering a sample of screened donors processed and cryopreserved over a 2-year period (2020 through 2021; n=274 donors) indicated total CD45+ WBC concentrations prior to cryopreservation of $1.2x10^8 \pm 0.5x10^8$/ml (mean ± standard deviation), which was not different from that measured following cryopreservation ($1.1x10^8 \pm 0.3x10^8$). The total number of CD34+ hematopoietic stem and progenitor cells (HSPC) per 65 ml unit volume (Fig 2A) also did not vary with cryopreservation ($6.3x10^7 \pm 3.2x10^7$ versus $6.9x10^7 \pm 2.7x10^7$, fresh and cryopreserved, respectively). Total and viable CD3+ T cells concentrations within the WBC population remained the same following cryopreservation (Fig 2B); whereas these parameters slightly, but significantly ($p<0.001$), increased for CD34+ cells after cryopreservation (Fig 2C), which was also reflected in the increased percentage of CD34+ cells (Fig 2D). Compared to the total nucleated cell population, each WBC, T cells and CD34+ cell populations slightly declined following cryopreservation (Fig 2E), which was likely due to loss of cryo-intolerant neutrophils (Moss and Higgins, 2016).

In addition to standard characterization performed on all specimens, a small subset was subjected to an expanded subset of lymphocyte analysis (Fig 2F). There was no significant difference in pre-freeze or post-thaw T cell, B cell or NK cell populations. Cryopreserved HPC, Marrow maintained colony-forming unit (CFU) potential after thawing; although, the number of lineage-committed progenitor cells was lower (Fig 2G). These data demonstrate that overall, the HPC, Marrow product is not dramatically altered by cryopreservation and thawing processes.

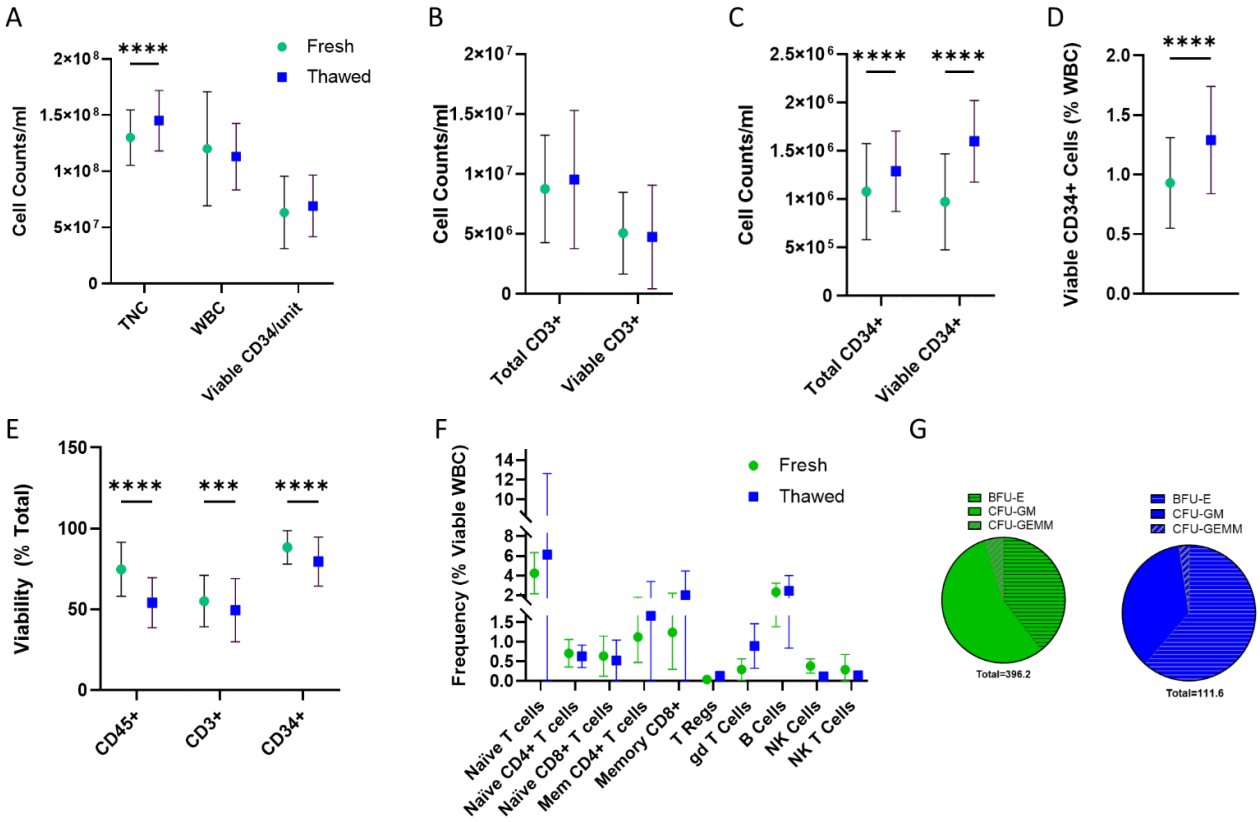

Figure 2. Characterization of Ossium donors processed in 2020 and 2021.

1.3.5.1 Engraftment

The ability of cryopreserved HPC, Marrow from two donors to stably engraft BM was evaluated *in vivo* in the non-lethally irradiated NSG mouse transplantation model at Indiana University (IUSM, Indianapolis, IN) (Fig 4). Engraftment at 8 and 16 weeks was compared to Umbilical Cord Blood (UCB). Human chimerism in peripheral blood at 8 weeks was similar between CD34+ cell sources (Fig 3A). By 16 weeks, chimerism was over 65% in the BM of mice infused with both HPC, Marrow donor sources (75.0±13.9 for Donor 1 and 66.6±25.5 for Donor 2), compared to an expected higher >95% (96.6±1.6) with UCB (Fig 3B). Human lymphocyte subsets in BM were similar between UCB and HPC, Marrow CD34+ cells with the exception of CD19+ B cells (Figs 3C-F). Analysis of peripheral blood at 16 weeks demonstrated approximately 40% chimerism for both donors, which was half that of UCB (Fig 3G). Extramedullary chimerism in spleen was above 50% for all cell sources (Fig 3H). The percentage of CD34+ cells from each input source varied from 10-15% (Fig 3I) and was remarkedly similar in BM collected from mice at the 16 weeks endpoint (Fig 4J). The BM collected from the two HPC, Marrow donors was then used to perform secondary transplantations into a new set of non-lethally irradiated NSG mice. At 16 weeks engraftment was detected in peripheral blood and BM, demonstrating the presence of long-term engrafting HSC in the original HPC, Marrow specimens (Figs 3K-L).

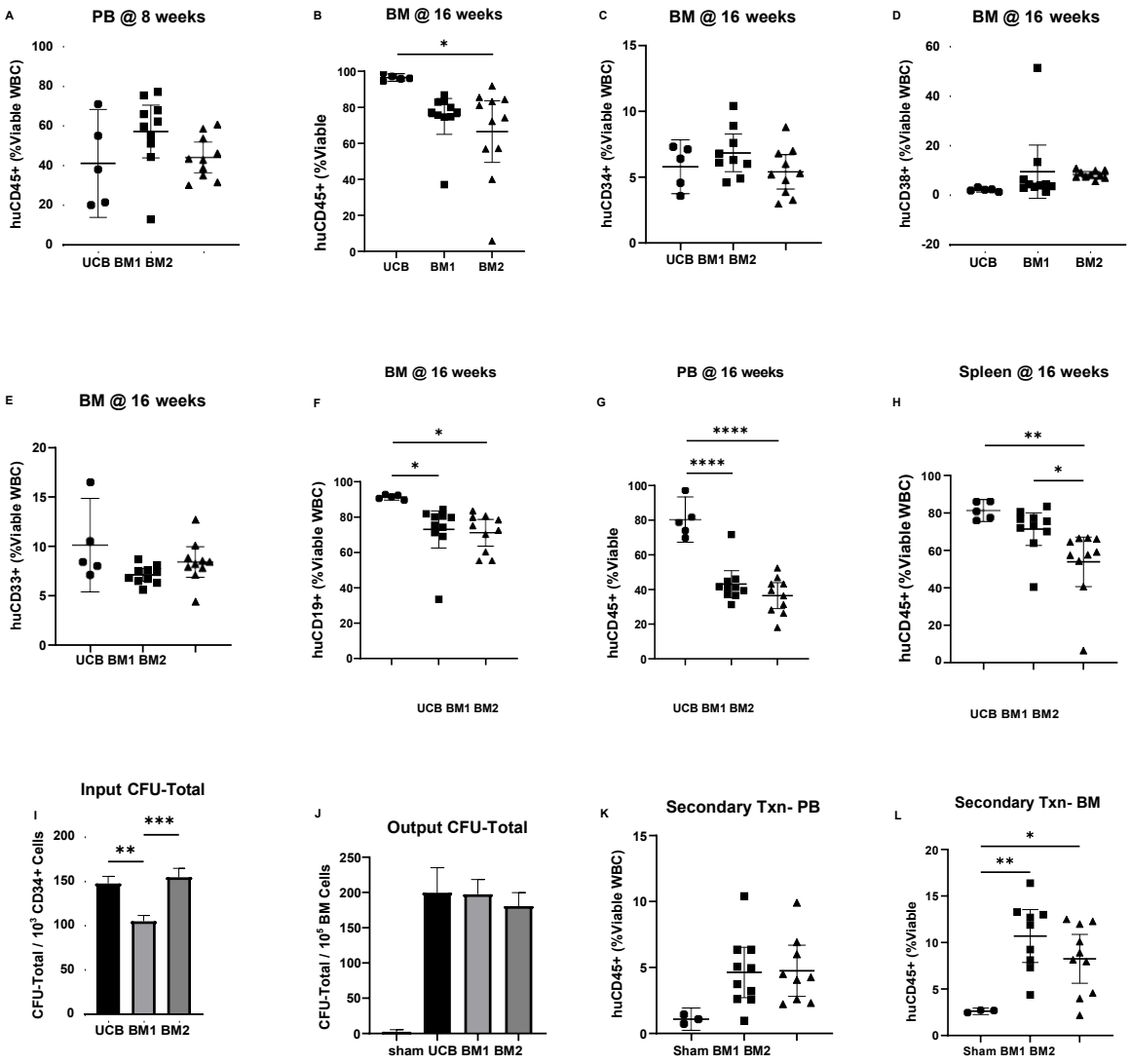

Figure 3. NSG mouse engraftment data.

A follow up NSG engraftment study was performed with one of the same donors at a different institution (Columbia University, New York, NY). In this experiment, two different doses were evaluated and compared to engraftment of live donor aspirated bone marrow prepared the same way with the same dosing. No differences in either dose or source were detected (Fig 4).

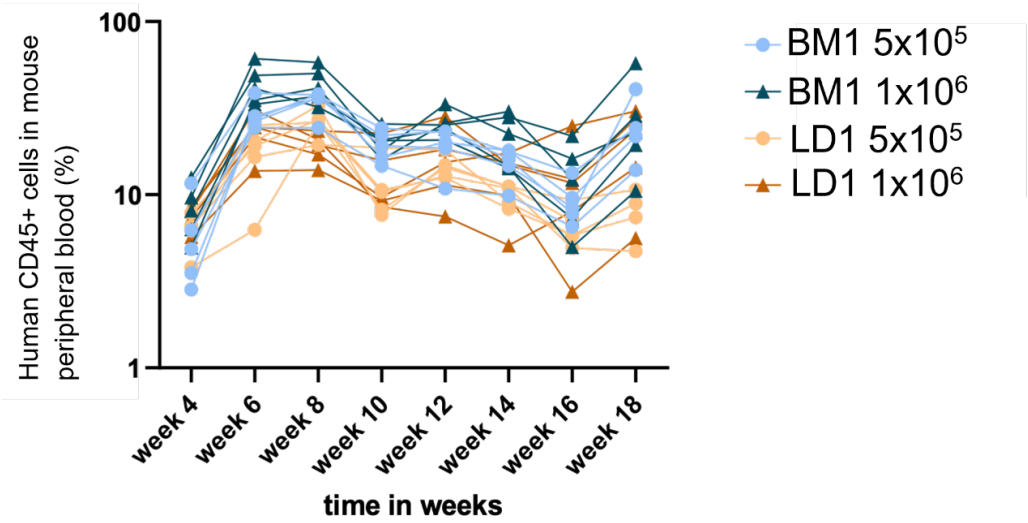

Figure 4. NSG mouse engraftment data comparing an Ossium processed donor (BM1) to a live donor aspirate (LD1) prepared the same way and tested at two different doses.

Another NSG engraftment study was performed at the University of Pennsylvania (Philadelphia, PA) with 5 different Ossium donors. In this study, the cells were pooled, and 3 different doses were evaluated. All doses yielded similar results (Fig 5).

