HEMISPHERx® BIOPHARMA, INC.

Advanced Therapies for the Human Immune System

NYSE American: HEB

Corporate Presentation

August 2019

Forward-Looking Statements

Some of the statements included in this presentation may be forward-looking statements that involve a number of risks and uncertainties. Among other things, for those statements, we claim the protection of safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. Any forward-looking statements set forth in this presentation speak only as of the date of this presentation. We do not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof.

Please review the “Risk Factors” section in our latest annual report on Form 10-K and subsequent quarterly reports on Form 10-Q. Corporate press releases and company filings are available at www.hemispherx.net. The information found on our website is not incorporated by reference into this presentation and is included for reference purposes only.

Hemispherx Overview

Hemispherx is an immuno-pharma company focused on the research and development of therapeutics to treat multiple types of cancers, as well as immune-deficiency disorders. Hemispherx has seen success in the field of immuno-oncology, which has guided the company's focus toward the potential use of Ampligen as a combinational therapy for the treatment of a variety of solid tumor types.

Our product Ampligen (rintatolimod) is being evaluated in multiple oncology indications, and also for the treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). With regulatory approval in Argentina, Ampligen is the world's only approved therapeutic for ME/CFS. Hemispherx is sponsoring multiple expanded access programs (EAP) for ME/CFS patients worldwide.

Ampligen has in the clinic demonstrated the potential for standalone efficacy in a number of solid tumors. We have also seen success in increasing survival rates and efficacy in the treatment of animal tumors when Ampligen is used in combination with checkpoint blockade therapies. Clinical trials to demonstrate the safety and efficacy of Ampligen in combination with checkpoint blockade drugs such as Keytruda (pembrolizumab) are now underway.

Alferon N Injection is approved in the U.S. and Argentina for the treatment of refractory or recurring external condylomata acuminate and Argentina for patients who have become intolerant to recombinant interferon. The company has developed and will be seeking FDA Pre-Approval Inspection of a high-volume, high-efficiency, upgraded manufacturing process to allow for the commercial viability of Alferon.

Investment Highlights

- Multiple Ampligen clinical trials are in process at major cancer centers, with five now underway; if successful, trials are expected to be a key value driver

- Clinical and commercial opportunities with Ampligen
  - Proven biological activity with an established safety profile
  - In mid-stage clinical testing for multiple cancer types
  - In late-stage development/pre-commercial for ME/CFS

- Ampligen's potential for both mono and combination therapy in oncology
  - Research collaborations are in place with multiple U.S. and European universities and medical centers
  - EAP for pancreatic cancer underway in Holland

- Ampligen has commercial approval for the treatment of ME/CFS in Argentina and is pending commercial launch in 2019; we are awaiting the FDA's authorization to ship product

- EAP for the treatment of ME/CFS further establishes Ampligen's safety profile, increases product awareness, provides a modest revenue stream and develops opinion leaders

- Commercialization of Alferon N injection in the U.S. and Argentina for the treatment of genital warts is pending and will take 18 months from final stage financing

Ampligen (rintatolimod) Development Pipeline

Disease / Indication	Pre-clinical	1	2	3	NDA	Approved	EAP
Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome*	●	●	●	●	U.S.***	Argentina	●
Ovarian, Colorectal, Renal Cell Carcinoma*, Breast and Melanoma* Cancers	●	●	●				
Pancreatic Cancer	●	●**					●
Bladder Cancer	●						

* Orphan Drug Indications in U.S.

** 2 year EAP experience in advanced pancreatic cancer, Ampligen generally well tolerated

*** Received complete response letter from FDA in February 2013. Continuing to identify the path toward approval, potentially with a subset of high responders.

Immuno-Oncology Thought Leader Perspectives

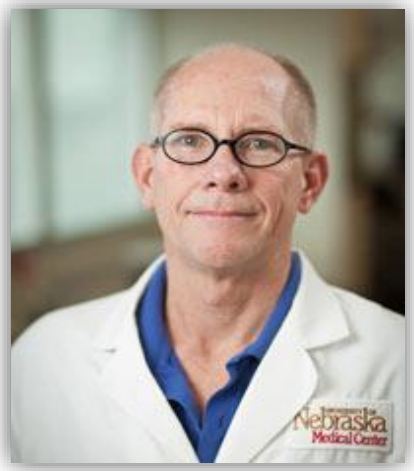
Ampligen

Ampligen is a selective activator of the TLR3 pathway. In combination therapy it shows characteristics that may potentially enhance the performance of checkpoint inhibitors (Theodorika, et al. (2017 & 2018)).

