EX-99.2 6 ea166468ex99-2_goodworks2.htm INVESTOR PRESENTATION

Exhibit 99.2

DIRECT BIOLOGICS™

Next-Generation Life Saving Solutions

Corporate Overview – October 2022

Disclaimer

This presentation ("**Presentation**") is for informational purposes only to assist interested parties in making their own evaluation with respect to the proposed offering (the "**Offering**") of Direct Biologics, LLC, a Wyoming limited liability company ("**Direct Biologics**") of Class B Units. The offering is being made in connection with, but is not subject to or conditioned upon, the consummation of a proposed business combination (the "**Business Combination**") between Good Works II Acquisition Corp. ("**Good Works**") and the Company (the "**Purpose**"). By accepting this Presentation, the recipient acknowledges and agrees that all of the information contained herein is confidential, that the recipient will distribute, disclose, and use such information only for such Purpose and that the recipient shall not distribute, disclose or use such information in anyway detrimental to Direct Biologics or Good Works. The information contained herein does not purport to be all-inclusive and none of Good Works, Direct Biologics, and IB Capital, LLC ("**IBC**") nor any of their respective affiliates nor any of its or their controlling persons, officers, directors, employees or representatives makes any representation or warranty, express or implied, as to the accuracy, completeness or reliability of the information contained in this Presentation. You should consult your own counsel and tax and financial advisors as to legal and related matters concerning the matters described herein, and, by accepting this Presentation, you confirm that you are not relying upon the information contained herein to make any decision.

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The offering of Direct Biologics' Class B Units is intended to be made in connection with, but is not subject to or conditioned upon, the consummation of the proposed Business Combination. In connection therewith, Direct Biologics and Good Works intend to enter into business combination or similar agreement and Good Works, or a to be formed entity, intends to file with the SEC a registration statement on Form S-4 whereby, upon the closing of the transaction, each Class B Unit will be canceled and converted into a number of shares of capital stock of a newly organized corporation or other business entity listed on a national securities exchange.

Participants in the Solicitation. Good Works and its directors and executive officers may be deemed participants in the solicitation of proxies from Good Works' shareholders with respect to the proposed Business Combination. A list of the names of those directors and executive officers and a description of their interests in Good Works is contained in Good Works' final prospectus relating to its initial public offering, July 13, 2021, which was filed with the SEC and is available free of charge at the SEC's website at www.sec.gov. Additional information regarding the interests of such participants will be contained in the proxy statement/prospectus for the proposed Business Combination when available.

Offering Summary

Private Placement Offering Summary

Issuer	• Direct Biologics, LLC
Offering Size	• Up to $100 million (including $5 million IB1[(1)] investment)
Pre-$ Valuation	• $500 million (20% discount to anticipated public market valuation of $625 million)
Potential Earnout	• $50 million (5.0 million shares) potential earnout contingent upon meeting a primary endpoint in the Phase 3 EXTINGuish trial by the end of 2023 • $350 million (35.0 million shares) potential earnout contingent upon BLA approval or EUA of ExoFlo™ by the end of 2024
Security	• Equity into the LLC (issued at 20% discount to $10.00 implied market price per share)
Investment Details	• LLC Units to be exchanged for registered shares (subject to lock-up period) following the closing of the proposed de-SPAC transaction • IB1[(1)] has invested $5 million in the private placement
Timing	• Private placement closing on rolling basis and proposed de-SPAC transaction expected to close in H1 2023

De-SPAC Transaction

Overview	• Direct Biologics has executed a definitive agreement for a business combination with Good Works II Acquisition Corporation ("Good Works II") (Nasdaq:GWII) • Good Works II is a SPAC with ~$25 million cash in trust, which is subject to further redemptions
Minimum Cash Condition	• The funds from Good Works II trust account (after giving effect to redemptions and after payment of all transaction fees and expenses), together with the net proceeds of the private placement, shall be at least $75 million

Selected abbreviations: BLA = Biologics License Application; EUA = Emergency Use Authorization; IB1 = IB Investments 1 LLC.

[1] IB1 (IB Investments 1 LLC) is an affiliate of I-Bankers Securities, Inc. and is owned by the CEO of IB Capital, LLC, the Placement Agent. No placement fees were paid on IB1's investment.

Private Placement Offering - Detailed Overview

Private Placement Offering as Described in Direct Biologics Units

	Fully Diluted Direct Biologics Units (in millions)	Price Per Unit for Private Placement (20% discount to de-SPAC transaction price)	Value for Purposes of Private Placement ($ in millions)
Pre-$ (Seller Equity)	113.1	$4.42	$500
Private Placement	22.6	4.42	100
Post-$	135.7		$600

Conversion Ratio ***0.553***

Private Placement Offering as Described in Good Works II Shares

	Good Works II Shares (in millions)	Price Per Share for Private Placement (20% discount to de-SPAC transaction price)	Value for Purposes of Private Placement ($ in millions)
Pre-$ (Seller Equity)	62.5	$8.00	$500
Private Placement	12.5	8.00	100
Post-$	75.0		$600

Value for Purposes of De-SPAC Transaction

Price Per Share for De-SPAC transaction	Value for Purposes of De-SPAC Transaction ($ in millions)
$10.00	$625
10.00	125
	$750

Does not include $50 million potential earnout contingent upon meeting a primary endpoint in the Phase 3 EXTINGuish trial by end of 2023 or $350 million potential earnout contingent upon BLA approval or EUA of ExoFlo™ by end of 2024.