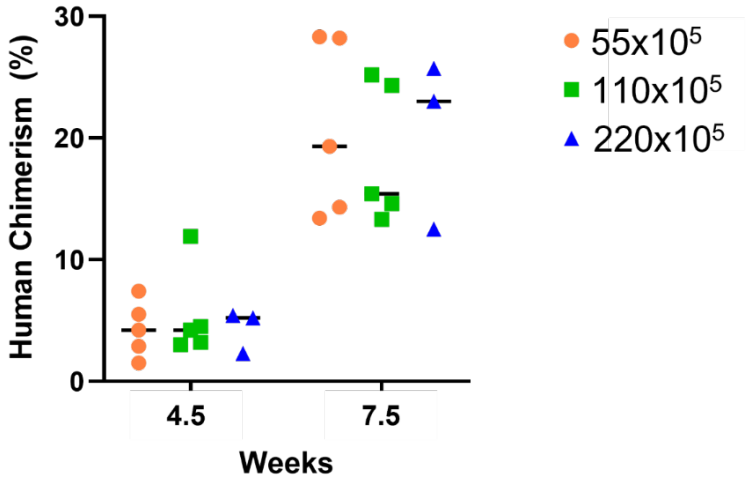

Figure 5. NSG mouse engraftment data comparing 5 Ossium processed donors (CD34 selected and pooled) at 3 different total Ossium processed donor Bone Marrow doses. Chimerism was comparable at each dose (study is continuing to 11.5 weeks).

1.3.6 Cryopreservation

A perceived restriction in the use of unrelated donors is the time necessary to find a donor, a delay which is thought to be associated with inferior patient outcomes. Ossium's partnered network of organ procurement organizations will allow for development of a large, genetically diverse bank of cryopreserved deceased donor HPC, Marrow that will be immediately available upon demand. Furthermore, very large volumes of bone marrow are obtained, yielding on average around 5 bags per deceased donor, corresponding to about 2.5 adult transplants per donor >1.4 x 10^8 CD34+ cells per transplant. Given early favorable results using MMUD and post-transplant cyclophosphamide, this bank reduces the transplantation wait time by greatly increasing the appropriate donor pool for each patient, thereby increasing the likelihood of finding a donor available to donate in a timely manner. The ability to select a MMUD would also benefit ethnically diverse patients who are less likely to find a matched unrelated donor on international donor registries.

Historically, the majority of donor HCT grafts for allotransplantation have been collected and infused fresh. However, cryopreservation of adult donor HCT grafts prior to transplantation has been used for decades routinely to treat patients with a variety of diseases when a patient's scheduled transplant is delayed or when there are coordination issues between the patient and their selected donor. More recently, the global COVID-19 pandemic caused a shift towards using cryopreserved grafts for a majority of allogeneic HPC grafts due to the disruptions in logistics of donor scheduling and in order to reduce risks to the donor (Auletta et al., 2021).

A retrospective comparison of outcomes from 7,397 allogeneic HCT procedures that used either fresh or cryopreserved stem cell grafts was performed (Hsu et al., 2021). There was no difference in engraftment,

relapse, non-relapse related mortality (NRM) or survival with cryopreserved (n=154) matched related or unrelated bone marrow (BM) grafts compared to fresh BM grafts. Conversely, multiple measures demonstrated worse outcomes with cryopreserved peripheral blood stem cell (PBSC) grafts compared to fresh (Fernandez-Sojo et al., 2021). In a separate study, outcomes of HCT in patients receiving PTCy therapy were compared to fresh graphs in order to study the impact of graft cryopreservation (Hamadani et al., 2020). There was no difference in engraftment, OS, aGVHD, or NRM in the 274 patients receiving cryopreserved grafts (18 BM and 256 PBSC). Rates of cGVHD and disease- free survival (DFS) were marginally lower with cryopreserved grafts. Although the number of cases using BM grafts was small, overall, these studies indicate that cryopreservation does not negatively impact outcomes of allogeneic HCT (with or without PTCy) when BM is the source of graft.

Low HPC cell counts, poor cell viability and other quality indicators have been associated with graft failure; thus, knowledge of pre-defined graft quality indicators from post-thawed samples (as will be available for Ossium HPC, Marrow products) may be associated with better engraftment outcomes. In contrast, cryopreserved cells may have a lower viability than fresh cells which may negatively impact engraftment.

Based upon the experience of using PTCy in the HLA-mismatched setting and advantage of immediate availability of Ossium's genetically diverse bank of cryopreserved HPC, Marrow, can be considered as potential graft source.

1.3.7 Previous Human Experience with Deceased Donor Bone Marrow

First bone marrow transplant was reported in 1957. In small series 6 patients successfully received bone marrow and at least 2 out of 6 patients received bone marrow from deceased donors (E. Donnall Thomas et al). In 1986 another report was published of a 12 year old male with acute lymphoblastic leukemia successfully received bone marrow from a deceased donor (Bruce Al Blazar et al). There are several additional studies reporting bone marrow transplant in at least 700 patients from deceased donors along with solid organ transplants.

2 HOPE Program (HOPE-I + HOPE-II) Eligibility

Patients may qualify if the following criteria are met (any exceptions made to the eligibility criteria should be pre-approved by Ossium Health):

- Patients are 12-80 years of age
- Their treating physician determined they are eligible for allogeneic bone marrow transplant
- Patient must be high-resolution, HLA partially or fully matched (4–8/8 allele matched at HLA-A, -B, -C, DRB1) to an available Ossium HPC, Marrow product
- Karnofsky performance status score ≥70% and HCT comorbidity index (HCT-CI) <5
- Their treating physician determined that the potential benefit outweighs the potential risks such as:
    - Patient is expected to live at least one year post transplant
    - Engraftment (neutrophil) is expected within 60 days of post transplant

2.1 Classification into HOPE-I or HOPE-II

All patients are reviewed for overall HOPE Program eligibility. Once the eligibility is determined, the patient will be enrolled into HOPE-I or HOPE-II.

2.1.1 HOPE-I Target Population

The following patients will be enrolled in HOPE-I program

1. Patients with malignant hematologic disease including:
    - Acute leukemia [acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), acute biophenotypic leukemia (ABL), or acute undifferentiated leukemia (AUL)], MDS without fibrosis, or chronic leukemia (CML, CLL) in the first remission or beyond with ≤5% marrow blasts and no circulating blasts or extra-medullary disease documented by bone marrow assessment
    - Fully chemosensitive non-Hodgkin's lymphomas, Hodgkin's lymphoma, or cutaneous T-Cell lymphoma in the first remission or beyond documented by PET/CT imaging and bone marrow assessment if previously involved
2. Patients who have never received prior allogeneic or prior autologous transplant
3. Patients where the minimum dose of 2.5 $\times 10^6$ CD34+ per kg is available with one single Ossium HPC, Marrow Product

2.1.2 HOPE-II Target Population

The following patients will be enrolled in HOPE-II:

1. Non-malignant hematologic indications such as severe aplastic anemia
2. Patients with malignant hematologic disease including:
    - Acute leukemia [acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), acute biophenotypic leukemia (ABL), or acute undifferentiated leukemia (AUL)], MDS with or without fibrosis, or chronic leukemia (CML, CLL) who are not in complete remission (active disease) with 5% - 20% marrow blasts
    - Chemosensitive non-Hodgkin's lymphomas, Hodgkin's lymphoma, or cutaneous T-Cell lymphoma who are not in complete remission (active disease) documented by PET/CT imaging and bone marrow assessment if previously involved
3. Any additional medical conditions not included in HOPE-I target population or HOPE II target population (as noted above) where patient is requiring allogenic transplants
4. Past history of auto or allogenic transplants
5. Where two Ossium donors are recommended by treating doctors
6. Patients requiring <50 mg/kg/IV on Day 3 and 4 PtCy dose post transplant
7. Patients with active disease or in remission with myeloproliferative neoplasms

Table 3: Summary Table of HOPE-P vs New HOPE

Criteria	HOPE-I (Group 1)	HOPE-II (Group 2)
Age	12-80	12-80
Disease status	Remission	Active disease or in Remission
Target Population	Hematologic malignancy patients in CR	Patients with Myeloproliferative Neoplasm Patients who received prior Allo HCT Patients with active disease Patients with Cardiac conditions for whom reduced PTCy dose is indicated Patients who may need two Ossium donors
Benefit vs Risk	Benefit outweighs risk (based om physician decision)	Benefit outweighs risk (based physician decision)

3 HOPE Program (HOPE-I + HOPE-II) Duration

A patient that receives Ossium HPC, Marrow as a part of the HOPE program will be followed as per standard follow up based on institutional practices. Information on GVHD, relapse, serious adverse events and adverse events will be collected for up to two years post transplant.

4 Risk/Benefit Assessment

Ossium HPC, Marrow under the HOPE program (HOPE-I + HOPE-II) is available for the patients who meet the criteria outlined in Section 2 and the physician has determined that the benefits outweighs the potentials risks as per their discretion. With the use of Ossium HPC, Marrow as a graft source the most relevant short term risk to patients are infusion related toxicity and primary graft failure which can occur with living donor bone marrow transplants as well. Extensive product analyses show a viable, quality graft with Total Nucleated Cell Count (TNC) and CD34+ content that is at least the same or often exceeds BM grafts obtained from healthy donors. Furthermore, preclinical data demonstrates the ability of Ossium HPC, Marrow to engraft in both primary and secondary transplant models in mice.

Cryopreserved hematopoietic cells are the standard of care for autologous transplants and their use has been increased in allogeneic transplants during the COVID-19 pandemic (Hsu et al., 2021; Fernandez-Soji et al., 2021). There are certain risks with infusion such as fluid retention, allergic reaction, changes in blood pressure, change in heart rate/rhythm, fever, chills, sweats, nausea, vomiting, diarrhea, cramping, headache, dyspnea, dimethyl sulfoxide (DMSO) toxicity, hemoglobinuria and acute renal failure, and in rare cases infusion reaction resulting in death. A recipient may develop or have seroconversion of an FDA-

listed relevant communicable disease. Due to stringent screening for Infectious Disease Markers (IDMs), the likelihood is rare.

The published experience using allogeneic cryopreserved grafts has mostly been in peripheral blood stem cells though bone marrow has also been described. To this end, most cryopreserved allogeneic hematopoietic cells have resulted in engraftment rates and outcomes similar to the use of fresh allogeneic hematopoietic cells (Hamandi et al., 2020).

Risks of a bone marrow transplant such as graft vs host disease (GVHD), graft failure, cytokine release syndrome (CRS) and infections as a part of the HOPE program may or may not be similar to conventional graft sources.

The common toxicities with conditioning treatments and post transplant therapies that will be used as a part of the HOPE program are the same as the standard of care using standard graft sources and can be found in U.S. Food and Drug Administration (FDA)-approved package insert for each drug.

Ossium cryopreserved HPC, Marrow provides an "on-demand" source of hematopoietic cell graft and will expand access to life saving hematopoietic cell transplantation for individuals comprising the expanding racially and ethnically diverse populations in the USA. Furthermore, the Ossium HPC, marrow bank would reduce the interval between diagnosis and time to transplant, which is a critical factor for post-transplant outcomes, and the large volumes of transplantable units from each donor will provide a unique opportunity for booster doses from the same source.

5. Donor Information

The following are the donor inclusion/exclusion for Ossium HPC, Marrow for the HOPE program (HOPE-I + HOPE-II).

5.1 Donor Inclusion Criteria

The following criteria for Ossium HPC, Marrow cells from deceased donors include:

1. Those who donated after brain death (DBD) or after circulatory death (DCD)
2. Male and female donors aged 7-55 years old who have authorization or authorized for organ and tissue procurement for research purposes.
3. Maximum warm ischemia time: 8 hours
4. Maximum cold ischemia time: 72 hours (defined as all the time after vertebral bodies are placed on wet ice)
5. Must undergo eligibility screening procedures, including an evaluation of medical history and relevant social behavior, per 21 CFR 1271 and the FDA's Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (2007). If a donor is deemed incomplete or ineligible but otherwise satisfies criteria 1-4 above, the treating physician may elect to use the donor due to urgent medical need by completing a Declaration of Urgent Medical Need form.

5.2 Donor Exclusion Criteria

The following criteria are exclusionary for donor marrow cells:

1. Evidence of septicemia, viremia, or bacteremia at time of death or positive blood culture
2. Active or recent cancer within the last 12 months of donation[1]

3. Reception of chemotherapy
4. Reception of gene-edited cell therapy at any time
5. Sexually transmitted infections acquired, treated, or untreated within the last 12 months[2]
6. Active or past history of neurological diseases such as Alzheimer's disease, dementia, or Creutzfeldt-Jakob disease (CJD)
7. History of rabies exposure and/or vaccine within past 12 months
8. If the colon or esophagus perforation reported during recovery
9. A positive/reactive result on the infectious disease panel[3]
10. Presence of donor-specific antibodies in the recipient. Recipient has positive anti-donor HLA antibodies against a mismatched HLA in the selected donor determined by either:
    a. positive crossmatch test of any titer (by complement-dependent cytotoxicity or flow cytometric testing) **or**
    b. presence of donor specific HLA antibodies (DSA) to any mismatched HLA allele/antigen at any of the following loci (HLA-A, -B, -C, –DRB1, DRB3, DRB4, DRB5, -DQA1, -DQB1, - DPA1, -DPB1) with median fluorescence intensity (MFI) >3000 by Luminex single antigen bead based solid phase immunoassay tested prior to SSA request and repeated if transplant is >30 days from prior HLA antibody testing

6. Study Process Workflow

6.1 Request for Ossium Product

A patient or physician can reach out directly to Ossium Health for request for participation in the HOPE program (HOPE-I+ HOPE-II). The patient signs an initial authorization form and agrees on consumer health data policy if applicable. If the patient contacts Ossium health directly, the treating physician may be contacted to provide additional information about Ossium HPC, Marrow. The treating physician completes the HOPE Program (HOPE-I + HOPE-II) Intake Form. This Intake Form is reviewed by Ossium Health to confirm participation in the program and the high resolution HLA information provided in the form is used to confirm if there is a HLA partially or fully matches (4-8/8 allele matched at HLA-A,-B,-C,-DRB1) to an available Ossium HPC, Marrow product. The treating institution will receive a business agreement for review as well.