Pawel Kalinski, MD, PhD, Vice Chair for Translational Research at the Department of Medicine and Director of Cancer Vaccine and Dendritic Cell Therapies at the Center for Immunotherapy at Roswell Park Comprehensive Cancer Center, Buffalo, N.Y.

"Ampligen is a selective activator of the TLR3 pathway, which selectively increases the production of factors which attract cytotoxic (killer) T cells while reducing suppressive regulator T cells in the tumor microenvironment. Such modulation of the tumor microenvironment is known to be important for antitumor effectiveness of checkpoint inhibitors, such as PD-1 blockers, and other immune therapies of solid tumors."

Immuno-Oncology Thought Leader Perspectives



Michael A. (Tony) Hollingsworth, PhD, head of pancreatic cancer research at UNMC's Buffett Cancer Center

"We are working hard to discover better treatments for pancreatic cancer. We believe Ampligen is an agent that holds tremendous promise - not only for pancreatic cancer, but also for a variety of other cancers."

Robert P. Edwards, MD, chair of gynecologic services at Magee-Women's Hospital of the University of Pittsburgh School of Medicine

"Ampligen has the potential to be clinically significant because a robust killer T-cell population in the tumor microenvironment without attracting Treg cells is important to help optimize checkpoint blockade induced tumor shrinkage."

Animal Experiments: Ampligen + Checkpoint Blockade Synergistically Increased Survival/Anti-tumor Response

- At the University of Nebraska, in a **pancreatic cancer** transgenic mouse model, combining Ampligen with an anti-PD-L1 drug shows a significant synergistic increase in median survival over control (p=0.029) (unpublished data Hollingsworth, et al.)
- At the University of Pittsburgh, in a mouse model of **colorectal carcinoma**, the combination of Ampligen plus anti-PD-1 showed a median survival increase of greater than 250% compared to anti-PD-1 alone (unpublished data Kalinski, et al.)
- At Augusta University, Ampligen synergistically induced a 300% increase in anti-tumor activity, when compared with anti-PD-L1 alone in a mouse **melanoma** model (unpublished data Hemispherx)
- These synergistic/anti-tumor responses at three different university centers using three different animal models in three different solid tumors have led to new collaborations and planned initiation of multiple combinational clinical trials with Ampligen and FDA-approved checkpoint blockade therapies

Clinical Trial Objective: Reprogram the Tumor Microenvironment to Convert 'Cold' Tumors Into 'Hot' Tumors that will be Responsive to Checkpoint Inhibitors

- Increase Intratumoral Teff cells
- Decrease Intratumoral Treg cells
- Goal is to unleash the cellular immune response to attack and destroy cancer cells and increase survival (Muthuswamy, et al. 2012)
- Ampligen is the only TLR3 agonist to promote selective attraction of CTLs (Teff) with concomitant increase in Teff/Treg ratio in the tumor microenvironment (Theodorika, et al. 2018)
- All of this with a generally well-tolerated safety profile

Five Ampligen Immuno-oncology Clinical Trials Initiated / Ongoing in the U.S.

- Phase 1 / 2 study of intraperitoneal chemo-immunotherapy in recurrent ovarian cancer at University of Pittsburgh Medical Center. Dr. R. Edwards, PI. Eleven of 12 patients enrolled and treated in the Phase I portion. https://clinicaltrials.gov/ct2/show/NCT02432378

- Phase 2a study of Ampligen as component of chemokine modulatory regimen on colorectal cancer metastatic to liver at Roswell Park Comprehensive Cancer Center. Dr. P. Boland, PI. Seven of 12 planned patients enrolled and treated. https://clinicaltrials.gov/ct2/show/NCT03403634

- Phase 2 study of metastatic triple-negative breast cancer using chemokine modulation therapy, including Ampligen and pembrolizumab at Roswell Park Comprehensive Cancer Center. Dr. M. Opyrchal, PI. Two of the planned 6 patients enrolled and treated. https://www.clinicaltrials.gov/ct2/show/NCT03599453

