## **Bonus Biogroup** Company Presentation, July 2023



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This presentation, both written and oral, includes statements that are or may be deemed, "forward-looking statements" within the meaning of applicable securities laws. In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately," "potential" or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these terms.

For example, when we discuss the addressable market sizes and growth potential of BonoFill and MesenCure, we are using forward-looking statements. Because such statements deal with future events, they are subject to various risks and uncertainties, and actual results, expressed or implied by such forward-looking statements, could differ materially from Bonus BioGroup's current beliefs, forecasts, and estimates. Factors that could cause or contribute to such differences include, but are not limited to risks and uncertainties associated with natural disasters and public health crises, such as the coronavirus disease (COVID) pandemic; the impact of global economic conditions; regulatory developments; our financing needs; research and development challenges; the demand and acceptance of our products and the other risk factors set forth in Bonus BioGroup's latest annual report and other filings with the Israeli Securities Authority ("ISA"). Any forward-looking statements that we make in this presentation, both written and oral, speak only as of the date of such statement, and, except as required by applicable law, we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation.

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Bonus Biogroup is an advanced clinical-stage biotechnology company developing 'next-generation' therapies for a variety of indications in the regenerative medicine field.



Our mission is to develop and deliver effective, safe, and affordable tissue engineering and cell therapy products to address severe diseases and conditions.

#### Our key assets in advanced clinical trials include:

**BonoFill™** is a live human bone graft for treating bone deficiencies based on the patient's own cells, which are grown outside their body.

MesenCure<sup>™</sup> is a cell therapy drug product consisting of viable, enhanced mesenchymal cells. It is designed to treat inflammation and tissue damage, including pneumonia and respiratory distress.



## **Our Vision:**

Empower millions of patients to live healthier and longer lives through scientific leadership and excellence, technological innovation, and patient-centric development.



Bonus Biogroup stands at the forefront of the industry as a pioneer in regenerative medicine, harnessing our unparalleled knowledge and expertise to develop a unique technological platform that revolutionizes cell therapy and tissue engineering.

By leveraging our deep understanding of the power and challenges of cellular therapeutics, we ensure cost-effectiveness, safety, and quality in our products. This leads to clinical success and enhances our prominent role in the biotech industry.

Dr. Shai Meretzki, Bonus Biogroup's Founder & CEO

## BonoFill™

Injectable live human bone graft

#### Expands bone grafting availability

Facilitates rapid return to normal functions and about 50% shorter hospitalization and recovery times

#### **Reduces surgery time by 70%**

Provides more treatment options for complicated patients

#### Reduces hospitalization and surgery costs by >50%

Reduces the need for revision surgeries

# Our products bring value to





#### According to an analysis by McKinsey & Company

## **MesenCure**<sup>™</sup>

Cell therapy for inflammation and tissue damage

#### **Reduces mortality by 68%**

Shortens the duration of hospitalization by 9 to 10 days

#### **Relieves ICU burden**

Provides more treatment options for severe patients

#### Reduces hospitalization and healthcare costs by ~40%

#### The MesenCure<sup>™</sup> opportunity

Cell therapy for inflammation and tissue damage Market Highlights: US only



US target market for treating respiratory distress, including pneumonia cases, Covidrelated, and otherwise



Reduction in hospitalization costs by using MesenCure in the US alone



Patients could be treated using MesenCure, each year in the US alone

#### The BonoFill<sup>™</sup> opportunity

Injectable live human bone graft Market Highlights: US only

~**6.2M** patients

US target market for treating bone deficiencies where BonoFill could be used

° ~70B USD

Reduction in surgery and hospitalization costs by using BonoFill: 15 Bn in orthopedics and 10 Bn in craniomaxillofacial applications, in the US alone

## ~130K patients

Patients could be treated using BonoFill, each year in the US alone

According to an analysis by McKinsey & Company (forecast 2030, both products)

## **CLINICAL STATUS**

Bonus Biogroup has released the results of the MesenCure Phase II trial and recently released interim results of a Phase II trial with BonoFill. We are now preparing for advanced-phase clinical trials in the U.S. with both products.