A product report including Comprehensive Report and Certificate of Analysis (Appendix 2), Declaration of Eligibility (Appendix 3) and Declaration of Urgent Medical Need (as applicable) available in Appendix 4 from Ossium Health will be provided to the treating institution for any matching product for consideration while subject treatment options are being evaluated. If the treating physician determines that the donor is suitable for the patient, the institution will order Ossium products by completing an Ossium Cryopreserved HPC, Marrow Product Request form (available in Appendix 5). The product will not be shipped until the HOPE Program agreement is executed, along with training of receipt/storing/ thawing requirements are completed by Ossium Health. Any additional requirements to execute the HOPE program (HOPE-I + HOPE-II) are determined by the treating physician and their institution.

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[1] Active cancers or recent cancers. Most skin cancers are not considered excluded

[2] Negative serology testing is required for the following STDs (Hepatitis B, Hepatitis C and HIV) and negative antibody for syphilis. For all other STDs, the acceptance is based on PI's discretion.

[3] Negative test result is required for CMV IgM, EBV IgM (if available), Toxoplasmosis IgM (if available), WNV, Chagas and HTLV. Positive results are acceptable based on PI's discretion for EBNA, EBV IgG, Toxoplasmosis IgG, Anti-CMV (only if CMV IgM is negative), and CMV IgG

6.2 Shipment and Dosing

Once the training and requirements outlined in section 6.1 are complete and the transplant date is planned, product shipment will be arranged by Ossium. The patient's weight is reconfirmed to finalize a target dose. Shipments are scheduled and tracked with a Qualified Shipping provider with associated documents enclosed. The details of the shipment and packing are available in the Appendix 6.

Ossium Production Team will complete a packaging and storage inspection to ensure the identity of the HPC, Marrow unit(s) (via ISBT DIN and bag Unique Serial Number) being moved from storage to shipment. Ossium Quality Control completes an independent bag inspection for visual quality and integrity. Transfers to shipper are timed and will not exceed 5 minutes to prevent thawing.

Product delivery will be scheduled to occur at least two days prior to the start of subject planned infusion. Product shipment will be arranged by Ossium. The details of the shipment and packaging is available in the Appendix 6. Once shipment is arranged, the airway bill and tracking information will be provided to the institution. Once the product is received, the institution will provide confirmation of product receipt to Ossium.

Upon receipt of the Ossium HPC, Marrow product, the institution will also complete a written confirmation that the product was received on the Record of Packaging and Receipt form (Appendix 7). A copy of the completed Record of Packaging and Receipt form will be sent from the institution to Ossium via email. The dosing checklist (Appendix 8) and infusion details (Appendix 9) will be completed on the day of the transplant. The institution will receive the following documents, along with the Ossium HPC, Marrow product: Declaration of Eligibility, Order Form, Record of Packaging and Receipt, Certificate of Analysis, Comprehensive Report, and Declaration of Urgent Medical Need (as applicable) and circular of information.

If the integrity of the Ossium HPC, Marrow is compromised at receipt (or at any time after receipt), the site should report to Ossium within 3 business days.

Any unused Ossium HPC, Marrow that has been thawed will be destroyed per local institutional biohazard destruction policies and documented on the Ossium Record of Packaging, Receipt and Accountability Form. Any unused Ossium HPC, Marrow that has not been thawed will be returned to Ossium Health, Inc.

6.3 Thawing and Infusion

Each participating institution is to thaw and infuse Ossium products following the Instructions for Use for the varitherm device if available. If the varitherm device is unavailable for use, investigational sites may thaw using a water bath following institutional practices and guidelines. Refer to the Instructions for Use in Appendix 10 and Investigator's Brochure documents.

In the event the Ossium HPC, Marrow cryobag is compromised in any way during thawing, notify Ossium as soon as possible who will perform an expedited search for additional available donor Ossium HPC, Marrow product, or an alternative donor to determine if one exists. Refer to the Investigator's Brochure for handling instructions and recommendations on product recovery for compromised cryobags.

6.4 Dosing and Administration

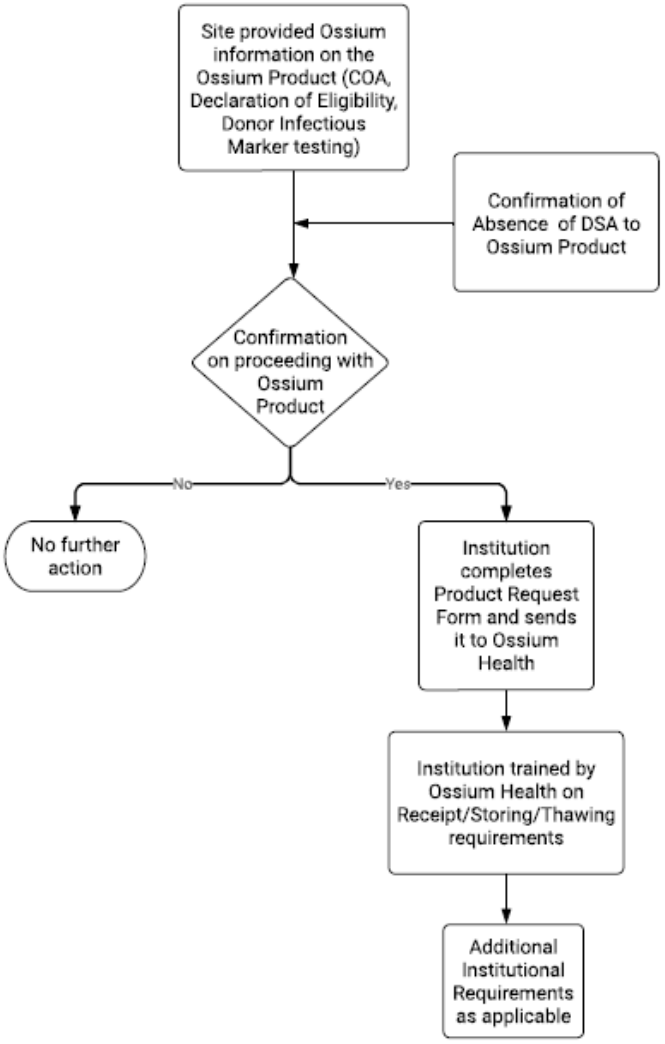
The target cell dose of pre-frozen Ossium HPC, Marrow is 3-8×10^6 CD34+ per kg patient weight for patients meeting the HOPE-II criteria with a minimum cell dose based on treating physician discretion and maximum cell dose of 8x10^6 CD34+/kg. Additionally, for HOPE-II criteria, if the minimum cell dose is not available with the planned donor, additional donor with a minimum match degree of 4/8 can be provided to the patient to allow for the target cell dose. For patients under HOPE-I program the planned target cell dose of pre-frozen Ossium HPC, Marrow is 2.5-8 x10^6 with a minimum cell dose based on treating physician discretion and maximum cell dose of 8x10^6 CD34+/kg.
There is no data available to date on if/how BMI affects safety and efficacy of the Ossium product.
The stem cell dose is in the range of hematopoietic stem cell doses used in allogeneic HCT. Previous studies used PBSC doses acceptable in traditional HCT (Guo et al., 2018; Guo et al., 2012; Guo et al., 2011; Hu et al., 2016). This dose was also found to be efficacious when previously cryopreserved grafts were used for HCT with PTCy prophylaxis for GVHD (Hamadani et al., 2020).

In regard to weight, a retrospective analysis study of 2503 adult patients receiving allogeneic hematopoietic cell transplantation found that Day +100 overall mortality in patients with higher BMI (i.e., overweight and obese patients) was no different than patients with normal BMI. Patients with extremely low BMI (i.e., underweight) or extremely high BMI (i.e., very obese) had a higher Day +100 mortality rate compared to patients with normal BMI. Underweight category patients represented 1% study population, very obese represented 10% study population (Doney et al, 2019).

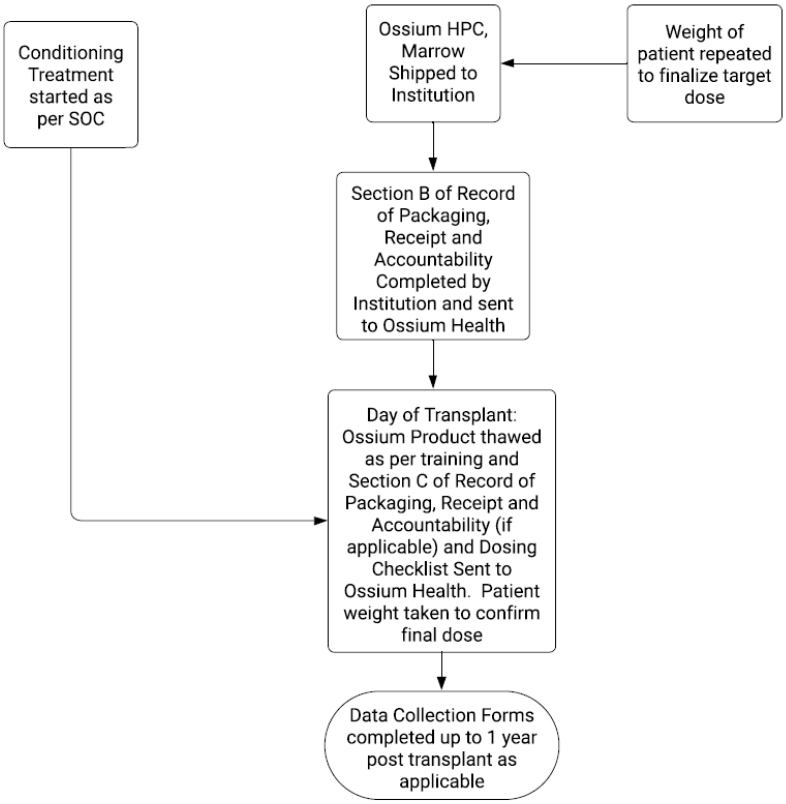
At the treating physician's discretion, additional Ossium HPC, Marrow product, if available, may be requested.

6.5 HOPE Program (HOPE + New HOPE) Workflow Chart

Activities Prior to Ossium Product Shipment



Shipment, Dosing and Post Transplant



7. Standard of Care Treatments

7.1 Conditioning Treatments

Institution will follow their standard care of planned conditioning treatment for the patient or the site protocol as planned. No additional institutional protocol changes are necessary for the patient to receive Ossium HPC, Marrow and participate in the HOPE Program (HOPE-I + HOPE-II).

7.2 Post Transplant Treatments

Institution will follow their standard of care planned post-transplant treatment plan for the patients or site protocol. There is no additional post-transplant treatment that is required for participation in the HOPE Program (HOPE-I + HOPE-II).

7.3 Supportive Care

Subjects should receive supportive care including transfusions, antiemetics, infection prophylaxis, and nutritional support according to institutional guidelines or site protocol.

8. HOPE Program (HOPE-I + HOPE-II) Follow Up

Institution will follow their standard of care follow up activities including labs and any assessments that are completed for monitoring of patient's health or site specific protocol. Information of the patient's engraftment, disease status, adverse events and occurrence of GVHD if applicable will be done as institutional protocol and the data will be provided to Ossium Health. Donor myeloid chimerism in whole blood (unsorted) to be completed; and CD3; CD33 subsets if available on Day 30 post transplant, Day 100 post transplant. The diagnosis and staging of acute and chronic GVHD will be done based on standard practices.

9. Adverse Events and Serious Adverse Events

9.1 Definition of Adverse Event

Adverse event (AE) means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)). An AE can be an unfavorable and unintended sign (including an abnormal laboratory finding), symptom, syndrome or disease associated with or occurring during the use of an Ossium HPC, Marrow whether or not considered related to it. All AEs related to Ossium HPC, Marrow should be reported in the data collection form within 5 days of occurrence for up to 2 years post transplant.

10. Data Collection

For each patient receiving Ossium HPC, Marrow through the HOPE Program (HOPE-I + HOPE-II), an intake form (available in Appendix 11) will be collected to confirm eligibility and availability of donor. Once the transplant is completed, a data collection form will be collected. The following information is collected in the data collection form(available in the Appendix 12) and timing of providing the information is shown below.