Five Ampligen Immuno-oncology Clinical Trials Initiated / Ongoing in the U.S. - Continued

- Phase 2 study of advanced ovarian cancer using cisplatin, pembrolizumab, plus Ampligen at University of Pittsburgh Medical Center. Up to 45 patients to be enrolled. Enrollment has commenced and the first patient has received treatment. https://clinicaltrials.gov/ct2/show/NCT03734692

- Phase 2 study investigating the effectiveness and safety of aspirin and Ampligen with or without interferon-alpha 2b (Intron A) compared to no drug treatments in a randomized three-arm study of patients with prostate cancer before undergoing radical prostatectomy. Roswell Park Comprehensive Cancer Center. Dr. G. Chatta, PI. IRB and FDA approval to proceed received; pending internal tasks before the study can be opened, with the goal of the end of June. Up to 60 patients to be enrolled. https://clinicaltrials.gov/ct2/show/NCT03899987

** In addition, an Early Access Program (EAP) in pancreatic cancer at Erasmus Medical Center in the Netherlands has been ongoing for more than a year. Prof. Casper van Eijck, PI. (see pages 40-41, https://www.pancreasclub.com/wp-content/uploads/2018/06/Poster-Abstracts.pdf)*

Additional Ampligen Clinical Trials Planned to Be Initiated in 2019-2020, Subject to Funding

- Phase 2 study of Ampligen plus pembrolizumab in refractory metastatic colorectal carcinoma at Roswell Park Comprehensive Cancer Center. Dr. P. Boland, PI. Up to 22 patients to be enrolled.

- Phase 2 study of advanced urothelial (bladder), melanoma and renal cell carcinoma, resistant to checkpoint blockade, using Ampligen plus checkpoint blockade at Roswell Park Comprehensive Cancer Center. Dr. M. Opyrchal, PI. Protocol design currently being finalized.

- First-line therapy for non-small cell lung cancer with SOC chemotherapy plus Ampligen and pembrolizumab at University of Nebraska Medical Center. Dr. V. Ernani, PI. Study design and budget being developed. However, we now anticipate an extended delay, as other studies with funding have moved ahead of the Ampligen project.

- Phase 2 study in advanced pancreatic cancer using checkpoint blockade plus Ampligen at University of Nebraska Medical Center. Dr. K. Klute, PI. Protocol and budget being developed.

- Seeking government-funded large Ampligen therapy breast cancer clinical trial to be conducted at multiple major cancer centers.

Expanded Access Program (EAP) with Ampligen Treatment in Pancreatic Cancer

- Location: Erasmus University, The Netherlands conducted by Professor Casper van Eijck
- Eligibility: Adults with metastatic or locally advanced pancreatic carcinoma following FOLFIRINOX
- Treatment: Ampligen (rintatolimod) 200 mg twice weekly for 2 weeks, then 400 mg twice weekly for a total treatment duration of 18 weeks. Ampligen stopped early for tumor progression.
- Systemic Immune-Inflammation Index and restaging scans/x-rays were performed every 6 weeks
- Initially approved for extremely advanced cases, now approved for all pancreatic cancer, regardless of stage

Interim Clinical Results from EAP in Advanced Pancreatic Cancer at Erasmus University

- 4 patients with advanced disease have survived >12 months on Ampligen without additional treatment
- Another 4 patients have survived >12 months since the start of the Ampligen protocol with palliative chemotherapy
- 15/24 patients died within 7 months
- All patients reported improvement of quality of life during treatment

Interim Clinical Results from EAP in Resected Patients with Pancreatic Carcinoma Treated with Ampligen at Erasmus University

- Of 5 resected patients, 2 died at 24 and 27 months after resection
- The other 3 patients are still alive with a mean survival of 26-plus months after resection and adjuvant Ampligen
- All patients reported improvement of quality of life during treatment