De-SPAC Transaction - Detailed Overview

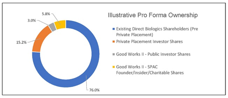
($ in millions, except per share/unit data)

Sources		
Seller Rollover Equity	$625	83.3%
Private Placement Proceeds	100	13.3%
Cash from SPAC Trust	25	3.3%
Total Sources	$750	100.0%
Uses		
Seller Rollover Equity	$625	83.3%
Cash to Company	100	13.3%
Estimated Transaction Costs	25	3.3%
Total Uses	$750	100.0%

Illustrative Pro Forma Valuation	
Pro Forma Good Works II Shares Outstanding (in millions)	82.3
Share Price	$10.00
Pro Forma Equity Value	$823
Less: Cash	(100)
Pro Forma Enterprise Value	$723

Illustrative Pro Forma Capitalization

Pro Forma Ownership	Good Works II Shares (in millions)	% Ownership
Existing Direct Biologics Shareholders (Pre Private Placement)	62.5	76.0%
Private Placement Investor Shares	12.5	15.2%
Good Works II - Public Investor Shares	2.5	3.0%
Good Works II - SPAC Founder/Insider/Charitable Shares	4.8	5.8%
Total Shares	82.3	100.0%



Assumes no additional redemption of current ~$25 million cash in SPAC trust and no excise tax under the Inflation Reduction Act. Does not include $50 million potential earnout contingent upon meeting a primary endpoint in the Phase 3 EXTINGuish trial by end of 2023 or $350 million potential earnout contingent upon BLA approval or EUA of ExoFlo™ by end of 2024.

DIRECT BIOLOGICS™

Company Overview

Overview

Who We Are

Late-stage biotechnology company focused on shepherding the next paradigm shift in medicine with its new platform of potential therapeutics called extracellular vesicles (EVs); the platform consists of a form of stem cell therapy without the cells, DNA or mitochondria

Our Mission

To revolutionize the standard of care (SoC) for patients globally by harnessing the natural power of regenerative EV technology

Value Proposition

Development and commercialization of ExoFlo™, the first MSC derived EV therapeutic candidate in Phase 3 clinical development, through expertise in manufacturing, R&D, quality assurance, clinical operations and regulatory affairs

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Executives

Mark Adams
Chief Executive Officer
Co-Founder

Joe Schmidt
President
Co-Founder

Jeff Mims
Chief Financial Officer

Tim Moseley, Ph.D.
Chief Science Officer

John Vacalis, J.D.
Chief Legal Officer

Vikram Sengupta, M.D.
Chief Medical Officer

Sascha Qian Sengupta, M.D.
Associate Chief Medical Officer

Key Investment Highlights

- Proprietary extracellular vesicle (EV) platform technology derived from bone marrow mesenchymal stem cells (bmMSCs)
- ExoFlo™ is a therapeutic candidate isolated from human bmMSCs, containing growth factors and EVs, including exosomes
- Ongoing "EXTINGuish COVID-19" Phase 3 clinical trial in acute respiratory distress syndrome (ARDS) induced by Covid-19, with submission of a Biologics License Application (BLA) and Emergency Use Authorization (EUA) planned in 2023
- Additional near-term Investigational New Drug (IND) clinical trials planned in all-cause ARDS, mild to moderate Covid-19, post-acute and chronic post-Covid-19 syndrome, ulcerative colitis, Crohn's disease and solid abdominal organ transplant
- Potential wide range of additional future opportunities for ExoFlo in other inflammation and tissue repair indications

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ExoFlo™

ExoFlo is a first-in-class, next-generation biologic leveraging the Company's proprietary EV platform technology

Source:

EVs isolated from human bmMSCs

Components:

Lipid nanovesicles containing 1,000+ regulatory chemokines and other natural signals including mRNA and miRNA

Mechanism:

Reduce inflammation, repair tissue by activating self-repair pathways and promote healing at the cellular level

DIRECT
BIOLOGICS
ExoFlo

Selected abbreviations: bmMSC = bone marrow mesenchymal stem cell; EV = extracellular vesicle; miRNA = micro ribonucleic acid; mRNA = messenger ribonucleic acid.

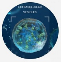
ExoFlo™

ExoFlo is a potent acellular EV product candidate that is anti-inflammatory, non-immunogenic and designed to bypass the drawbacks of traditional stem cell therapies

EXTRACELLULAR VESICLE
MESENCHYMAL STEM CELLS

EVs are derived from human bmMSCs and play a critical role in immune regulation and regeneration

- Clinicians increasingly recognize that the mechanism of transplanted MSCs is not engraftment or differentiation in the target tissue, but rather cell-to-cell communication known as paracrine signaling
- ExoFlo contains an array of over 1,000 growth factors and chemokines, including exosomes, which deliver mRNAs and miRNAs secreted from MSCs
- EVs are paracrine mediators of anti-inflammatory response, immune regulation, tissue regeneration and repair



EVs bypass the drawbacks of traditional stem cell therapies

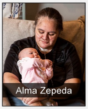
- The secreted EVs of bmMSCs can reproduce similar biological activity to MSCs without requiring the transplantation of MSCs themselves
- The small size of the EVs in ExoFlo will avoid capillary thrombosis, but are still powerful anti-inflammatory and non-immunogenic therapeutic signals
- EVs have a wide array of regulatory proteins to stimulate many processes within the normal healing cascade

EVs regulate the immune response and promote tissue repair

- ExoFlo provides molecular and protein signals that have been shown to stimulate bioactivity and direct cellular communication
- By activating and recruiting local cells, ExoFlo can reduce overactive inflammatory response and restore healing

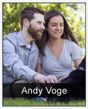
Selected abbreviations: bmMSC = bone marrow mesenchymal stem cell; EV = extracellular vesicle; miRNA = micro ribonucleic acid; mRNA = messenger ribonucleic acid; MSC = mesenchymal stem cell.