- We have successfully completed a Phase II clinical trial using MesenCure to treat pneumonia and respiratory distress in severe Covid patients.
- Ongoing communications with the FDA are underway toward an advanced clinical trial in the U.S. for treating severely ill respiratory distress patients with MesenCure.
- We have published interim results of a Phase II trial using BonoFill to treat facial bone deficiencies and have completed study enrollment.
- Our ongoing Phase II trial for treating critical-sized bone defects in the limbs has demonstrated efficacy and safety in reported cases.



The company is exploring additional applications for treating inflammation and tissue damage through the technological platform underlying our products.

## Effective use of proceeds

# **\$60** million USD

## 18% premium

# **1.56 ILS** per share

# **\$12.5** million USD

#### **Funds raised**

in public and private placements

#### Average premium

above the closing share price on the relevant date

#### Average share price

throughout the last round, during which we raised \$11.5 million

#### **Cash reserves**

as of 03.31.23, expected to support operations until early 2025

#### In 2022, we relocated to the new Bonus Biogroup Center:

## Advanced GMP facility for R&D and manufacturing of tissue engineering and cell therapy products

- GMP compliant according to FDA and EMA requirements
- It includes two production halls for BonoFill and MesenCure, as well as QC labs
- Production capacity suitable for commercial activity
- Home to Israel's most advanced R&D center for cell therapy and tissue engineering



In January 2023, Israel MoH certified the manufacturing facility and process of MesenCure to comply with GMP standards in accordance with the recommendations of the WHO.









## BonoFill<sup>™</sup>: A live human bone graft



## BonoFill is a living bone graft composed of mesenchymal cells sampled from the patient's own adipose tissue.

These cells are seeded onto biodegradable mineral particles and cultivated within a unique bioreactor system. The result is a ready-to-use graft designed for treating bone deficiencies across a variety of indications.

#### **Competition & alternatives**

## **BonoFill**<sup>™</sup>

Injectable live human bone graft



Bone Grafts and Substitutes

Tissue Engineering in R&D

#### Features

Requires additional bone harvesting surgery: leading to high complexity, cost, and low success rates

#### **BonoFill features**

More effective and available than existing treatments and less expensive

Cadaveric or other inanimate substitutes: suitable only for small bone deficiencies A live bone graft, also suitable for large bone deficiencies

Does not include all ingredients for the regeneration of large bone deficiencies: **still in early academic research** 

BonoFill is in the most advanced clinical development stage

Bonus Biogroup revolutionizes technology and science in the development and production of bones



In just seven weeks, BonoFill led to the complete regeneration of a critical-sized bone defect in a preclinical study.

#### Journal of Orthopaedic Surgery and Research RESEARCH ARTICLE Open Access

Check for updates

Autologous cell-coated particles for the treatment of segmental bone defects—a new cell therapy approach







BonoFill treatment has been completed successfully in dozens of patients and demonstrated safety and efficacy in regenerating bones in the face and limbs, even in patients who failed other treatments.

## Clinical Trial to Treat Facial Bone Deficiencies Using BonoFill

- ✓ Phase II clinical study in 30 transplants
- ✓ 90% success following 20 transplants
- Complete bone healing in three months
- Reducing the recovery time to half to onethird of the period required today
- ✓ Full safety profile demonstrated
- ✓ Enrollment completed

## Clinical Trial to Treat Critical Bone Defects in the Limbs Using BonoFill

- ✓ Phase II clinical study in up to 40 transplants
- ✓ Efficacy demonstrated in reported cases
- ✓ Full safety profile demonstrated
- ✓ Expected completion of enrollment in early 2024

#### Examples from a Clinical Trial to Treat Critical Bone Defects in the Limbs using BonoFill

#### **Before treatment**

- Significant constant pain
- Limited weight bearing
- >5 cm long bone gap
- Three previous, other treatments failed



#### A year after BonoFill

- Complete healing and gap closure
- No pain
- Normal weight bearing
- Normal function
- No adverse events



#### Danny Yaakobson participated in a triathlon and rode 91 km just one year after receiving BonoFill.



#### Examples from a Clinical Trial to Treat Critical Bone Defects in the Limbs using BonoFill

## Rehabilitation from complex fracture of the forearm bones





#### **Before treatment**

- Constant pain
- No weight bearing
- Two previous, other treatments failed



#### A year after BonoFill

- Complete healing
- Normal weight bearing
- Normal function, no pain
- No adverse sevens