Ampligen in ME/CFS

Overview

- ME/CFS is a medical disorder with biochemical and immune abnormalities, and with promising early work in identifying biomarkers
- The only treatment with a New Drug Application (NDA) filed with the U.S. FDA for the treatment of ME/CFS; a Phase 3 trial was completed and a confirmatory Phase 3 trial will be required; continuing to identify a path toward approval, potentially with a subset of high responders (Hemispherx unpublished data)
- FDA designated orphan drug status, for which the criteria is “a medically plausible basis for expecting the drug to be effective in the rare disease”
- Failure of Rituximab makes this “only game in town”
- FDA authorized a compassionate care program (EAP) for use in ME/CFS for up to 100 patients at a time in approved clinics
- Ampligen has been granted commercial approval by the Argentine Republic for severe ME/CFS

Etiologic / Pathogenic Basis of ME/CFS Establishes ME/CFS as a Medical Disorder

- More than 100 recent articles now establish this as a medical disorder, not a mental disorder
- Pathogenic basis likely to be multifactorial with a strong immune system component
- Two immunologic signatures have been associated with greater disease severity:
  - Low NK cell cytotoxicity (Strayer, et al. 2015)
  - Levels of inflammatory cytokines in serum (Montoya, et al. 2017)
- Ampligen is a well-documented immuno-modulator of both innate and adaptive immunity including activation of NK cell cytotoxicity
- Ampligen has been generally well-tolerated when administered intravenously, intraperitoneally and intranasally

Clinical Safety Record of Ampligen (dsRNA)

- Ampligen has been generally well-tolerated, with almost 100,000 IV doses administered in humans, as well as an intra-nasal and intra-peritoneal safety profile
- Approved as safe for commercial use in Argentina
- Numerous orphan drug designations have been granted by FDA and EMA
- FDA authorized EAP, Ampligen now being given at two major clinics for “compassionate” use
- No evidence of Ampligen-induced autoimmunity
- Safety profile shows that Ampligen has been generally well-tolerated

Alferon N Injection (interferon alfa-n3)

- Approved in the U.S. for the treatment of refractory or recurrent external genital warts in patients ages 18 or older
- Approved in Argentina for the treatment of patients refractory to or intolerant to recombinant alpha interferon
- The worldwide market for recombinant alpha interferon is approximately $4.3 billion, and the incidence of neutralizing antibodies induced against Alferon is very low (<0.2%) compared to recombinant interferons (12-40%) ($p<0.001$) (Strayer, et al. (2012)), thus creating a substantial business opportunity for replacement therapy
- Alferon produces minimal neutralizing antibodies because it is a natural alpha interferon
- The global market is wide open, as there is no natural alpha interferon competitor worldwide to serve as a replacement therapy for refractory patients due to neutralizing antibodies in recombinant alpha interferon therapies

Alferon N Injection (interferon alfa-n3)

- Alferon was approved by the FDA and in Argentina based upon a manual manufacturing technique utilizing 6-liter glass flasks
- Hemispherx has developed a new modern, high-volume, high-efficiency manufacturing technique utilizing an automated 600-liter bioreactor so as to create an adequate volume of production and price point to allow a commercial launch of Alferon
- Hemispherx has a U.S. marketing alliance with distributor Asembia; reimbursement approved by major insurers
- We anticipate sales of ~$94 million per year using our one bioreactor with a single shift, pending a successful FDA pre-approval inspection
- Again, the global market is wide open, as there is no natural alpha interferon competitor worldwide to serve as a replacement therapy for refractory patients due to neutralizing antibodies in recombinant alpha interferon therapies

6-liter flask

600-liter bioreactor

Alferon N Injection Development Pipeline

Disease / Indication	Pre-clinical	Phase I	Phase II	Phase III	Approved
Genital HPV (condylomata acuminata)	●	●	●	●	US and Argentina
Refractory to Recombinant IFN	●	●	●	●	Argentina
Intolerant to Recombinant IFN	●	●	●	●	Argentina
MERS*	●				
Influenza A (H7N9) Virus	●				

* Orphan Drug Indication in EU

Milestones Accomplished in 2018

- Completed the manufacture of 2 commercial size lots amounting to over 16,000 vials of Ampligen
- First 8,000 vial lot of Ampligen has completed rigorous tests and is released to supply expanded access programs in the United States, Europe and Canada for ME/CFS and pancreatic cancer
- Second commercial size lot has passed testing for human use and will be used to initiate commercial sales, as a result of our unrestricted commercial approval for severe ME/CFS in Argentina and ongoing oncology studies
- Expanded our existing scientific collaboration to advance the clinical development of Ampligen at Roswell Park Comprehensive Cancer Center
- University collaborators published new data showing Ampligen's positive role in reprogramming the malignant tumor microenvironment (Theodorika, et al. (2017 & 2018))
- Signed Clinical Trial Agreement with Roswell Park Comprehensive Cancer Center to Study Ampligen in Combination with Checkpoint Inhibitors in a Phase 2A Study in Urothelial Carcinoma, Renal Cell Carcinoma and Melanoma