ExoFlo™ for Compassionate Use



Virginia mother reunited with newborn after going into Covid-19 induced coma(1)

"In a last-ditch effort, Zepeda was given ExoFlo… an investigational therapeutic available under compassionate emergency use by the FDA."



Cleveland Clinic performs first-in-world full multi-organ transplant to treat rare appendix cancer(2)

"Andy underwent a procedure perfected and performed by Dr. Lightner [of Cleveland Clinic's Center for Regenerative Medicine and Surgery]. She administered MSC derived [EVs], a… novel treatment for solid organ transplants."

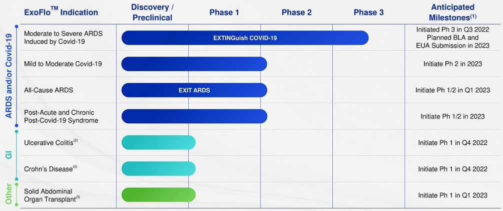
Selected abbreviations: EV = extracellular vesicle; FDA = Food and Drug Administration; MSC = mesenchymal stem cell.

ExoFlo is an investigational product, the safety and efficacy of which continues to be evaluated in ongoing or planned clinical trials. The experiences described above may not be representative of other experiences or future experiences with the investigational product. ExoFlo has not been approved for any use in any jurisdiction and may not be in the future.

[1] Please see https://www.fox5dc.com/news/virginia-mother-reunited-with-newborn-after-going-into-coma-due-to-covid-19, which includes more information.

[2] Please see https://my.clevelandclinic.org/patient-stories/581-man-undergoes-first-in-world-multi-organ-transplant-to-treat-rare-appendix-cancer, which includes more information.

Clinical Pipeline



	ExoFlo™ Indication	Discovery / Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones[1]
ARDS and/or Covid-19	Moderate to Severe ARDS Induced by Covid-19		EXTINGuish COVID-19			Initiated Ph 3 in Q3 2022 Planned BLA and EUA Submission in 2023
	Mild to Moderate Covid-19					Initiate Ph 2 in 2023
	All-Cause ARDS		EXIT ARDS			Initiate Ph 1/2 in Q1 2023
	Post-Acute and Chronic Post-Covid-19 Syndrome					Initiate Ph 1/2 in 2023
GI	Ulcerative Colitis[2]					Initiate Ph 1 in Q4 2022
	Crohn's Disease[2]					Initiate Ph 1 in Q4 2022
Other	Solid Abdominal Organ Transplant[3]					Initiate Ph 1 in Q1 2023

Selected abbreviations: ARDS = acute respiratory distress syndrome; BLA = Biologics License Application; EUA = Emergency Use Authorization.

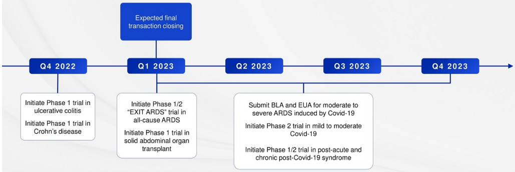
[1] Estimated dates only; actual milestones may differ materially.

[2] Medically refractory.

[3] At risk of worsening allograft function with conventional immunosuppressive therapy alone.

Direct Biologics Upcoming Anticipated Milestones

Direct Biologics anticipates significant news flow in the next 12 months



Expected final transaction closing

Q4 2022

- Initiate Phase 1 trial in ulcerative colitis
- Initiate Phase 1 trial in Crohn's disease

Q1 2023

- Initiate Phase 1/2 "EXIT ARDS" trial in all-cause ARDS
- Initiate Phase 1 trial in solid abdominal organ transplant

Q2 2023 **Q3 2023** **Q4 2023**

- Submit BLA and EUA for moderate to severe ARDS induced by Covid-19
- Initiate Phase 2 trial in mild to moderate Covid-19
- Initiate Phase 1/2 trial in post-acute and chronic post-Covid-19 syndrome

Selected abbreviations: ARDS = acute respiratory distress syndrome; BLA = Biologics License Application; EUA = Emergency Use Authorization.
Estimated dates only; actual milestones may differ materially.

DIRECT BIOLOGICS™

ExoFlo™ for ARDS induced by Covid-19

Acute Respiratory Distress Syndrome (ARDS)

ARDS is an inflammatory lung injury that occurs when fluids build up in air sacs in the lungs and is often fatal; ARDS can be caused by many conditions, including Covid-19, influenza, pneumonia and trauma

No Approved Products in US

- There are currently no approved treatments for ARDS in the US despite decades of clinical trials[1]
- Current mainstay of management is low tidal volume mechanical ventilation

Significant Unmet Need in US

- 40-50% mortality rate among patients with moderate to severe ARDS
- $100,000-150,000 average cost of ICU stay for ARDS
- Annual intensive care expenditure exceeding $80 billion with ARDS representing 15% of the cause for ICU admissions

Direct Biologics' Solution: ExoFlo™

Compelling clinical data suggest the potential of ExoFlo to treat moderate to severe ARDS induced by Covid-19 with a favorable tolerability profile

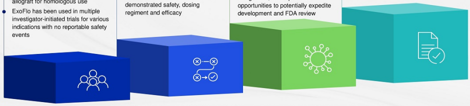
ExoFlo has been shown to reduce inflammation and activate local cells to repair tissue damage; ExoFlo reduces neutrophils and increases CD4 & CD8 T Cells

Selected abbreviation: ARDS = acute respiratory distress syndrome.
Moderate to severe ARDS as defined by classic Berlin criteria.