- Conditioning and Post Transplant Data Collection Form (within 5 days of transplant)
- Neutrophil Engraftment (ANC ≥ 500/µL for 3 consecutive days, within 5 days post neutrophil engraftment or by Day 28 whichever is earlier)
- Platelet Engraftment (≥ 20,000/µl for 3 consecutive days in absence of transfusion for 7 consecutive days, within 5 days post platelet engraftment or by Day 56 whichever is earlier)
- Donor myeloid chimerism in whole blood (unsorted); and CD3; CD33 subsets if available(within 5 days of completion or periodic reporting on Day 30 post transplant, Day 60 post transplant and Day 100 post transplant).
- Disease Evaluation (within 5 days post bone marrow aspirate/bone marrow biopsy or periodic reporting on Day 180,Day 365, Day 545 and Day 730)
- aGVHD, late onset aGVHD and cGVHD Information (within 5 days of diagnosis and period reporting on Day 30, Day 60, Day 100, Day 180, Day 365, Day 545 and Day 730 post-transplant)
- SAE Information associated with Ossium HPC, Marrow Product, not related to transplant procedure (if applicable, within 24 hrs of event. If no SAE, periodic reporting on Day 180,Day 365, Day 545 and Day 730 post-transplant)
- AE associated with Ossium HPC, Marrow Product, not related to transplant procedure (if applicable, within 5 days of event, If no AE, periodic reporting on Day 180,Day 365, Day 545 and Day 730 post-transplant)

Data collection is the responsibility of the hospital staff at the institution under the supervision of the site treating physician. The treating physician is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

11. Abbreviations

AE	Adverse Event
BM	Bone Marrow
CTCAE	Common Terminology Criteria for Adverse Events
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMV	Cytomegalovirus
Cy	Cyclophosphamide
DMSO	Dimethyl Sulfoxide
DNA	Deoxyribnucleic Acid
DSA	Donor-Specific Antibodies
EBV	Epstein-Barr Virus
FDA	Food and Drug Administration
FISH	Fluorence in situ Hybridization
GMP	Good Manufacturing Practices
GVHD	Graft Versus Host Disease
HCT	Hematopoietic Cell Transplantation
HCT-CI	HCT-Specific Co-Morbidity Index
HIPAA	Health Insurance Portability and Accountability Act
HLA	Human Leukocyte Antigens
HSV	Herpes Simplex Virus
HTLV	Human T-Lymphotrophic Virus
IB	Investigator's Brochure
IgG	Immunoglobulin G
IgM	Immunoglobulin M
MMUD	Mismatched unrelated donor
NMDP	National Marrow Donor Program
NRM	Non-relapse related mortality
OS	Overall Survival
PBSC	Peripheral blood stem cell
PFT	Pulmonary Function Tests
PTCy	Post-Transplant Cyclophosphamide
QC	Quality Control
RIC	Reduced Intensity Conditioning
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TC	Transplant Centers
TNC	Total Nucleated Cell Count
UCB	Umbilical Cord Blood
US	United States
VZV	Varicella Zoster Virus
WNV	West Nile Virus

12. References

Anasetti, C., Logan, B. R., Lee, S. J., Waller, E. K., Weisdorf, D. J., Wingard J. R., …Blood and Marrow Transplant Clinical Trials Network. (2012). Peripheral-blood stem cells versus bone marrow from unrelated donors. New England Journal of Medicine, 367(16), 1487-1496.

Auletta, J. J., Novakovich, J. L., Stritesky, G. L., Newman, J., Fridy-Chesser, S., Hailperin, K., & Devine, S. M. (2021). Meeting the Demand for Unrelated Donors in the Midst of the COVID-19 Pandemic: Rapid Adaptations by the National Marrow Donor Program and Its Network Partners Ensured a Safe Supply of Donor Products. Transplantation and Cellular Therapy, 27(2), 133-141.

Bacigalupo, A., Lamparelli, T., Barisione, G., Bruzzi, P., Guidi, S., Alessandrino, P.E., …Gruppo Italiano Trapianti Midollo Osseo (GITMO). (2006). Thymoglobulin prevents chronic graft-versus-host disease, chronic lung dysfunction, and late transplant-related mortality: long-term follow-up of a randomized trial in patients undergoing unrelated donor transplantation. Biology of Blood and Marrow Transplantation, 12, 560-565.

Bashey, A., & Solomon, S.R. (2014). T-cell replete haploidentical donor transplantation using post-transplant CY: an emerging standard-of-care option for patients who lack an HLA-identical sibling donor. Bone Marrow Transplantation, 49, 999-1008.

Berz, et al. (2007). Cryopreservation of Hematopoietic Stem Cells. American Journal of Hematology. Jun; 82(6): 463–472

Blazar BR, Lasky LC, Perentesis JP, Watson KV, Steinberg SE, Filipovich AH, Orr HT, Ramsay NK. (1986). Successful donor cell engraftment in a recipient of bone marrow from a cadaveric donor. Blood, 67(6):1655-60.

Blood and Marrow Transplant Clinical Trials Network (2013). Technical Manual of Procedures, v3.0.

Brunstein, C.G., Fuchs, E.J., Carter, S.L., Karanes, C., Costa, L.J., Wu, J., … Blood and Marrow Transplant Clinical Trials Network. (2011). Alternative donor transplantation after reduced intensity conditioning: results of parallel phase 2 trials using partially HLA-mismatched related bone marrow or unrelated double umbilical cord blood grafts. Blood, 118, 282-288.

Chakraverty, R., Orti, G., Roughton, M., Shen, J., Fielding, A., Kottaridis, P., …Mackinnon, S. (2010). Impact of in vivo alemtuzumab dose before reduced intensity conditioning and HLA-identical sibling stem cell transplantation: pharmacokinetics, GVHD, and immune reconstitution. Blood, 116, 3080-3088.

Choi S.W., & Reddy, P. (2014). Current and emerging strategies for the prevention of graft- versus-host disease. Nature Reviews Clinical Oncology, 11, 536-547.

Dehn, J., et al., Selection of unrelated donors and cord blood units for hematopoietic cell transplantation: guidelines from the NMDP/CIBMTR. Blood, 2019. 134(12): p. 924-934.

Dominietto, A., et al. Transplant-related Mortality and Long-term Graft Function are Significantly Influenced by Cell Dose in Patients Undergoing Allogeneic Marrow Transplantation. Blood. 2002;100(12):3930-3934.

Doney, K., McMillen, K., Buono, L., Deeg, H.J., Gooley, T. (2019). Impact of Body Mass Index on Outcomes of Hematopoietic Stem Cell Transplantation in Adults. *Biology of Blood and Marrow Transplantation*, 25(3), 613-620. doi: 10.1016/j.bbmt.2018.10.006.

Fernandez-Sojo, J., Azqueta, C., Valdivia, E., Martorell, L., Medina-Boronat, L., Martinez-Llonch, N., … Villa, J., Querol, S. (2021). Cryopreservation of unrelated donor hematopoietic stem cells: the right answer for transplantations during the COVID-19 pandemic? Bone Marrow Transplant 56, 2489–2496. *https://doi.org/10.1038/s41409-021-01367-x*

Ferrebee, J. W., Atkins, L., Lochte, H. L., … Thomas, E. D. (1959). The collection storage, and preparation of viable cadaver marrow for intravenous use. Blood 14(2), 140-147. *https://doi.org/10.1182/blood.V14.2.140.140*

Furst, D., et al., High-resolution HLA matching in hematopoietic stem cell transplantation: a retrospective collaborative analysis. Blood, 2013. 122(18): p. 3220-9.

Gauntner, T.D., et al. Association of CD34 Cell Dose with 5-year Overall Survival after Peripheral Blood Allogeneic Hematopoietic Cell Transplantation in Adults with Hematologic Malignancies. Transplant Cell Therapy 2022;28:88-95.

Gragert, L., et al., HLA match likelihoods for hematopoietic stem-cell grafts in the U.S. registry. N Engl J Med, 2014. 371(4): p. 339-48.

Guo, M., Hu, K. X., Yu, C. L., Sun, Q. Y., Qiao, J. H., Wang, D. H., …Ai, H. S. (2011).Infusion of HLA-mismatched peripheral blood stem cells improves the outcome of chemotherapy for acute myeloid leukemia in elderly patients. Blood, 117(3), 936-941.doi:10.1182/blood-2010-06-288506

Guo, M., Hu, K. X., Liu, G. X., Yu, C. L., Qiao, J. H., Sun, Q. Y., …Ai, H. S. (2012). HLA-mismatched stem-cell microtransplantation as postremission therapy for acute myeloidleukemia: long-term follow-up. J Clin Oncol, 30(33), 4084-4090.doi:10.1200/JCO.2012.42.0281

Guo, M., Chao, N. J., Li, J. Y., Rizzieri, D. A., Sun, Q. Y., Mohrbacher, A., …Microtransplantation Interest, G. (2018). HLA-Mismatched Microtransplant in Older Patients Newly Diagnosed With Acute Myeloid Leukemia: Results From the Microtransplantation Interest Group. JAMA Oncol, 4(1), 54-62.doi:10.1001/jamaoncol.2017.2656

Hamadani, M., Zhang, M., Tang, X., Mingwei, F., Brunstein, C., Chhabra, S., … Horowitz, M. M. (2020). Graft Cryopreservation Does Not Impact Overall Survival after Allogeneic Hematopoietic Cell Transplantation Using Post-Transplantation Cyclophosphamide for Graft-versus-Host Disease Prophylaxis. Biology of Blood and Marrow Transplantation, 26(7), 1312-1317.

Horowitz, M.M., Gale, R.P., Sondel, P.M., Goldman, J.M., Kersey, J., Kolb, H.J., ...Bortin,

M.M. (1990). Graft-versus-leukemia reactions after bone marrow transplantation. Blood, 75, 555-562.

Hsu, J. W., Farhadfar, N., Murthy, H., Logan, B. R., Bo-Subait, S., Frey, N. …Wingard, J. R. (2021). The Effect of Donor Graft Cryopreservation on Allogeneic Hematopoietic Cell Transplantation Outcomes: A Center for International Blood and Marrow Transplant Research Analysis. Implications during the COVID-19 Pandemic. Transplantation and Cellular Therapy, 27(6), 507-516.

Hu, K. X., Sun, Q. Y., Guo, M., Qiao, J. X., Yu, C. L., Qiao, J. H., Dong, Z., Sun, W. J., Zuo, H. L., Huang, Y. J., Cai, B., & Ai, H. S. (2016). A Study of Human Leukocyte Antigen Mismatched Cellular Therapy (Stem Cell Microtransplantation) in High-Risk Myelodysplastic Syndrome or Transformed Acute Myelogenous Leukemia. *Stem cells translational medicine*, *5*(4), 524–529. https://doi.org/10.5966/sctm.2015-0196

Jimenez, A.M., et al. Post-Transplant Cyclophosphamide (PTCy) is Associated with Superior GvHD-free, Relapse-free (GRFS) in HLA-Mismatched Unrelated Donor (MMUD) Hematopoietic Cell Transplantation. 2022 Tandem Meetings, Abstract #406.

Kekre, N., & Antin, J.H. (2014). Hematopoietic stem cell transplantation donor sources in the 21st century: choosing the ideal donor when a perfect match does not exist. Blood, 124, 334- 343.

Kollman, C., Howe, C.W., Anasetti, C., Antin, J.H., Davies, S.M., Filipovich, A.H., … Confer, D.L. (2001). Donor characteristics as risk factors in recipients after transplantation of bone marrow from unrelated donors: the effect of donor age. Blood, 98, 2043-2051.

Kollman, C., Spellman, S.R., Zhang, M.J., Hassebroek, A., Anasetti, C., Antin, J.H., … Eapen, M. (2016). The effect of donor characteristics on survival after unrelated donor transplantation for hematologic malignancy. Blood, 127, 260-267.

Kongtim, P., Cao, K., & Ciurea, S.O. (2016). Donor Specific Anti-HLA Antibody and Risk of Graft Failure in Haploidentical Stem Cell Transplantation. Advances in Hematology, 2016, 1-10.

Kröger, N. (2012). Allogeneic stem cell transplantation for elderly patients with myelodysplastic syndrome. Blood, 119(24), 5632-5639.

Kosuri, S., et al., Prospective Evaluation of Unrelated Donor Cord Blood and Haploidentical Donor Access Reveals Graft Availability Varies by Patient Ancestry: Practical Implications for Donor Selection. Biol Blood Marrow Transplant, 2017. 23(6): p. 965-970.

Lee, S.J., et al., High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. Blood, 2007. 110(13): p. 4576-83.

Lee, D.W., Santomasso, B.D., Locke, F.L… Neelapu, S. S. (2018).. ASBMT Consensus Grading for Cytokine Release Syndrome and Neurological Toxicity Associated with Immune Effector Cells. Biology of Blood and Marrow Transplantation, 25(4), 625-638.

Luznik, L., O'Donnell, P.V., Symons, H.J., Chen, A.R., Leffell, M.S., Zahurak, M., …Fuchs, E.J. (2008). HLA-haploidentical bone marrow transplantation for hematologic malignancies using

nonmyeloablative conditioning and high-dose, post transplantation cyclophosphamide. Biology of Blood and Marrow Transplantation, 14, 641-650.

Monzr M. Al Malki et al. (2024). Post-transplant cyclophosphamide-based graft-*versus*-host disease prophylaxis following mismatched unrelated donor peripheral blood stem cell (PBSC) transplantation. JCO 42, 6503-6503

Mayumi, H., Umesue, M., & Nomoto, K. (1996). Cyclophosphamide-induced immunological tolerance: an overview. Immunobiology, 195, 129-139.

NMDP website. How does a patient's ethnic background affect matching? *https://bethematch.org/transplant-basics/matching-patients-with-donors/how-does-a-patients-ethnic-background-affect-matching/*

Olsson, R. F., Logan, B. R., Chaudhury, S., Zhu, X., Akpek, G., Bolwell, B. J., …Cooke, K. R. (2015). Primary graft failure after myeloablative allogeneic hematopoietic cell transplantation for hematologic malignancies. Leukemia, 29(8), 1754-1762.