## Regeneration of a large 40 cc bone defect following valgus knee repair



#### **Before treatment**

- Impaired walking
- Constant pain
- Limited weight bearing



#### A year after BonoFill

- Normal walking
- No pain
- Normal functions
- No adverse events

#### **Examples from a Clinical Trial to Treat Facial Bone Deficiencies Using BonoFill**

# Before<br/>treatmentfuree months<br/>after BonoFill6 months<br/>after BonoFillImage: Select colspan="3">Of the select colspan="3">Select colspan="3"Image: Select colspan="3">Select colspan="

- Before treatment, the bone height was 2.9 mm
- Three months after transplantation, the bone reached a height of 15.6 mm
- At the end of the six months follow-up period, bone regeneration was achieved, enabling continued reconstructive activities

# Before<br/>treatmentThree months<br/>after BonoFillSix months<br/>after BonoFillImage: Descent region of the second region of

- Before treatment, the bone height was 6.6 mm
- Three and six months after transplantation, the bone reached a height of 14.8 and 15.8 mm, respectively
- Bone regeneration enables continued reconstructive activities

## BonoFill revolutionizes the safety and efficacy of bone grafting

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**Rejection failure is minimized:** Grown from cells sampled from the adipose tissue of the patient

**Tailor-made for the best healing outcome:** Designed to precisely fit the anatomical deficiencies of patients

**Diversified cell culture to accelerate regeneration:** Cells are in a spectrum of differentiation stages to maximize efficacy

**Biodegradable 3D matrix mimicking natural bone:** FDA- and EMA-approved mineral scaffold, safe and promotes bone regeneration

**Proprietary and scalable bioreactor:** Enable costeffective production with large throughput and reproducibility of a safe and high-quality product

**Versatile applications:** Accommodates a range of bone deficiencies - available upon demand and in large quantities

# Biogroup



## **MesenCure<sup>™</sup>**

A cell therapy drug for treating inflammation and tissue damage consisting of enhanced mesenchymal cells from healthy donors



The drug has been shown to be safe and effective in treating pneumonia and respiratory distress in severe COVID-19 patients.



About 100,000 doses of MesenCure can be produced from a single cell-bank donor.



A unique manufacturing process gives MesenCure the ability to treat a wide range of inflammation and tissue damage.



MesenCure reduced life-threatening cytokine release syndrome, which occurred as a result of cancer immunotherapy.



The drug is being tested in a number of additional indications for the treatment of acute and chronic inflammations and tissue damage.

**Competition & alternatives** 

## **MesenCure**<sup>™</sup>

Cell therapy drug for treating inflammation and tissue damage



#### Features

#### Steroids, mechanical ventilation, *etc*.: **Do not cure the disease**

#### **MesenCure features**

Equipped with wide and varied therapeutic capabilities

Treat a single cause of the disease: **Limited** efficacy in a variety of conditions Treats both inflammation and tissue damage

Based on natural cells: Limited potency and efficacy MesenCure is the only cell therapy that achieved success in clinical development





Phase II clinical trial for the treatment of pneumonia and respiratory distress with MesenCure was completed

- 50 severe COVID-19 patients suffering from pneumonia and respiratory distress were treated with MesenCure
- ~90% of the patients suffered significant comorbidities
- Dosage: Up to three doses of the drug
- MesenCure safety and efficacy were demonstrated compared to a control group of 150 similar severe patients who received the standard treatment.

#### Main Results of the Phase II Trial with MesenCure



reduction in mortality



days reduced from hospitalization time for highly complex patients\*



reduction in the risk of invasive ventilation



of patients treated with MesenCure were discharged from the hospital up to two days after treatment



reduction in inflammation marker CRP, and rapid improvement in respiratory function, and markers of tissue damage

Full safety profile

\* Patients with a hospital length of stay longer than seven days



# MesenCure rapidly healed pneumonia and improved respiratory functions

Before MesenCure treatment, the lungs were congested with inflammatory infiltrates, obstructing breathing (representative patients)



Approx. 30 days after MesenCure treatment, breathing is normal, and pneumonia dramatically reduced