[1] Though there are no approved ARDS treatments in the US, there are other biotechnology companies looking to enter the space.

Initial Focus on Moderate to Severe ARDS Induced by Covid-19

Direct Biologics' strategic initial focus on moderate to severe ARDS induced by Covid-19 has enabled the Company to develop ExoFlo^{TM} pursuant to an expedited regulatory path



Treated Patients During Discretionary Period

- In 2019-2021, during the FDA's discretionary enforcement period for certain regenerative medicines, ExoFlo was launched as a tissue allograft for homologous use
- ExoFlo has been used in multiple investigator-initiated trials for various indications with no reportable safety events

Completed Successful Phase 1 and Phase 2 Trials

- In April 2020, the first in-human study for ExoFlo demonstrated that 17 out of 24 hospitalized patients with ARDS induced by Covid-19 experienced reversal of hypoxia following treatment with ExoFlo
- The Phase 2 "EXIT COVID-19" trial demonstrated safety, dosing regiment and efficacy

Ongoing Phase 3 Clinical Trial Under RMAT Designation

- In July 2022, the Company initiated its multicenter, double-blinded, placebo-controlled, randomized pivotal Phase 3 trial of ExoFlo in ARDS induced by Covid-19
- ExoFlo also received RMAT designation, which provides opportunities to potentially expedite development and FDA review

Planned Submission of BLA and EUA of ExoFlo in Moderate to Severe ARDS Induced by Covid-19 in 2023

Selected abbreviations: ARDS = acute respiratory distress syndrome; BLA = Biologics License Application; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; RMAT = Regenerative Medicine Advanced Therapy.
Moderate to severe ARDS as defined by classic Berlin criteria.

Current US Standard of Care for Covid-19

	Small Molecule Drugs	Vaccines, Monoclonal Antibodies	MSC Cellular Therapies	Direct Biologics' Approach: ExoFlo^{TM}
Provenance	Synthetic	Synthetic	Natural with synthetic adulterants	Natural
Tolerability	Reported allergic reactions, organ injury	Reported allergic reactions, organ injury	Reported pulmonary emboli ("lung clots", allergic reaction)	No reportable AEs observed in Phase 1 and 2 clinical trials
Mechanism of Action	Antiviral	Antiviral	Anti-inflammatory, regenerative properties	Anti-inflammatory, regenerative properties
Response to SARS-CoV-2 Variants	Potential for variant independent response	Waning efficacy response (2 monoclonal antibodies already lost EUA)	Potential for variant independent response	Potential for variant independent response
Ability to treat ARDS	No mortality reduction, only dexamethasone (steroid) helps	No mortality reduction, not effective	Potential limited by difficulty of redosing and scaling	Potential for mortality reduction and global delivery

Selected abbreviations: AE = adverse event; ARDS = acute respiratory distress syndrome; EUA = Emergency Use Authorization; EV = extracellular vesicle; MSC = mesenchymal stem cell.
These data are derived from different clinical trials at different time points in time, with differences in trial design and patient populations. **No head-to-head clinical trials have been conducted.**

ExoFlo^{TM} Phase 3 Pivotal Trial Design and Path to Approval

EXTINGuish COVID-19 Phase 3 Trial Design

In July 2022, Direct Biologics initiated a multicenter, double-blinded, placebo-controlled, randomized clinical trial to evaluate the safety and efficacy of ExoFlo in treating patients with severe to critical Covid-19, including those with moderate to severe ARDS caused by Covid-19

Up to 610 hospitalized, adult patients with severe to critical Covid-19, including those with moderate to severe ARDS

Treatment Arm: SoC + Drug

Dosing: ExoFlo-15 mL diluted to 100 mL in normal saline infused intravenously over 1 hour; infusion repeated 72 hours later if patient has not recovered

Placebo Arm: SoC + Placebo

Dosing: equivalent volume (100 mL) of normal saline infused intravenously over 1 hour; infusion repeated 72 hours later if patient has not recovered

Primary endpoints:

- 60-day mortality among patients with severe to critical Covid-19 (full study population)
- 60-day mortality among a subset of patients with moderate to severe ARDS
- Primary safety endpoint: incidence of SAEs

Planned BLA submission in 2023

- Direct Biologics plans to complete an interim efficacy analysis based on 50% enrollment (305 patients)
- If the interim analysis reaches statistical significance, Direct Biologics plans to submit a BLA with the data and suspend enrollment in the trial
- If additional data is required, full enrollment of 610 patients will be completed before BLA submission

Selected abbreviations: ARDS = acute respiratory distress syndrome; BLA = Biologics License Application; mL = milliliters; SAE = serious adverse event; SoC = standard of care.
Severe to critical Covid-19 as defined by the Food and Drug Administration (FDA) and moderate to severe ARDS as defined by classic Berlin criteria.