Pagel, J.M., et al. Rapid Donor Identification Improves Survival in High-Risk First-Remission Patients with Acute Myeloid Leukemia. J Oncol Practice, 2020. Jun;16(6):e464-e475.

Perkins, J., Kim, J., Anasetti, C., Fernandez, H., Perez, L.E., Ayala, E., … Field, T.L. (2012). Maximally Tolerated Busulfan Systemic Exposure in Combination with Fludarabine as Conditioning before Allogeneic Hematopoietic Cell Transplantation. Biology of Blood and Marrow Transplantation, 18, 1099-1107.

Pidala J., Lee S.J., Ahn, K.W., Spellman, S., Wang, H.L., Aljurf, M., … Anasetti, C. (2014). Nonpermissive HLA-DPB1 mismatch increases mortality after myeloablative unrelated allogeneic hematopoietic cell transplantation. Blood, 124, 2596-2606.

Pidala, J., Alousi, A., & MacMillan, M. (2015). A Randomized, Phase II, Multi-Center, Open Label, Study Comparing Sirolimus to Prednisone in Patients with Minnesota Standard Risk, Ann Arbor 1/2 Confirmed Acute Graft-Versus-Host Disease. BMT CTN Clinical Trials Network.

Potter, V.T., Krishnamurthy, P., Barber, L.D., Lim, Z., Kenyon, M., Ireland, R.M., …Mufti, G.J. (2014). Long-term outcomes of alemtuzumab-based reduced-intensity conditioned hematopoietic stem cell transplantation for myelodysplastic syndrome and acute myelogenous leukemia secondary to myelodysplastic syndrome. Biology of Blood and Marrow Transplantation, 20, 111-117.

Przepiorka, D., Weisdorf, D., Martin, P., Klingemann, H. G., Beatty, P., Hows, J., & Thomas, E. D. (1995). 1994 Consensus Conference on Acute GVHD Grading. Bone Marrow Transplantation, 15(6), 825-828.

Shaw, B.E., Russell, N.H., Devereux, S., Das-Gupta, E., Mackinnon, S., Madrigal, J.A., … Byrne, J.L. (2005). The impact of donor factors on primary non-engraftment in recipients of reduced intensity conditioned transplants from unrelated donors. Haematologica, 90, 1562- 1569.

Shaw, B.E., et al., Development of an Unrelated Donor Selection Score Predictive of Survival after HCT: Donor Age Matters Most. Biol Blood Marrow Transplant, 2018. 24(5): p. 1049-1056.

Shaw, B.E., Jimenez-Jimenez, A. M., Burns, L. J., Logan, B. R., Khimani, F., Shaffer, B. C., …Bolanos-Meade, J. (2021). National Marrow Donor Program- Sponsored Multicenter, Phase II Trial of HLA-Mismatched Unrelated Donor Bone Marrow Transplantation Using Post-Transplant Cyclophosphamide. Journal of Clinical Oncology, 29 (18), 1971-1982.

Seshan, V. E., (2018). Clinical Trial Design and Data Analysis Functions. Retrieved from https://cran.r-project.org/web/packages/clinfun/clinfun.pdf

Thomas ED, Lochte HL Jr, Lu WC, Ferrebee JW. (1957). Intravenous infusion of bone marrow in patients receiving radiation and chemotherapy. N Engl J Med, 257(11), 491-6.

U. S. Census Bureau (2020). 2020 Census Statistics Highlight Local Population Changes and Nation's Racial and Ethnic Diversity. Retrieved from *https://www.census.gov/newsroom/press-releases/2021/population-changes-nations-diversity.html*

United States Food and Drug Administration (US FDA) (2015). Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products. Retrieved from: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-design-early-phase-clinical-trials-cellular-and-gene-therapy-products*

Wadsworth K, Albrecht M, Fonstad R, Spellman S, Maiers M, Dehn J. Unrelated donor search prognostic score to support early HLA consultation and clinical decisions. Bone marrow transplantation 2016; 51(11): 1476-1481. doi: 10.1038/bmt.2016.162

Walker, I., Panzarella, T., Couban, S., Couture, F., Devins, G., Elemary, M., …Canadian Blood and Marrow Transplant Group. (2016). Pretreatment with anti-thymocyte globulin versus no anti-thymocyte globulin in patients with haematological malignancies undergoing haemopoietic cell transplantation from unrelated donors: a randomised, controlled, open- label, phase 3, multicentre trial. The Lancet Oncology, 17, 164-173.

Appendix 1 (Regulatory Links)

1. Code of Federal Regulations. 45 CFR Part 46. Protection of Human Subjects. https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46
2. Code of Federal Regulations. 21 CFR Part 1271.Human Cells, Tissues, and Cellular and Tissue-Based Products. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-L/part-1271
3. Attachment B - Deceased Donor Intervention Research 45 CFR part 46. Issues Surrounding Deceased Donor Intervention Research under 45 CFR part 46. https://www.hhs.gov/ohrp/sachrp-committee/recommendations/august-12-2020-attachment-b-deceased-donor-intervention/index.html
4. National Academies of Sciences, Engineering, and Medicine. 2017. Opportunities for Organ Donor Intervention Research: Saving Lives by Improving the Quality and Quantity of Organs for Transplantation. Washington, DC: The National Academies Press. https://doi.org/10.17226/24884
5. Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use. https://www.fda.gov/media/109176/download

Appendix 2 (Product Comprehensive Report and Certificate of Analysis)

OSSIUM HEALTH™

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DIN: _____ GRID: _____

Product Comprehensive Report and Certificate of Analysis

Processing & Storage Facility:	Ossium Health, Inc.
Product Type:	Cryopreserved HPC, Marrow
Product Description:	Allogeneic Investigational Product
Donor Type:	Unrelated Donor
Donor Sex:	
Donor Date of Birth:	
Donor's Age at Collection:	yrs
ABO/Rh:	
Donor Race:	
Donor Ethnicity:	
Eligibility Determination:	☐ Eligible ☐ Incomplete ☐ Ineligible
Donor CMV Status:	

Processing Details	
Collection Date/Time and Zone:	
Process, Test and Freeze Date:	
Product Modification:	Red Blood Cell Reduced
Product Additives:	☐ Plasma-Lyte A ☐ 10% DMSO, ☐ 5% DMSO
Specific Anticoagulant Name:	☐ None ☐ Not Specified
3rd Party Blood Component Name:	Human Serum Albumin USP
Processing Type:	Proprietary
Bag Type:	☐ Charter Medical Cell Freeze® 250 ☐ Origen Cryostore™ 250
Storage Temperature:	-150°C or colder

Bag Serial Number, Unique ID and Division Code	Volume (mL)	CD34+ Cell Count x 10^7/bag	CD45+ Cell Count x 10^9/bag	CD3+ Cell Count x 10^8/bag
	65 mL			

Total Quantity of Bags: **Total Volume for all Bags: mL**

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DIN: _____ GRID: _____

Testing Summary

Test	Method	Result
Total Viable Nucleated Cell Count (TNC)*	Flow Cytometry CD45+	x 10 all bags
Total CD34+/all bags	Flow Cytometry	x 10 for all bags
Viability*	7-AAD Flow Cytometry	%
CFU-GM/GEMM Count	Progenitor Assay	per 10^5 TNC
Hematocrit (%)	Automated Cell Counter	%
Total viable CD3+ Cell Count*	Flow Cytometry	x 10 all bags
Final Sterility: Bacterial	14-Day Culture	
Final Sterility: Fungal	14-Day Culture	

*This test was developed, and its performance characteristics determined by Ossium Health. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.

HLA Preliminary Report										
A	B	C	DRB1	DRB3	DRB4	DRB5	DQB1	DQA1	DPB1	DPA1
Source							Typing Date			

HLA Confirmatory Typing										
A	B	C	DRB1	DRB3	DRB4	DRB5	DQB1	DQA1	DPB1	DPA1
Source							Typing Date			

Donor Infectious Disease Markers

Laboratory and Test Kit Certification
• All required tests were performed by a laboratory certified by the Clinical Laboratory Improvement Amendments (CLIA) or that meets equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS). • All required tests were performed using test kits approved by the U.S. Food and Drug Administration (FDA) for donor screening.
Blood Collection Date:

Test	Interpretation
Hepatitis B Virus (HBV)	
HBsAg (hepatitis B surface antigen screening test)	
Anti-HBc Total (hepatitis B core antibody, IgG + IgM)	
HBV NAT (nucleic acid test/PCR)	

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DIN: _____ GRID: _____

Test	Interpretation
Hepatitis C Virus (HCV)	
Anti-HCV	
HCV NAT (nucleic acid test/PCR)	
Human T-Lymphotropic Virus (HTLV)	
Anti-HTLV I/II (HTLV Antibodies)	
Human Immunodeficiency Virus (HIV)	
Anti-HIV-1 and anti-HIV-2 +O (HIV antibodies)	
HIV-1 NAT (nucleic acid test/PCR)	
Syphilis, WNV, Chagas	
Syphilis	
WNV NAT (nucleic acid test/PCR)	
Trypanosoma cruzi (Chagas)	
Cytomegalovirus (CMV), Epstein Barr Virus (EBV), Toxoplasma	
Anti-CMV Total (IgG + IgM)	
CMV IgG antibody	
CMV IgM antibody	
EBV IgG	
EBV IgM	
Toxoplasma IgG	
Toxoplasma IgM	
Immunohematology	
ABO/Rh:	**Confirmatory ABO:**

Comments:

☐ N/A

Review

Role	Print Name	Signature	Date
Completed by:			
Verified by:			
Laboratory Director:			
Quality Assurance:			

Appendix 3 (Declaration of Eligibility)

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Declaration of Eligibility

Identification Information	
DIN:	GRID:

SECTION 1 Eligibility Determination

Based on a review of the health history screening, infectious disease testing, physical assessment, and other medical records the donor eligibility is:

- **A.** ☐ **ELIGIBLE** → Section 2 is N/A. Complete Section 3
- **B.** ☐ **INELIGIBLE** → Complete Sections 2 and 3
- **C.** ☐ **INCOMPLETE (FDA Eligibility)*** → Complete Sections 2 and 3

**Note: Post Collection Amendment of Donor Eligibility may follow, as applicable; and product shipped in quarantine per 21 CFR 1271.60*

SECTION 2 Documentation of Eligibility Determination

Due to urgent medical need for transplantation, it is acceptable to transplant cells from the above product. Details of donor screening and testing completed, not completed and/or reasons for ineligibility or incomplete eligibility, as applicable, have been provided here and as part of the Declaration of Urgent Medical Need documentation prior to shipment.

A. INFECTIOUS DISEASE TESTING ☐ **Not Applicable** (All testing and results meet FDA regulations)

1. ☐ Some of the infectious disease testing was not performed according to FDA regulations. → Label 1
2. ☐ None of the infectious disease testing was performed according to FDA regulations. → Label 1
3. ☐ Some of the infectious disease testing indicates risk factors for relevant communicable diseases. → Label 2

B. DONOR SCREENING RESULTS ☐ **Not Applicable** (Screening results meet FDA regulations)

1. ☐ Health history screening indicates the presence of risk factors of relevant communicable diseases. → Label 3
2. ☐ Physical assessment indicates physical evidence of risk factors for relevant communicable diseases. → Label 3
3. ☐ Review of medical records indicate risk factors for relevant communicable diseases. → Label 3
4. ☐ Health history screening, physical assessment, and/or review of available relevant medical records was not performed per FDA requirements. → Label 1

SECTION 3: Responsible Party Making Eligibility Determination

I determined the donor's eligibility:

Printed Name **Signature** **Date**

My establishment is:

Institution Name	Ossium Health
Street address	5742 W. 74th St.
City/State/Zip Code	Indianapolis, IN 46278

Appendix 4 (Declaration of Urgent Medical Need)

OSSIUM HEALTH®

Declaration of Urgent Medical Need
Ossium Health Cryopreserved HPC, Marrow Product

Ossium Health®
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Identification Information	
DIN:	Recipient Name or RID:
GRID:	Recipient DOB or Study Subject #:

SECTION 1 Ineligibility / Incomplete Status	
Evaluation of donor infectious disease marker testing, answers to donor health history screening questionnaire, donor physical assessment, and review of readily available medical records indicate eligibility status of:	
☐ **INELIGIBLE**	• There are identified risk(s) of communicable disease transmission to the transplant recipient and donor screening/testing has been completed per FDA and Ossium Health requirements.
☐ **INCOMPLETE**	• Donor screening and/or testing was not fully performed per FDA or Ossium Health requirements. There may be an unidentified communicable disease risk to the recipient. • If the eligibility status is unable to be completed per FDA and Ossium Health regulations, regardless of any previously identified communicable risk, the eligibility status will remain incomplete.