## MesenCure is revolutionizing the treatment of pneumonia and respiratory distress

**Highly effective in treating respiratory distress in severe COVID-19 patients:** The cell culture process is designed to enhance the effectiveness

**Effective by acting against different stages of the inflammatory process:** Rescues from multi-system failure and death and is also suitable for those suffering from comorbidities

The cells are administered intravenously and reach the **lungs:** The cells reduce cytokine storm and pneumonia, encouraging repair of lung damage

The treatment has additional benefits on top of reducing pneumonia: The cells reduce the risk of damage to other organs, such as the heart, liver, and kidneys

**High production capacity, safe and easy-to-use drug:** About 50k doses of the drug can be produced from one liter of adipose tissue from a single donor

<u>MesenCure applications</u>

Acute respiratory distress



Other inflammations: local and systemic, acute and chronic



Tissue regeneration



Bonus

Biogroup

## Preclinical development

**BonoFill:** Our exclusivity in the manufacture and commercialization of a live human bone graft is guaranteed by three patent families. This covers the entire bone rehabilitation market for any relevant indication.

**CR-01** 

**MesenCure:** Two patent families protect our unique mesenchymal cells with enhanced therapeutic capacity. These cells, with their unique gene expression profile, are used to treat inflammation, tissue damage, and more.

**Tissue Engineering and Other Applications:** We have a patent family dedicated to the creation and embedding of artificial blood vessel networks within tissue implants. Another patent family protects the composition and method of transporting active compounds to stimulate blood vessel growth in tissues.



## **Intellectual Property**

- Seven patent families
- **28** approved patents
- □ 15 patent applications
- □ In the US, Europe, and beyond

Major Predicted Events 2023 - 2024

- Obtain FDA approval for an advanced clinical trial with MesenCure in the U.S.
- Initiate recruitment of centers for an advanced clinical trial with MesenCure in the US.
- Begin patient enrollment and treatment with MesenCure in the US.
- Publish results from a Phase II Clinical Trial for treating critical bone defects in the limbs using BonoFill.
- Release the results of Phase II Clinical Trial for treating facial bone deficiencies using BonoFill.
- Secure FDA approval for an advanced-phase clinical trial with BonoFill in the US.

## **Products and applications pipeline**

PRODUCT CANDIDATE	Preclinical R&D	Phase I	Phase II	Phase III
MesenCure for respiratory distress				
BonoFill for facial bone deficiencies				
<b>BonoFill</b> for treating critical bone defects in the limbs				
<b>MesenCure</b> for treating other inflammations and tissue damage				
<b>BonoFill</b> for bone augmentation in osteoporosis				
Vascularized bone grafts				
Soft tissue grafts				

## Proven track record of success

#### Shai Meretzki, Ph.D., Founder & CEO

Yossi Rauch, MBA, Executive Chairman



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Dr. Meretzki is a seasoned leader in the Life Science field, having founded several biotech companies, including Pluristem, where he served as CEO and CTO. He holds a Ph.D. in biotechnology from the Technion - Israel Institute of Technology, in collaboration with the Weizmann Institute of Science, Israel. His proven operational, management, and leadership abilities are instrumental in driving Bonus Biogroup's success.

#### Dror Ben David, Ph.D., COO



#### Tomer Bronshtein, Ph.D., VP BD

Mr. Rauch brings a wealth of financial expertise to his role, having served as the Chief Economist and Manager of the Economics Department at Leumi PIA, Israel's largest mutual fund company at the time. He holds an MBA in Finance & Accounting and Computers & Information Systems from Tel Aviv University and a BA in Economics and Business Administration from Bar-Ilan University.



Yoni Livne, CPA, CFO



Atara Novak, Ph.D., VP R&D



Vered Kivity, Ph.D., MBA, VP Reg.



Corinne Chemouny, Pharm.D., VP QA









25th International Conference on Oral and Maxillofacial Surgery



#### אניות: בראת הנדסת רקשות ד"ר הופר ברושטיין שימורים ביוסכולוגיים

מאז הנחתה על הירח, יידרשו עוד כארבעה עשורים של התקדשות פדעית כדי להתואל להביא שהדומה לרשוי שהלות מצבים קשים, ולא רק להרות להתו מחלה, כלי שהיה הנא עד אינ לשהל, הדמי הכובה וגידול של רקומות וגירים אנשישה יודים הבעבודה, מה את הקשיה למעולם מנו מדע בידיני, הוא למעולה המציחות ליבים, באש אשר עצוי לייבוי כבר בשות 2000. הנכופה של למעולי הכול למינודי הדול בשנה.