Compelling Outcomes from Phase 2 EXIT COVID-19 Trial

The trial yielded reduction in multiple clinically relevant endpoints in Covid-19 patients with moderate to severe ARDS in the high dose ExoFlo^{TM} treatment arm

Trial Design

Double-blinded, placebo-controlled, randomized clinical trial of 102 adult Covid-19 patients with moderate to severe ARDS

- Randomized 1:1:1 into 3 treatment arms
  1. Placebo + SoC
  2. Low Dose ExoFlo-10 mL + SoC
  3. High Dose ExoFlo-15 mL + SoC
- Treatment consisted of one to two 60-minute infusions of ExoFlo dosed 72 hours apart
- Topline endpoints: 60-day mortality, time to discharge, 7-day change in PaO2/FiO2 ratio, VFDs and the incidence of SAEs
- SoC was defined as per NIH guidelines and consisted of remdesivir, dexamethasone and other medications

Results(1)

- For 60-day mortality, the High Dose treatment arm demonstrated an absolute risk reduction of 17.7% compared to placebo plus SoC and a relative risk reduction of 37.6%
- Subgroup analysis restricted to patients on HFNC, BiPAP and mechanical ventilation demonstrated an absolute risk reduction of 26.1% with a relative risk reduction of 42.9%
  - The subgroup was not pre-specified in the Phase 2 trial design, but will be pre-specified for purposes of the pivotal Phase 3
- No AEs or SAEs were deemed attributable to ExoFlo

Safety and Efficacy Endpoints from Phase 2 EXIT COVID-19 (N=102)

Endpoint	High Dose ExoFlo	Placebo	Notes
60-day Overall Mortality Rate (%)	**29.4%**	**47.1%**	Relative risk reduction in 60-day mortality = 37.6% Absolute risk reduction in 60-day mortality = 17.7%
Median Time to Discharge (Days)	**22**	**NR (31)**(2)	15 mL dose IP reduced length of stay by approximately 9 days
7-day Change in PaO2/FiO2 (mmHg)	**56**	**49**	15 mL dose IP showed higher 7-day change in PaO2/FiO2
Ventilator Free Days (Days)	**41**	**34**	15 mL dose IP reduced mechanical ventilation time by 7.3 days
SAEs	**10**	**16**	44% fewer SAEs in the High Dose treatment arm

Subgroup Analysis of Patients on HFNC, CPAP, BiPAP and Mechanical Ventilation

Endpoint	High Dose ExoFlo	Placebo	Notes
60-day Overall Mortality Rate (%)	**34.8%**	**60.9%**	Relative risk reduction in 60-day mortality = 42.9% Absolute risk reduction in 60-day mortality = 26.1%

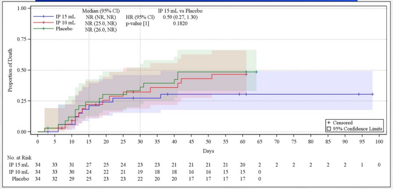
Selected abbreviations: AE = adverse event; ARDS = acute respiratory distress syndrome; BiPAP = bilevel positive airway pressure; CPAP = continuous positive airway pressure; HFNC = high-flow nasal cannula; IP = intraperitoneal; mL = milliliters; mmHg = millimeters of mercury; NIH = National Institutes of Health; NR = not reached; PaO2/FiO2 = partial pressure of oxygen in arterial blood to fraction of inspired oxygen; SAE = serious adverse event; SoC = standard of care; VFDs = ventilator free days.
Moderate to severe ARDS as defined by classic Berlin criteria.

[1] The Low Dose treatment arm did not reach statistical significance compared to the placebo arm.

[2] 31 days for Placebo was estimated via nonparametric extrapolative methods by biostatisticians.

EXIT COVID-19: Phase 2 Trial Results

Phase 2 EXIT COVID-19: % Mortality Vs Time

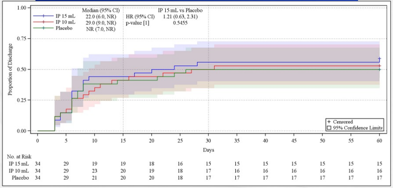


No. at Risk	0	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100
IP 15 mL	34	33	31	27	25	24	23	23	21	21	21	21	20	2	2	2	2	2	2	1	0
IP 10 mL	34	33	30	24	22	21	19	18	18	16	16	15	15	0							
Placebo	34	32	29	25	23	23	22	20	20	17	17	17	17	0							

Selected abbreviations: CI = confidence interval; IP = intraperitoneal; mL = milliliters; NR = not reached.

EXIT COVID-19: Phase 2 Trial Results (continued)

Phase 2 EXIT COVID-19: Time to Discharge



No. at Risk	0	5	10	15	20	25	30	35	40	45	50	55	60
IP 15 mL	34	29	19	19	18	16	15	15	15	15	15	15	15
IP 10 mL	34	29	23	20	19	18	17	16	16	16	16	16	16
Placebo	34	29	21	20	20	18	17	17	17	17	17	17	17

Selected abbreviations: CI = confidence interval; IP = intraperitoneal; mL = milliliters; NR = not reached.
Time to discharge is the interval in days from randomization to discharge from the hospital. The interval is censored to 60 days if the subject did not discharge.

EXIT COVID-19: Phase 2 Trial Results Comparison

The Phase 2 trial results suggest that ExoFlo$^{\text{TM}}$ could be more effective than Remdesivir and Tocilizumab for the treatment of ARDS induced by Covid-19

	Remdesivir 29-day Mortality(1)(2)	Tocilizumab 28-day Mortality(3)	ExoFlo 30-day Mortality	ExoFlo 60-day Mortality
Absolute Risk Reduction	-1.4%	-0.3%	8.8%	17.7%
Relative Risk Reduction	-7.2%	-1.5%	24.9%	37.6%

Selected abbreviation: ARDS = acute respiratory distress syndrome.
These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. **No head-to-head clinical trials have been conducted.**

[1] Figures based on post hoc analysis of subgroup of patients with similar oxygen requirements at baseline to those enrolled in EXIT COVID-19.

[2] Beigel JH, et al. Remdesivir for the Treatment of Covid-19 - Final Report. N Engl J Med. 2020 Nov 5;383(19):1813-1826.