Documents marked below provide details on the eligibility status:

1. Risk Assessment – Relevant Medical Records Including Physical Findings

☐ Assessment was not performed per requirements. (Additional details, if applicable):

☐ Donor relevant medical records indicate the presence of risk factors of relevant communicable diseases. (Additional details, if applicable):

☐ Donor physical assessment indicates the presence of risk factors of relevant communicable disease agents or disease. (Additional details, if applicable):

☐ Physical Findings (if applicable):

2. Risk Assessment – Infectious Disease Marker Testing

☐ Required tests were not performed and/or sample was not collected within the required time frame. (Additional details, if applicable):

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Declaration of Urgent Medical Need
Ossium Health Cryopreserved HPC, Marrow Product

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Identification Information	
DIN:	Recipient Name or RID:
GRID:	Recipient DOB or Study Subject #:

☐ Some or all tests were not performed in a CMS approved laboratory and/or were not FDA licensed, approved, or cleared donor screening tests, performed in accordance with the manufacturer's instructions. (Additional details, if applicable):

☐ Testing indicates positive result(s). (Additional details, if applicable):

3. Incomplete Eligibility – Missing Information

☐ No additional FDA required donor screening or testing is available; unit shipped as quarantined per 21 CFR 1271.60 (as applicable)

☐ Additional FDA required donor screening and/or testing will follow; unit shipped as quarantined per 21 CFR 1271.60 (as applicable)
(Additional details, if applicable):

Completed by:

Printed Name Signature Date

SECTION 2 Transplant Center Acknowledgment

Due to the donor's ineligible or incomplete status, urgent medical need must be documented for Ossium Health to proceed with shipment. Urgent medical need indicates the benefits associated with the transplantation of this product outweighs the potential or unknown risk of disease transmission considerations from the product.
After reading the above statement and reviewing the relevant documentation, I elect to: (Mark one box below)

☐	Receive the cryopreserved product
☐	Decline receiving the cryopreserved product and release the unit(s) from the search

Transplant Physician:

Printed Name Signature Date

Important: Return completed form to Ossium Health as soon as possible prior to the start of the recipient's preparative regimen or shipment of cryopreserved product, whichever occurs first.
For PRESERVE I Study: PRESERVE@ossiumhealth.com
For HOPE Program: HOPE@ossiumhealth.com

Appendix 5 (Cryopreserved HPC, Marrow Product Request)

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Cryopreserved HPC, Marrow Product Request

Section One - Completed by Transplant Coordinator or designee
Date Requested:
DIN:
GRID:
Recipient Name or RID (for PRESERVE I):
Recipient DOB or Study Subject ID (for PRESERVE I):
Transplant study/program: ☐ PRESERVE I ☐ HOPE Program ☐ Other (specify)

Section Two - Completed by the Transplant Center
Proposed Shipment Date:
Planned Patient Prep Start Date:
Planned Infusion Date:
Total number of bags requested:
Additional product samples requested: *(Each product bag has 2 attached segments)*
Patient weight (kg):

Section Three - Cryopreserved Product Transport / Delivery Information	
• The address below is to be noted as the delivery information for shipping the cryopreserved product from Ossium Health, Inc. to the transplant center. • Frozen product samples will be sent with the product unless otherwise noted.	
Attn/Name:	
Location Name:	
Address:	
City, State, Postal Code, & Country:	
Phone:	Email

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Section Four - All Transplant Centers Must Complete

Regarding the HPC, Marrow product selected:

- I am aware the donor's CMV status is ☐ POSITIVE ☐ NEGATIVE.
- I verify that the ABO and Rh type and degree of HLA match are acceptable to proceed for the above recipient. Furthermore, the patient's transplant center has policies for determining the appropriate volume and the appropriate dose of red blood cells, cryoprotectants, and other additives. In addition, the necessary procedures are in place for receipt, storage, and infusion of the cryopreserved product at the transplant center.
- Proceeding with a cryopreserved product from Ossium Health, Inc. creates the following obligations for your transplant program:
  - Documentation in the patient's medical record that the patient is consented and eligibility for transplant has been confirmed by the treating physician.
  - Documentation in the patient's medical record that the patient has been informed of the plans to use a cryopreserved product.
  - Provision of updates to your assigned case manager or coordinator of the patient's condition.
  - Notification to your assigned case manager or coordinator if the proposed conditioning date or infusion date changes from the proposed plan.
  - Acknowledgement that if the product is not infused, Ossium Health® will be notified.

Section Five - Urgent Medical Need ☐ (Check if applicable)

I have been informed by the Ossium Health® Medical Director of the circumstances for this donor's ☐ **INCOMPLETE** or ☐ **INELIGIBLE** eligibility determination. As the Ordering Physician it is my decision to proceed with transplantation of this product due to the urgent medical need of the patient.

Additional Notes/Comments:

Roles	Print Name	Signature	Date *(DDMMMYYYY)*
Form Completed By:			
Ordering Physician:			

Appendix 6 (Shipment, Packaging and Labeling)

Shipment and Packaging

This procedure is written to comply with Department of Transportation (DOT) and International Air Transport Association (IATA) biological material shipping regulations as a measure of protecting the transporter, recipient, and community from potential exposure. The ultimate responsibility is on the shipper, Ossium Health.

All biological materials shipped from Ossium Health are classified as Exempt Human Specimens. Exempt human specimens are not regulated; however, they must be triple packed and labeled correctly as described below.

No test specifications are needed. The shipper can assemble their own materials as listed below:

1. A primary leak proof container contains the specimen.
    a. The sample may not total more than 500mL of liquid or 500g of solid material.
        i. Two or more containers may be combined but together must not exceed the amounts listed above.
    b. The primary container must be surrounded by absorbent material.
        i. The quantity must be sufficient enough to absorb all sample if released.
2. A secondary leak proof container holds the primary container surrounded by absorbent material.
    a. The primary container(s) should fit snugly within the secondary container.
    b. The secondary container cannot serve as the outer shipping container.
    c. Examples of acceptable secondary containers include:
        i. 50mL conical tubes
        ii. Sealed plastic bags
        iii. Other sealed plastic containers
3. The outer shipping container should be rigid and made of fiberboard or plastic.

Packaging Labeling

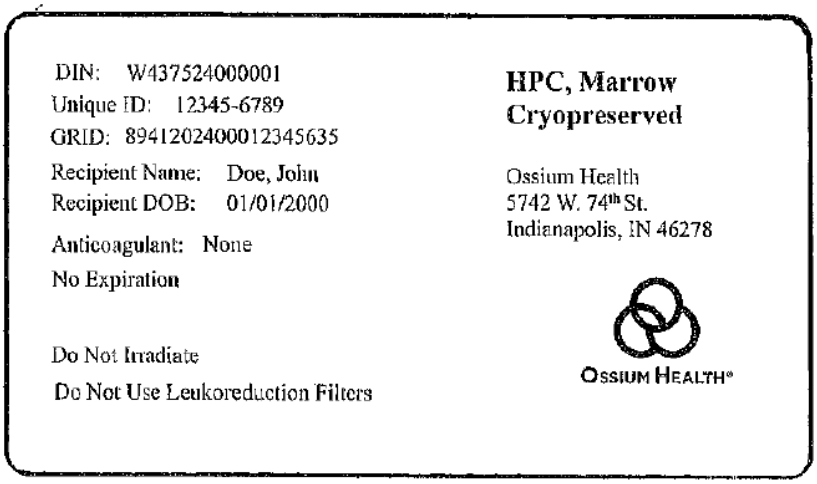
1. Appropriate markings must be present on any package surface except the bottom.
2. The following markings are always required:
    a. Shipper name, address, and contact info
    b. Receiver name (consignee), address, and contact info
    c. The words “EXEMPT HUMAN SPECIMEN”
    d. Biohazard symbol
3. When shipping dry ice, A Class 9 UN1845 dry ice label and the net quantity of dry ice in the package is required.
4. Shipments are not limited to the above labels. Additional labels may be affixed to the box (e.g., fragile, refrigerate upon arrival, freeze upon arrival, etc.).

Product Labeling

All labels are clear, legible, indelible, and secured on all products to enable tracking of the cellular product through the processing steps to storage.

An example of the final product label is provided below, with a clinical label provided on the investigational product bag and a tie tag which is attached to the bag at the time of shipment:

HPC, Marrow Final Product Label



Cryopreserved HPC, Marrow Product Warning Labels

Appendix 7 (Record of Packaging, Receipt and Accountability)

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logistics@ossiumhealth.com

Record of Packaging, Receipt and Accountability

Refer to the Accompanying Product Comprehensive Report and Certificate of Analysis for Additional Information

Section A: Release (To be completed by Ossium Health)				
DIN:	GRID:			
RID (PRESERVE I):				N/A ☐
Study Subject # (PRESERVE I):				N/A ☐
Recipient Name: (HOPE/Other)				N/A ☐
Recipient DOB: (HOPE/Other)				N/A ☐
Product Type: Cryopreserved HPC, Marrow				
Collection Date/Time (EST/EDT):				
Number of product bags				
Number of product samples:				
Cable/Zip Tie #s				

Accompanying documents required to be included:

- **OHC-FRM-0242** *Declaration of Eligibility*
- **OHC-FRM-0244** *Chain of Custody Cryopreserved HPC, Marrow* (or Cryoport equivalent)
- **OHC-FRM-0245** *Dosing Checklist* (PRESERVE Study only)
- **OHC-FRM-0286** HPC, Marrow Dosing Checklist (HOPE Program and others)
- **OHC-FRM-0247** *IFU for Thawing Cryopreserved HPC, Marrow Using the varitherm*
- **OHC-FRM-0249** *Product Comprehensive Report and Certificate of Analysis*
- **OHC-FRM-0277** *Summary of Records HPC, Marrow*
- **OHC-IFU-0005** *HPC, Marrow Instructions for Use*
- **OHC-FRM-0258** *Declaration of Urgent Medical Need Ossium Health Cryopreserved HPC, Marrow Product* ☐ N/A
- **OHC-FRM-0289** *Exceptional Release for Urgent Medical Need* ☐ N/A

I have examined the identification on all products, tubes, and accompanying documents. I verify they all accurately reflect the information listed above.

Ossium Health Releaser: Print Name *Signature* *Date:*

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Section B: Transplant Center Instructions
• Follow Instructions for Receiving and Returning LN2 Dry Shipper – HPC, Marrow • **DO NOT OPEN CRYOSHIPPER IF THE RECIPIENT'S TRANSPLANT IS DELAYED > 5 DAYS OR HAS BEEN CANCELLED. THE HPC, MARROW CAN NOT BE RETURNED TO OSSIUM HEALTH ONCE THE DRY SHIPPER HAS BEEN OPENED. Contact Ossium Health for instructions (see email at bottom of page).**

Section B: Receipt (To be completed by TC)			
Received:	Date: (*DDMMMYYYY*)	Time: *(24 hr)*	Time Zone:
Data logger temperature at time of arrival:_____°C (Must be ≤ -150 °C)		TC thermometer temperature at time of arrival _____°C (Must be ≤ -150 °C)	
Number of product bags: _____		Number of product samples (segments):_____	
Time cryoshipper opened (24hr)			__ __:__ __
Cryoshipper arrived in good condition?			☐ YES ☐ NO*
Cable/Zip Ties intact and numbers match page 1?			☐ YES ☐ NO*
Required labeling and documentation present and complete?			☐ YES ☐ NO*
Data logger and TC temperature **≤ -150 °C**			☐ YES ☐ NO*
Were bags intact when removed from dry shipper?			☐ YES ☐ NO*
Were bags transferred to institutional storage within **5 minutes?**			☐ YES ☐ NO*
***For any NO response contact Ossium Health immediately. Place product in quarantine at ≤ -150 °C. DO NOT administer product until a resolution is reached.**			

Cryopreserved product(s) inspected, and form completed by:

TC Representative: Print Name ***Signature*** ***Date:*** *DDMMMYYYY*

Return a copy of completed form to:

For PRESERVE I Study: PRESERVE@ossiumhealth.com
HOPE Program: hope@ossiumhealth.com
All Others: bonemarrow@ossiumhealth.com

Appendix 8 (Dosing Checklist)

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HPC, Marrow Dosing Checklist

Identification Information			
Recipient Name:		DIN:	
Recipient DOB:		GRID:	
Recipient Day of Infusion Weight: kg		Varitherm SN:	Most recent calibration Date:
Date of Thaw/Infusion:		Water Bath SN:	Most recent calibration Date:
Time Zone:		Make/Model Water Bath: ☐ N/A	

NOTE: Please use 24-hour clock to record time

Unique Bag ID: *Ex. 711668-0123 or A0*					
Thaw Start Time:					
Thaw Stop Time:					
Volume (mL):					

Unique Bag ID: *Ex. 711668-0123 or A0*					
Thaw Start Time:					
Thaw Stop Time:					
Volume (mL):					

Thawing Checklist

#	CHECKLIST QUESTIONS	YES	NO*
1	Was the donor information verified and matched?		
2	Was the patient/recipient information verified and matched for each bag?		
3	Were the bags intact prior to thaw?		
4	Were the bags intact after the thaw procedure?		
5	Was the thawing procedure completed as per study requirements for each bag?		
6	Was product free of clumping post thaw per visual inspection of each bag?		
7	Did you receive confirmation from sponsor that there was no temperature excursion prior until receipt of product at your institution for all the bags?		
8	Was the temperature within acceptable limits during the storage time at your institution before the thaw?		

Provide details for any **NO response on the next page, including Unique Bag ID(s), and notify Ossium Health at HOPE@ossiumhealth.com (HOPE Program) or BoneMarrow@ossiumhealth.com (all others).*

Confidential and Proprietary OHC-FRM-0286 Rev. 03 Page 1 of 2

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NOTE: Prior to infusion gently mix product bags to ensure cells remain in suspension

For **NO** responses to Thawing Checklist questions, please list the Unique Bag ID and provide an explanation of the occurrence. Mark N/A if not applicable.
☐ N/A

Signatures

I hereby certify that all information above is accurate.