ם שוק ההון מגלה עניין רב בפיתורים ביוטנולוגיים לריפוי מחלות ובהנדסת רקמות בפרט. את לעיתים, על פני השקטר בפיתוח תרופות קובבטינליות בשל ירידה בתוקלת השולית ל אותן תרופות, עליה בהובאות המ"ס, ומשואות הולכות ופוחתות של תעשיית התרופות סמותאת.



רבית הפעילות הכלכית במשוק שבן. דכת הקטות להשוא שיקונית התמקדת ום באיברים מלאכותיים. לדוגמה, מפרקים "אכותיים או תחליםי עום לעיפול בחסרי שמק מספה, לאשלי להשולת עם באימול וייצו

שינים ושד. איברים מלאמתיים יעילים. בעיקר, בזמת ימולום להחזיר לרקבה מידה מסומת של עורה וחוזק ותסקורים משוסים הסית, למשל תפקודים במניים. לעולים הם משמשים גם נפיגום להמשך תהליך התחדש הרקבה וש ארגבר. Biogroup

Meet us at AAOS 2023 Annual Meeting 7-11 March, Las Vegas

AAOS

מל הפוטנציאל המשמעותי של בונופיל-2 לטיפול בחסרי עצם קריטיים

ואת פרופ' נמרוד רוון, מנהל חסיבה אורתופדית שיקומית מרכז רפואי

חברת בונוס ביוגרופ מנייסת בימים אלה חולים לניסוי קליני בחמישה מרכזים רפואיינ

באמצעות בונופיל-2, מוצר הנדסת רקמות חדשני, בונפיל-2 הוא שתל חי של עצם

אנושית המבוסס על תאים בעלי פוטנציאל לבניית עצם הנדנמים מרקחת השומן שי

המטופל ואשר מנודלים, בהמשך, מחוין לגופו. לאחר השתלתו, צפוי שתל העצם

העמק-עפולה ונשיא האינוד הישראלי לאורתופדיה

ובשברים בלתי מתאחים (בשיתוף חברת בונוס ביונרופ)



The Jackson Laboratory EU Symposium

#### Preclinical to Clinical Development of Next-Generation Mesenchymal Cell Therapy: From CAR-T Induced CRS in Humanized Models to Rescuing Severe COVID-19

#### Patients and Beyond 16 JUNE Paris Tomer Bronshtein PhD

#### Bonus Biogroup's technological and scientific strides have garnered significant recognition and appreciation in the field.

#### **Selected Publications include**

 ◆ Ben-David *et al.* Autologous cell-coated particles for the treatment of segmental bone defects-a new cell therapy approach.
J Orthop Surg Res. 2019 Jul 1;14(1):198.

◆ Tzur *et al.* Safety and Efficacy Results of BonoFill First-in-Human, Phase I/IIa Clinical Trial for the Maxillofacial Indication of Sinus Augmentation and Mandibular Bone Void Filling. J Oral Maxillofac Surg. 2021 Apr;79(4):787-798.e2.

- ◆ Bronshtein *et al.* BLOOD 2021, Vol. 138, No. , Pages 2172
- Bronshtein et al. CYTOTHERAPY 2022, Vol. 24, No. 5, Pages S31-S32
- Kushnir et al. CYTOTHERAPY 2022, Vol. 24, No. 5, Pages S24-S25
- Novak et al. CYTOTHERAPY 2022, Vol. 24, No. 5, Pages S46-S46

# Biogroup





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## **The Bonus Biogroup Advantage**



Demonstrated clinical successes across diverse products and indications.



Targeting multi-billion-dollar markets with minimal competition.



Proprietary platform technology with broad applicability across various indications.



Significant barriers to entry for potential competitors.



Established GMP-compliant production facilities scaled for commercial activity.



Leadership team comprises seasoned executives and scientists with a proven success record.