[3] Rosas IO, et al. Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia. N Engl J Med. 2021 Apr 22;384(16):1503-1516.

Phase 1 Clinical Trial Demonstrated Positive Results

An independent pilot study of ExoFlo$^{\text{TM}}$ at the start of the pandemic demonstrated positive results in ARDS induced by Covid-19

Trial Origin

- In April 2020, independent investigators performed an IRB-approved clinical trial using ExoFlo to treat 24 patients with moderate to severe ARDS due to Covid-19
- The independent pilot study demonstrated reversal of hypoxia following treatment with ExoFlo
- The results of this trial were used as Phase 1 data to support Direct Biologic's IND submission allowing the Company to proceed directly into the Phase 2 "EXIT COVID-19" trial

Trial Outcome

- After a single dose, 17 of 24 patients demonstrated reversal of hypoxia
  - Discharged from hospital within 5-6 days
  - 50% median time to recovery from a single dose compared to that observed over a 10-day course of Remdesivir (11 days)

Discharged within
5-6 days

Patients
17/24

Time to recovery
50% of Remdesivir

Selected abbreviations: ARDS = acute respiratory distress syndrome; IND = Investigational New Drug; IRB = Institutional Review Board.

ExoFlo$^{\text{TM}}$ Expanded Access Protocol for Intermediate Population

Positive Data to Date

Open-label, compassionate use study demonstrated positive outcomes in patients with moderate to severe ARDS induced by Covid-19 to date

Background and Methods

- The Company is actively enrolling the open-label clinical trial of ExoFlo in adult Covid-19 patients with moderate to severe ARDS under an expanded access protocol authorized by the FDA
- Single arm study, eligible patients receive up to 3 doses of High Dose intravenous ExoFlo, which is administered in 72-hour intervals
- Endpoints include 60-day mortality, 7-day change in PaO2/FiO2, TTD, VFDs and the incidence of SAEs
- Safety assessed for every patient

Data Readout(1)(2)

- Safety analysis performed by the independent DSMB for the first 50 patients
  - No SAEs related to ExoFlo
- Ad hoc efficacy analysis also performed which revealed the following outcomes for 26 patients
  - 30-day mortality rate was 25.8%, outperforming historical SoC mortality rates of 45% to 55% or greater
  - 7-day change in PaO2/FiO2 was + 132 mmHg, reflecting an improvement in oxygenation
  - Median TTD: 6.8 days
  - VFDs for non-intubated patients: 43.6 days
  - Proportion of non-intubated patients progressing to intubation: 8.3%

Selected abbreviations: ARDS = acute respiratory distress syndrome; DSMB = Data and Safety Monitoring Board; FDA = Food and Drug Administration; mmHg = millimeters of mercury; PaO2/FiO2 = partial pressure of oxygen in arterial blood to fraction of inspired oxygen; SAE = serious adverse event; SoC = standard of care; TTD = time to discharge; VFDs = ventilator free days.
Moderate to severe ARDS as defined by classic Berlin criteria.

[1] 60-day mortality rate not shown in data readout due to timing of efficacy analysis; 60-day mortality is expected at a future date.

[2] Eligibility for expanded access trial was partly determined based on patient exclusions from the Phase 2 trial due to high disease severity. Therefore, patients in expanded access have inherently greater disease severity.

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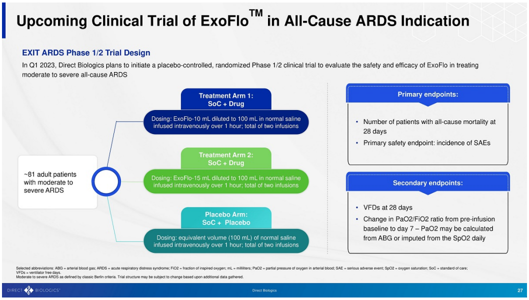
Additional Planned ExoFlo$^{\text{TM}}$ Clinical Trials



Upcoming Clinical Trial of ExoFlo^{TM} in All-Cause ARDS Indication

EXIT ARDS Phase 1/2 Trial Design

In Q1 2023, Direct Biologics plans to initiate a placebo-controlled, randomized Phase 1/2 clinical trial to evaluate the safety and efficacy of ExoFlo in treating moderate to severe all-cause ARDS

~81 adult patients with moderate to severe ARDS

Treatment Arm 1: SoC + Drug

Dosing: ExoFlo-10 mL diluted to 100 mL in normal saline infused intravenously over 1 hour; total of two infusions

Treatment Arm 2: SoC + Drug

Dosing: ExoFlo-15 mL diluted to 100 mL in normal saline infused intravenously over 1 hour; total of two infusions

Placebo Arm: SoC + Placebo

Dosing: equivalent volume (100 mL) of normal saline infused intravenously over 1 hour; total of two infusions

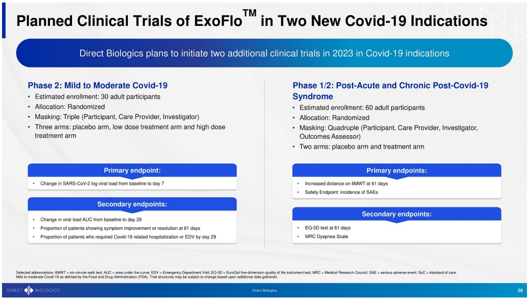
Primary endpoints:

- Number of patients with all-cause mortality at 28 days
- Primary safety endpoint: incidence of SAEs

Secondary endpoints:

- VFDs at 28 days
- Change in PaO2/FiO2 ratio from pre-infusion baseline to day 7 – PaO2 may be calculated from ABG or imputed from the SpO2 daily

Selected abbreviations: ABG = arterial blood gas; ARDS = acute respiratory distress syndrome; FiO2 = fraction of inspired oxygen; mL = milliliters; PaO2 = partial pressure of oxygen in arterial blood; SAE = serious adverse event; SpO2 = oxygen saturation; SoC = standard of care; VFDs = ventilator free days.
Moderate to severe ARDS as defined by classic Berlin criteria. Trial structure may be subject to change based upon additional data gathered.