Roles	Print Name	Signature	Date *(DDMMMYYYY)*
Person Responsible for Thawing Product			
Person Authorized to Receive Product			
Treating Physician			

Please return this completed form to Hope@ossiumhealth.com (HOPE Program) or BoneMarrow@ossiumhealth.com (all others).

Appendix 9 (Infusion Details)

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DIN: _____ GRID: _____

HOPE Program Infusion Details

Identification Information	
Patient Name:	Date of Thaw/Infusion:
DOB:	

1. Please provide details on the infusion process:
   a. Were the HPC, Marrow products thawed at the bedside?
      ☐ Yes ☐ No
      i. If No, please provide distance/time to bedside:_____
   b. Was a blood filter used? ☐ Yes ☐ No
      i. If a blood filter was used confirm if it was a standard 170-260 micron? ☐ Yes ☐ No
      ii. If No, specify filter size:_____
      iii. If no blood filter was used, is that your standard practice?
      ☐ Yes ☐ No
   c. Were the cells pushed via a syringe? ☐ Yes ☐ No
   d. If there was a difference of procedures between the bags infused please provide details: _____
      _____
2. Please provide the infusion start time and stop time for each bag.

Unique Bag ID				
Infusion start time				
Infusion stop time				
Was entire bag infused (YES/NO)				
If No, please provide volume infused				
Was any infusion issue noticed post-thaw (YES/NO)				
If yes, please provide details				

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DIN: _____ GRID: _____

Unique Bag ID				
Infusion start time				
Infusion stop time				
Was entire bag infused (YES/NO)				
If No, please provide volume infused				
Was any infusion issue noticed post-thaw (YES/NO)				
If yes, please provide details				

Unique Bag ID				
Infusion start time				
Infusion stop time				
Was entire bag infused (YES/NO)				
If No, please provide volume infused				
Was any infusion issue noticed post-thaw (YES/NO)				
If yes, please provide details				

Form Completed by:

Print Name Signature Date

Please return the completed form to hope@ossiumhealth.com

Appendix 10 (Instructions for Use – Varitherm)

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INSTRUCTIONS FOR USE

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This Instructions for Use contains information on how to thaw and prepare for administration Ossium Health® Cryopreserved HPC, Marrow.

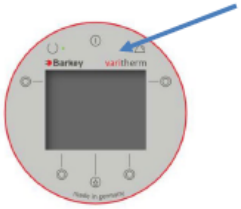
Important Information You Need to Know Before Thawing and Preparing Ossium Health® Cryopreserved HPC, Marrow for Administration.

- HPC, Marrow product must be transported and stored at or below -150°C per institutional practices until ready to thaw. Place the cryogenic container close to the Barkey varitherm thawing and heating device.
- Extreme caution must be used when handling the cassette(s) containing the frozen HPC, Marrow to ensure physical damage to the bags does not occur.
- Do not lift product by the tie tag to remove it from cassette.
- Do not hold or carry product by the tie tag.
- Verify correct patient (RID or Recipient Name) and product (DIN) before thawing.
- Refer to the Barkey Varitherm Instructions for Use V1 manual for complete safety instructions and operating directions before using the device.

Preparing to thaw Ossium Health® Cryopreserved HPC, Marrow

A. Preparing to thaw Ossium Health® Cryopreserved HPC, Marrow using the Barkey varitherm thawing and heating device.

1. Place the Varitherm on a sturdy and level surface away from other devices that generate strong electromagnetic fields.
2. Connect to power and press the top power button on the operating panel to turn the instrument on.



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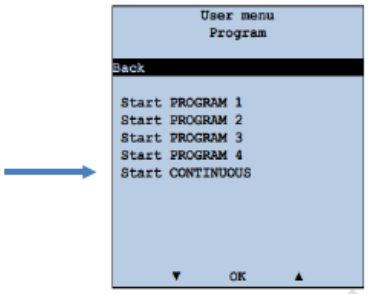
3. At a minimum of one (1) hour prior to thawing cryopreserved HPC, Marrow, run the device in CONTINUOUS mode by selecting Continuous program shortcut from the main screen or via the program list under the user menu.



   a. Set the temperature to 40 °C

   b. Warming cushions fill with water which circulates to allow the device to reach the set temperature and equilibrate.

   c. CONTINUOUS mode maintains the device in a ready state until the operator presses **Stop**.

B. Thawing Ossium Health® Cryopreserved HPC, Marrow

1. Press **Stop** to end the Continuous program (cushions will drain).

2. Be ready to quickly identify product and transfer to the varitherm. You will have no more than 2 minutes to do this while the cushions are filling. See B.3.c.

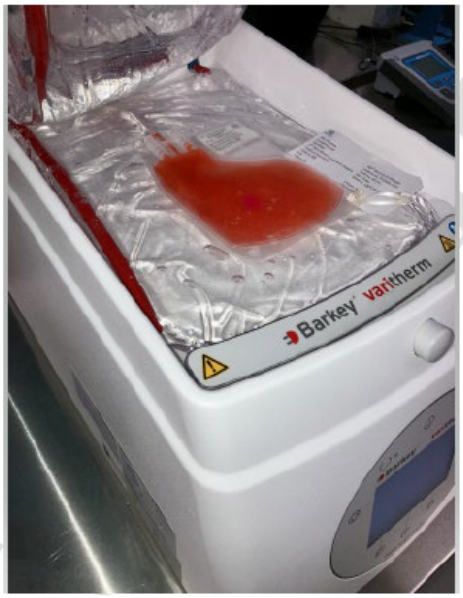
   NOTE: DO NOT place frozen bag in the varitherm at this time. The first minute of the thaw program is a wait time to allow the cushions to fill with water. The bag thaw time is a minimum of 3 minutes and a maximum of 5 minutes. This allows the operator up to two (2) minutes to place the cryopreserved bag in the device.

3. Select Program 1 shortcut from the main screen, or from the main menu and press OK to launch program. Program specifications are shown in Appendix A.

   a. The program begins and the six (6) minute countdown is displayed.

b. Set a timer for a one (1) minute WAIT to allow the cushions to fill.

c. Open the lid and immediately position the cryopreserved bag centrally between the warming cushions as shown, taking care to avoid the red paddle.



4. Close the lid and **record thaw start time** on form **OHC-FRM-0245**, *Dosing Checklist*.

NOTE: DO NOT attempt to change the program. Preset parameters dictate thawing temperature, duration, and the function of the paddle attachment.

a. The screen will display the temperature and time remaining.

5. The device will beep and display a message when the program is complete. The cushions will begin to drain.

a. **Record thaw stop time** on form **OHC-FRM-0245**, *Dosing Checklist*.

6. Open lid and carefully remove marrow bag from between the cushions.

a. Gently massage bag and observe for leaks.

b. Wipe outside of bag with sterile isopropyl alcohol (IPA) or an approved disinfectant per institutional protocol.

c. The product is now ready for administration .

d. Gently mix the product bag and infuse as soon as possible after thawing, preferably within 60 minutes.

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If the infusion is delayed post thaw, then mix product bag periodically to ensure that the cells remain in suspension. **RECOMMENDATION:** Do not thaw the next bag until the infusion of the first is near completion.

7. Repeat steps B. 2. through B.6. for each additional bag to be thawed.

8. Document the thaw according to institutional procedures. It is the responsibility of the end user to document accordingly.

C. Error Messages and Alarms

Condition	Message / Alarm	Resolution
Leak inside varitherm	Heating cushion or conserve has leaked! Intermittent acoustic sound and warning message	1. Press "OK" to confirm. 2. Turn off device and unplug it from the power source. 3. Remove the saturated paper from the heating chamber. 4. Clean the heating cushion and the heating chamber by wiping with sterile IPA and allow to dry. 5. Replace the filter paper (dry-paper).
Overtemperature condition	! Error ! Overtemperature! Warning tone sounds	1. Switch off the device and allow it to cool down
Excess air in heating cushions	! Error ! Device Error!	Please refer to the following link for instructions on bleeding out the air: https://vimeo.com/724841326/c8273309e1
Tank is empty or water level is low	! Error ! Tank is Empty!	1. Switch off the device 2. Add water per the Operator's Manual
Program failure or loss	! Error ! Device Error!	Contact Barkey Corporation at +1-866-227-5393

D. Upon completion of thawing

1. Clean the heating cushions.

   a. Wipe off any visible moisture or condensation with a dry wipe.

2. Use a wipe saturated with sterile IPA to clean the product-facing sides of the heating cushions.

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NOTE: Avoid wetting the filter paper below the heating cushions. Never spray alcohol directly onto any part of the device.

E. Alternate thawing

1. If varitherm is unavailable for use, the following procedure will be used to thaw Ossium Health® Cryopreserved HPC, Marrow
2. HPC, Marrow product must be transported and stored at or below -150°C per institutional practices until ready to thaw. Place the cryogenic container near the water bath.
3. Do not expose HPC, Marrow to temperatures warmer than -150°C for longer than 5 minutes.
4. Extreme caution must be used when handling the cassette(s) containing the frozen HPC, Marrow to ensure physical damage to the bags does not occur.
5. Do not lift product by the tie tag to remove it from cassette.
6. Do not hold or carry product by the tie tag.
7. Verify correct recipient (RID or Recipient Name) and product (DIN) before thawing.

F. Thawing Ossium Health Cryopreserved HPC, Marrow

1. Follow institutional procedures for thawing.
2. Place the water bath on a sturdy and level surface.
3. Connect to power and turn the instrument on per institutional procedure.
   a. Set the temperature to 37 °C.
   b. Allow water bath to reach the set temperature before proceeding.
4. Prepare to transfer one (1) cryopreserved bag from frozen storage (freezer or monitored dry shipper or equivalent) and perform product and recipient identification as applicable per institutional protocol.

5. **Record thaw start time** on the Form **OHC-FRM-0245** *Dosing Checklist* and per institutional procedure as applicable.

6. **Record thaw stop time** on the Form **OHC-FRM-0245** *Dosing Checklist* and per institutional procedures as applicable.

7. Carefully remove HPC, Marrow bag and wipe dry.

   a. Gently massage bag and observe for leaks.

   b. Wipe outside of bag with sterile isopropyl alcohol (IPA) or an approved disinfectant per institutional protocol.

   c. The product is now ready for administration.

   d. Gently mix the product bag and infuse as soon as possible after thawing, preferably within 60 minutes.

If the infusion is delayed post thaw, then mix product bag periodically to ensure that the cells remain in suspension. **RECOMMENDATION**: Do not thaw the next bag until the infusion of the first is near completion.

8. Repeat steps F.2 through F.7 for each additional bag to be thawed.

9. Document the thaw according to institutional procedures and complete Form **OHC-FRM-0245** *Dosing Checklist*. It is the responsibility of the end user to document accordingly.

G. At completion of thawing

1. Clean and disinfect the water bath according to institutional procedures.

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APPENDIX A

Thaw Program 1 Settings for Varitherm

Setpoint temperature	**40**	**°C**
Heating duration	**6**	**min**
Paddle delay	**1**	**min**
Paddle duration	**5**	**min**
Paddle active	**5**	**min**
Paddle inactive	**0**	**min**

Appendix 11 (HOPE Program Intake Form)

HOPE Program

In partnership with NMDP, Ossium Health is sponsoring the PRESERVE I clinical trial (NCT05589896) to characterize the safety and effectiveness of cryopreserved bone marrow from qualified organ donors. The HOPE Program expands access to patients outside of the PRESERVE I clinical study.
If you would like to learn more or have any questions, please contact Ossium Health at hope@ossiumhealth.com or (628) 677-4863.

This form is to be completed by the treating physician team
Your patient has already consented to the release of their medical information for the purpose of finding a potential bone marrow donor. This form enables us to determine if we have a match for your patient. We can share the copy of the patient authorization upon request.

* Indicates required question

Physician Information

1. Physician Name *

2. Physician Email *

3. Physician Medical Center / Hospital *

4. Physician Office Address *

5. Physician Phone Number *

Patient Information

6. Patient Name *

7. Patient mailing address *

8. Date of birth *

Example: January 7, 2019

9. Sex assigned at birth *
Mark only one oval.

- ◯ Male
- ◯ Female

10. Race *
Check all that apply.

- ☐ White
- ☐ Black or African American
- ☐ Asian
- ☐ American Indian or Alaska Native
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Declined
- ☐ Unknown
- ☐ Other:

11. Ethnicity *

Mark only one oval.

- ◯ Hispanic or Latino
- ◯ Not Hispanic or Latino
- ◯ Not Reported
- ◯ Unknown

12. Patient weight *

_____

13. Patient weight (unit) *

Mark only one oval.

- ◯ kg
- ◯ lb

Patient Disease Information

14. Disease indication at the time of diagnosis *

Mark only one oval.

- ◯ Acute Lymphoblastic Leukemia (ALL)
- ◯ Acute Myeloid Leukemia (AML)
- ◯ Acute Leukemia of ambiguous origin
- ◯ Other Myeloid Neoplasms (including ABL and AUL)
- ◯ Myelodysplastic Syndrome
- ◯ Other: _____

15. Date of diagnosis *

_____

Example: January 7, 2019

16. Pre-transplant disease status *

Mark only one oval.