Planned Clinical Trials of ExoFlo^{TM} in Two New Covid-19 Indications

Direct Biologics plans to initiate two additional clinical trials in 2023 in Covid-19 indications

Phase 2: Mild to Moderate Covid-19

- Estimated enrollment: 30 adult participants
- Allocation: Randomized
- Masking: Triple (Participant, Care Provider, Investigator)
- Three arms: placebo arm, low dose treatment arm and high dose treatment arm

Primary endpoint:

- Change in SARS-CoV-2 log viral load from baseline to day 7

Secondary endpoints:

- Change in viral load AUC from baseline to day 29
- Proportion of patients showing symptom improvement or resolution at 61 days
- Proportion of patients who required Covid-19 related hospitalization or EDV by day 29

Phase 1/2: Post-Acute and Chronic Post-Covid-19 Syndrome

- Estimated enrollment: 60 adult participants
- Allocation: Randomized
- Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
- Two arms: placebo arm and treatment arm

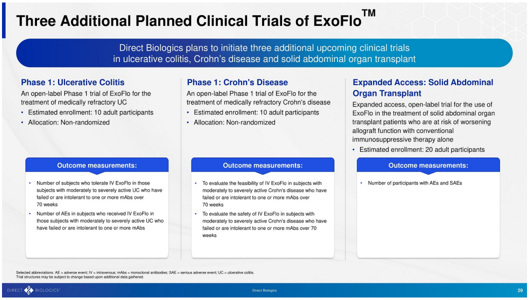
Primary endpoints:

- Increased distance on 6MWT at 61 days
- Safety Endpoint: incidence of SAEs

Secondary endpoints:

- EQ-5D test at 61 days
- MRC Dyspnea Scale

Selected abbreviations: 6MWT = six-minute walk test; AUC = area under the curve; EDV = Emergency Department Visit; EQ-5D = EuroQol five-dimension quality of life instrument test; MRC = Medical Research Council; SAE = serious adverse event; SoC = standard of care.
Mild to moderate Covid-19 as defined by the Food and Drug Administration (FDA). Trial structures may be subject to change based upon additional data gathered.



Three Additional Planned Clinical Trials of ExoFlo^{TM}

Direct Biologics plans to initiate three additional upcoming clinical trials in ulcerative colitis, Crohn's disease and solid abdominal organ transplant

Phase 1: Ulcerative Colitis

An open-label Phase 1 trial of ExoFlo for the treatment of medically refractory UC

- Estimated enrollment: 10 adult participants
- Allocation: Non-randomized

Outcome measurements:

- Number of subjects who tolerate IV ExoFlo in those subjects with moderately to severely active UC who have failed or are intolerant to one or more mAbs over 70 weeks
- Number of AEs in subjects who received IV ExoFlo in those subjects with moderately to severely active UC who have failed or are intolerant to one or more mAbs

Phase 1: Crohn's Disease

An open-label Phase 1 trial of ExoFlo for the treatment of medically refractory Crohn's disease

- Estimated enrollment: 10 adult participants
- Allocation: Non-randomized

Outcome measurements:

- To evaluate the feasibility of IV ExoFlo in subjects with moderately to severely active Crohn's disease who have failed or are intolerant to one or more mAbs over 70 weeks
- To evaluate the safety of IV ExoFlo in subjects with moderately to severely active Crohn's disease who have failed or are intolerant to one or more mAbs over 70 weeks

Expanded Access: Solid Abdominal Organ Transplant

Expanded access, open-label trial for the use of ExoFlo in the treatment of solid abdominal organ transplant patients who are at risk of worsening allograft function with conventional immunosuppressive therapy alone

- Estimated enrollment: 20 adult participants

Outcome measurements:

- Number of participants with AEs and SAEs

Selected abbreviations: AE = adverse event; IV = intravenous; mAbs = monoclonal antibodies; SAE = serious adverse event; UC = ulcerative colitis.
Trial structures may be subject to change based upon additional data gathered.

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Manufacturing, IP & Future Opportunities

Scalable Manufacturing Capabilities

The Company's proprietary EV technology is positioned to scale with global demand, including meeting rigorous FDA manufacturing requirements

- cGMP manufacturing facilities across the US, including state-of-the-art R&D facilities at the Center for Novel Therapeutics at UC San Diego and QC lab in St. Louis
- Cell banks derived from healthy human donors are GTP compliant and have master files with the FDA
- Treatment with bmMSC derived EVs rather than transplantation of MSCs allows for minimal batch-to-batch variability as the product can be derived from a single donor rather than harvesting from multiple donors
- Substantial progress in the development of proprietary technology using bioreactors capable of mass producing ExoFlo™, significantly increases the yield of EV production while simultaneously reducing manufacturing costs
- Key trade secrets and portfolio of patents protecting IP extensively in the US and in select jurisdictions throughout the world

Direct Biologics already has substantial cGMP manufacturing capabilities and clinical experience with ExoFlo established during the FDA's discretionary enforcement period for certain regenerative medicines

Selected abbreviations: bmMSC = bone marrow mesenchymal stem cell; cGMP = current Good Manufacturing Practices; EV = extracellular vesicle; FDA = Food and Drug Administration; GTP = Good Tissue Practice; MSC = mesenchymal stem cell; QC = quality control.

Robust Intellectual Property

Direct Biologics works to maintain its competitive position by utilizing a multi-layered approach that includes filing and prosecuting US and foreign patent applications and protecting proprietary know-how as trade secrets

Patent and Trade Secret Strategy

- Focused on obtaining patents covering product technology, manufacturing and delivery processes, including the proprietary manufacturing process of refining EV therapeutics from bmMSCs and other regenerative cells
- The EV technology platform is protected by a variety of patents pending in the US and OUS, as well as closely guarded trade secrets
- Key trade secrets serve to keep manufacturing processes undisclosed
- Patents pending covering product technology, manufacturing and delivery processes, and release and stability assays
- Additional patent applications in process to obtain a range of coverage for future opportunities

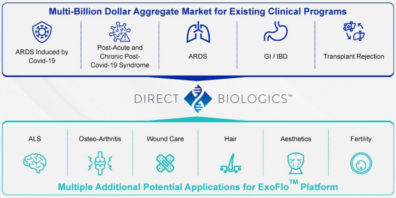
Pending Patent Examples

- Applications related to MSC secretomes, methods of making them and their use in treating and preventing a variety of conditions including wounds, skin disorders, orthopedic disorders/injuries and spinal disorders/injuries
- Application related to a composition comprising a MSC secretome preparation and one or more biomolecules that selectively bind to one or more microbial immunogens, as well as a method of treating a microbial infection
- Application related to a method of isolating platelet rich derived exosomes, platelet rich plasma derived exosome preparation and a method of treating orthopedic or spinal pathology comprising administering a platelet rich plasma derived exosome
- Application related to methods of treating certain hair and skin disorders
- Application related to bacterial and viral infections and subsequent inflammation related disorders

Selected abbreviations: bmMSC = bone marrow mesenchymal stem cell; EV = extracellular vesicle; MSC = mesenchymal stem cell; OUS = outside the United States.

Long Term Opportunities

Direct Biologics' initial focus is on critical unmet needs with applications across inflammation and tissue repair


Multi-Billion Dollar Aggregate Market for Existing Clinical Programs
ARDS Induced by Covid-19
Post-Acute and Chronic Post-Covid-19 Syndrome
ARDS
GI / IBD
Transplant Rejection
DIRECT BIOLOGICS™
ALS
Osteo-Arthritis
Wound Care
Hair
Aesthetics
Fertility
Multiple Additional Potential Applications for ExoFlo™ Platform

Product Extensions

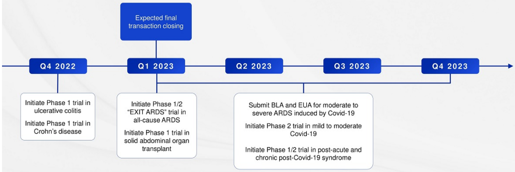
MDI – ExoFlo formulation for outpatient pulmonary indications

Lyophilized ExoFlo (powder formulation) – room temperature stable for ease of distribution (e.g., international markets)

Selected abbreviations: ARDS = acute respiratory distress syndrome; ALS = amyotrophic lateral sclerosis; GI = gastrointestinal; IBD = inflammatory bowel disease; MDI = Metered Dose Inhaler.
Direct Biologics plans to utilize the data from investigator-initiated studies in these and other indications to advance its clinical pipeline in these applications.

Direct Biologics Upcoming Anticipated Milestones

Direct Biologics anticipates significant news flow in the next 12 months



Q1 2023: Expected final transaction closing

Q4 2022
- Initiate Phase 1 trial in ulcerative colitis
- Initiate Phase 1 trial in Crohn's disease

Q1 2023
- Initiate Phase 1/2 "EXIT ARDS" trial in all-cause ARDS
- Initiate Phase 1 trial in solid abdominal organ transplant

Q2 2023 – Q3 2023
- Submit BLA and EUA for moderate to severe ARDS induced by Covid-19
- Initiate Phase 2 trial in mild to moderate Covid-19
- Initiate Phase 1/2 trial in post-acute and chronic post-Covid-19 syndrome

Q4 2023

Selected abbreviations: ARDS = acute respiratory distress syndrome; BLA = Biologics License Application; EUA = Emergency Use Authorization.
Estimated dates only; actual milestones may differ materially.

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Appendix

AmnioWrap

Although it is not the Company's primary focus, Direct Biologics' marketed product, AmnioWrap, is currently a revenue-generating product

AmnioWrap
AmnioWrap2
AmnioWrap3
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- ✓ Placental-based allografts that contain a collagen extracellular matrix and a wide array of regulatory proteins including growth factors, cytokines and chemokines
- ✓ Addresses a wide variety of clinical needs for skin and dermal substitute applications by supporting the healing cascade in the treatment of acute and chronic wounds
- ✓ Technology marketed under three brands
  1. AmnioWrap – a single layer amnion allograft sized appropriately for ocular applications
  2. AmnioWrap2 – a tri-layer amnion allograft ideal for acute and chronic wound application in the outpatient clinic setting (reimbursed with a respective Q code)
  3. AmnioWrap3 – a tri-layer amnion allograft sized appropriately for surgical placement; targeting hospital and ASC surgical procedures
- ✓ The AmnioWrap2 product is in the process of being sold (expected completion in Q4 2022)
- ✓ AmnioWrap3 is being evaluated in an investigator-initiated trial for the prevention and healing of incisional hernias
- ✓ Multi-billion dollar addressable market

Selected abbreviation: ASC = ambulatory surgery center.