- 1st Complete Remission(CR1)
- 2nd Complete Remission(CR2)
- ≥3rd Complete Remission (CR3)
- Not Applicable

17. Has the patient had a prior autologous or allogeneic HCT? *

Mark only one oval.

- Yes
- No

18. Is your patient a candidate for allogeneic bone marrow transplant? *

Mark only one oval.

- Yes
- No

Patient HLA Information

Please email the patient's HLA report to hope@ossiumhealth.com or provide the allele designations below.

19. Please confirm that you emailed the patient's HLA report to Ossium Health.

Mark only one oval.

- Yes. I emailed the report
- No. I did not email the report & will provide the allele designations in the following fields
- Other: _____

20. If the HLA report was not shared via email, please provide the following information

First A allele designation

21. If the HLA report was not shared via email, please provide the following information

Second A allele designation

22. If the HLA report was not shared via email, please provide the following information

First B allele designation

23. If the HLA report was not shared via email, please provide the following information

Second B allele designation

24. If the HLA report was not shared via email, please provide the following information

First C allele designation

25. If the HLA report was not shared via email, please provide the following information

Second C allele designation

26. If the HLA report was not shared via email, please provide the following information

First DRB1 allele designation

27. If the HLA report was not shared via email, please provide the following information

Second DRB1 allele designation

28. If the HLA report was not shared via email, please provide the following information

First DQB1 allele designation

_____

29. If the HLA report was not shared via email, please provide the following information

Second DQB1 allele designation

_____

30. If the HLA report was not shared via email, please provide the following information

First DPB1 allele designation

_____

31. If the HLA report was not shared via email, please provide the following information

Second DPB1 allele designation

_____

Patient Health Status

32. HCT-CI Score (if available) *

_____

33. Karnofsky Performance Status (if available) *

_____

34. Cardiac Function (LVEF) at rest is ≥45% based on most recent evaluation *
Mark only one oval.

- ◯ Yes
- ◯ No

35. Pulmonary Function ≥50% based on DLCO (adjusted if needed for hemoglobin),*

FEV1 and FVC based on most recent evaluation
Mark only one oval.

Yes

No

36. Liver Function shows total bilirubin ≤2.0 and ALT and AST ≤3x ULN based on most recent evaluation *
Mark only one oval.

Yes

No

37. Renal Function shows creatinine ≤1.5x of normal range for age based on most recent evaluation*
Mark only one oval.

Yes

No

38. Patient is expected to live at least 1 year post bone marrow transplant *
Mark only one oval.

Yes

No

39. Engraftment (neutrophil) is expected within 60 days post transplant *

Mark only one oval.

Yes

No

40. Any additional comments/questions? *

Signature

By typing your name below, you are signing this application electronically.

41. Signature of physician *

42. Date of signature *

Example: January 7, 2019

Appendix 12 (HOPE DATA COLLECTION FORM)

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HOPE Data Collection Form

This form is to be completed by the physician's care team of the patient that received Ossium HPC, Marrow through the HOPE Program. Additional information on medical history and medications may be collected if required. The patient is to be followed for up to 1 year post transplant.

For each section, please (1) enter the data, (2) sign and date below such section, and (3) submit this form to Ossium within the applicable timelines. The following are the timelines for each section:

Section 1: Conditioning and Transplant Information on Page 2: To be entered within 5 days post transplant

Section 2: Neutrophil Engraftment on Page 4: To be entered within 5 days post neutrophil engraftment or within 28 days post-transplant whichever is earlier

Section 3: Platelet Engraftment on Page 5: To be entered within 5 days post platelet engraftment or within 56 days post-transplant whichever is earlier

Section 4: Donor Chimerism on Page 6: To be entered within 5 days of completion or periodic reporting at Day 30, Day 60 and Day 100 post-tranplant

Section 5: Disease Evaluation on Page 7: To be entered within 5 days post bone marrow aspirate/bone marrow biopsy or periodic reporting on Day 180 and Day 365 post-transplant

Section 6: aGVHD, late onset aGVHD and cGVHD* Information on Page 8: To be entered within 5 days of diagnosis and periodic reporting at Day 30, Day 60, Day 100, Day 180 and Day 365 post-transplant

Section 7: SAE Associated with Ossium HPC, Marrow Product (Report SAEs related to Ossium HPC, Marrow only, transplant related SAEs need not be reported) on Page 10: To be entered within 24 hours of event. If no SAE, periodic reporting on Day 180 and Day 365 post-transplant. Death to be reported irrespective of causality to Ossium HPC, Marrow

Section 8: AE Associated with Ossium HPC, Marrow Product (Report AEs related to Ossium HPC, Marrow Product only, transplant procedure related AEs need not be reported) on Page 11: To be entered within 5 days of event. If no AE, periodic reporting on Day 180 and Day 365 post-transplant

*cGVHD: Please use your standard evaluation form or we can provide template if required and provide details of treatment provided

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Section 1:

Conditioning and Transplant Information (To be entered within 5 days post-transplant)		
1	Conditioning Regimen Administered	○ MAC (Busulfan and Fludarbine) ○ MAC (Fludarbine and Total Body Irradiation) ○ RIC (Fludarbine, Pre-HCT Cyclophosphamide, Total Body Irradiation) ○ Other, Specify:
2	Dose of Conditioning Regimen Administered	Rx*: Dose: Rx*: Dose: Rx*: Dose: Rx*: Dose:
2a	Start and Stop date of Conditioning Regimen Administered	Rx*: Start Date: Stop Date: Rx*: Start Date: Stop Date: Rx*: Start Date: Stop Date: Rx*: Start Date: Stop Date:
3	# of months patient has searched with no match (if applicable)	
4	Date of transplant	DD MM YYYY
5	Weight on day of transplant	○ lbs ○ kg
6	Method used to thaw Ossium HPC, Marrow	○ Water bath ○ Electric warmer (Varitherm) ○ Other, specify:
7	Temperature of water bath if use of water bath	○ C ○ F
8	Time thaw began (HH:MM)	
9	Time thaw completed (HH:MM)	
	Bag ID #	
10	Ossium HPC, Marrow Infusion Start Time (HH:MM)	
11	Ossium HPC, Marrow Infusion Stop Time (HH:MM)	

*Rx=Name of Drug

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Section 1:

12	Was entire volume of Ossium HPC, Marrow infused?	○ Yes ○ No, Specify:
13	Was cyclophosphamide administered on Day 3?	○ Yes ○ No, Specify:
14	Was cyclophosphamide administered on Day 4	○ Yes ○ No, Specify:
15	Was there any other prophylactic GVHD treatment?	◉ Yes ○ No
If Yes, please provide the following information		
15a	Rx*: Dose: Start Date: Stop Date (If applicable): Rx*: Dose: Start Date: Stop Date (If applicable): Rx*: Dose: Start Date: Stop Date (If applicable): Rx*: Dose: Start Date: Stop Date (If applicable): Rx*: Dose: Start Date: Stop Date (If applicable):	

Signature of Physician: _____ **Date:** _____

*Rx=Name of Drug

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Section 2:

Neutrophil Engraftment Information (To be entered within 5 days of neutrophil engraftment or within 28 days post-transplant whichever is earlier)			
16	Was neutrophil engraftment achieved?	○ Yes ○ No	
If Yes, please provide the following information			
16a	Absolute Neutrophil Count on all 3 days	Neutrophil Count with units	Date
		Day 1:	DD MMM YYYY
		Day 2:	DD MMM YYYY
		Day 3:	DD MMM YYYY

Signature of Physician:_____ **Date:**_____

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Section 3:

Platelet Engraftment Information (To be entered within 5 days of Platelet engraftment or within 56 days post-transplant whichever is earlier)			
17	Was platelet engraftment achieved?	○ Yes ○ No	
If Yes, please provide the following information			
17a	Platelet count on all 3 days	Platelet Count with units	Date
		Day 1:	DD MMM YYYY
		Day 2:	DD MMM YYYY
		Day 3:	DD MMM YYYY

Signature of Physician:_____ **Date:**_____

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Section 4:

Donor Chimerism (To be entered within 5 days of completion if done or periodic reporting at Day 30, Day 60 and Day 100)		
18	Was chimerism testing performed?	○ Yes ○ No
If Yes, please provide the following information		
18a	Date donor chimerism was performed	DD MMM YYYY
18b	Unsorted/Whole blood % donor cells (numeric or fixed %)	
18c	T cells: CD3+ % donor cells (numeric or fixed %)	
18d	Myeloid cells: CD33+ % donor cells (numeric or fixed %)	

Signature of Physician:_____**Date:**_____

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Section 5:

Disease Evaluation (To be entered within 5 days of bone marrow aspirate/bone marrow biopsy or periodic reporting on Day 180 and Day 365 post-transplant)		
19	Was bone marrow aspirate performed to evaluate disease status post transplant?	○ Yes ○ No
If Yes, please provide the following information		
19a	Date bone marrow aspirate was performed	DD MMM YYYY
19b	Blasts in bone marrow aspirate (numeric or non-numeric)	
20	Was bone marrow biopsy performed to evaluate disease status post transplant)?	○ Yes ○ No
If yes, please provide the following information		
20a	Date bone marrow biopsy was performed	DD MMM YYYY
20b	Blasts in bone marrow biopsy (numeric or non-numeric)	

Signature of Physician:_____ **Date:**_____

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Section 6:

aGVHD , late onset aGVHD and cGVHD* Information (To be entered within 5 days of diagnosis and period reporting at Day 30, Day 60, Day 100, Day 180 and Day 365 post-transplant)		
21	Date of GVHD assessment	DD MMM YYYY
22	Did patient have GVHD diagnosis?	○ Yes ○ No If yes, please specify type of GVHD:
If yes for aGVHD or late onset aGVHD please provide the following information		
22a	Date of acute GVHD diagnosis	DD MMM YYYY
22b	Maximum overall grade	○ Grade I ○ Grade II ○ Grade III ○ Grade IV
22c	Date of acute GVHD resolution (if available)	DD MMM YYYY
22d	Was skin assessed	○ Yes ○ No
22d(i)	If yes, Skin stage	○ Stage 0 ○ Stage 1 ○ Stage 2 ○ Stage 3 ○ Stage 4
22e	Was liver stage (bilirubin) assessed?	○ Yes ○ No
22e(i)	If yes, liver stage (bilirubin)	○ Stage 0 ○ Stage 1 ○ Stage 2 ○ Stage 3 ○ Stage 4
22f	Was upper GI assessed?	○ Yes ○ No
22f(i)	If yes, upper GI stage	○ Stage 0 ○ Stage I
22g	Was lower GI assessed?	○ Yes ○ No
22g(i)	If yes, lower GI stage	○ Stage 0 ○ Stage 1 ○ Stage 2 ○ Stage 3 ○ Stage 4

*cGVHD: Please use your standard evaluation form or we can provide template if required and also provide details of treatment provided

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Section 6:

23	Treatment Provided for acute GVHD	Rx*: Start Date:	Dose: Stop Date (If applicable):
		Rx*: Start Date:	Dose: Stop Date (If applicable):
		Rx*: Start Date:	Dose: Stop Date (If applicable):
		Rx*: Start Date:	Dose: Stop Date (If applicable):
		Rx*: Start Date:	Dose: Stop Date (If applicable):

Signature of Physician:_____**Date:**_____

Version 1.5

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OSSIUM HEALTH®

Section 7:

SAE Information (Report SAEs related to Ossium HPC, Marrow Product only except death, transplant procedure related SAEs need not be reported. To be entered within 24 hours. If no SAE, periodic reporting on Day 180 and Day 365 post-transplant). Additional pages to be entered for each SAE		
24	Did the patient have any serious adverse event	○ Yes ○ No
If yes, please provide the following information		
24a	Date of onset	DD MMM YYYY
24b	SAE Category	○ Death ○ Life threatening situation ○ In-patient hospitalization or prolongation of existing hospitalization ○ Persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions ○ Congenital abnormality/Birth defect ○ Required intervention to prevent permanent impairment or damage ○ Other serious medical events
24c	SAE Description	
24d	Maximum CTCAE severity Grade	○ Grade 1 ○ Grade 2 ○ Grade 3 ○ Grade 4 ○ Grade 5
24e	What is relationship between the reported adverse event to the Ossium HPC, Marrow Product (Not related to transplant procedure)	○ Definite ○ Probable ○ Possible ○ Unlikely ○ Unrelated

Signature of Physician:_____ **Date:**_____

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Section 8:

AE Information (Report AEs related to Ossium HPC, Marrow Product only, transplant procedure related AEs need not be reported. To be entered within 5 days. If no AE, periodic reporting on Day 180 and Day 365 post-transplant. Additional pages to be completed for each AE)		
25	Did the patient have any adverse event or serious adverse event associated with Ossium HPC, Marrow Product (Not related to transplant procedure)	○ Yes ○ No
If yes, please provide the following information		
25a	Date of onset	DD MMM YYYY
25b	AE Description	
25c	Maximum CTCAE Severity Grade	○ Grade 1 ○ Grade 2 ○ Grade 3 ○ Grade 4 ○ Grade 5
25d	What is relationship between the reported adverse event to the Ossium HPC, Marrow Product (Report AEs related to Ossium HPC, Marrow Product only, transplant procedure related AEs need not be reported.)	○ Definite ○ Probable ○ Possible ○ Unlikely

Signature of Physician:_____**Date:**_____