Milestones Accomplished in 2018

- IRB Approval of Clinical Study in Metastatic Triple Negative Breast Cancer in Collaboration with Roswell Park Comprehensive Cancer Center
- Initiated 12 patient clinical study in colorectal cancer at Roswell Park Comprehensive Cancer Center in combination with Ampligen, Intron A, and Celecoxib, data expected by 2020
- Initiated 6 patient clinical study in triple negative breast cancer at Roswell Park Comprehensive Cancer Center in combination with Ampligen, Intron A, Celecoxib and pembrolizumab, data expected by 2020
- Within the 1st Quarter we expect to initiate a 45 patient clinical study in ovarian cancer at University of Pittsburgh Medical Center in combination with Ampligen, Cisplatin and pembrolizumab, data expected by 2021
- First shipment of Ampligen delivered for sale in Netherlands and currently pursuing additional countries throughout Europe and Canada utilizing the Early Access Program (EAP)

Milestones Accomplished in 2018

- Opened FDA-Approved reimbursement based expanded access program (511) for ME/CFS to new enrollees at approved clinical sites in Nevada and North Carolina, based on FDA authorization to treat up to 100 patients
- Completed initial shipments of Ampligen to the two FDA-authorized 511 clinical sites to treat ME/CFS patients
- Continuing to identify path toward approval for ME/CFS, with work progressing on Ampligen responder subset (Hemispherx unpublished data)
- Completed data analysis of an intranasal human safety study of Ampligen plus FluMist®, intra-nasal safety generally well tolerated
- University of Pittsburgh safety study established Ampligen as generally well-tolerated intraperitoneally for ovarian cancer patients
- Burn rate reduction maintained through 2018 and still accomplished milestones

Milestones Accomplished in 2019

- Initiated 12-patient clinical study in colorectal cancer at Roswell Park Comprehensive Cancer Center combining Ampligen, Intron A, and celecoxib, data expected by 2020. See full details of the study at ClinicalTrials.gov.
- Extended the Early Access Program (EAP) at the Erasmus Medical Center in the Netherlands using Ampligen in the treatment of patients with pancreatic cancer. The EAP is approved by the Dutch Health Inspectorate until March 9, 2020 to treat pancreatic cancer patients diagnosed with any stage of the serious disease. Patients receive Ampligen as a maintenance therapy after completing standard care. Read the full release.
- Our stockholders participated in a Rights Offering and we raised $5.3 million. Further, subsequent to the end of the quarter steps were taken to increase stockholder equity by an additional $4.4 million.

Milestones Accomplished in 2019

- Received an interim report from Dr. Edwards' team on recurrent Ovarian Cancer Phase 1/2 study of intraperitoneal chemo-immunotherapy at University of Pittsburgh Medical Center. See full details of the study at ClinicalTrials.gov.
- An additional round of more extensive and comprehensive pre-clinical animal pancreatic cancer studies were initiated at the University of Nebraska to reconfirm the successful results seen in the initial animal studies. Two pancreatic cancer tumor types will be examined using both anti-PD-1 in addition to the prior anti-PD-L1 in order to fine tune the focus of the proposed future pancreatic cancer clinical trial and reduce the chances of error in clinical trial design.
- Our stockholders voted in favor to grant the Board of Directors the authority to effect a 44-1 reverse stock split of the company's issued and outstanding shares of Common Stock. The proposal passed by approximately 55% of all issued and outstanding shares and approximately 86% of the shares actually voted were voted in favor of the reverse split.

Milestones Accomplished in 2019

- Two patients are enrolled in a 6-patient clinical study in triple negative breast cancer at Roswell Park Comprehensive Cancer Center combining with Ampligen, Intron A, celecoxib and pembrolizumab, data expected by 2020. See full details of the study at ClinicalTrials.gov.
- The Phase 2 study at Roswell Park to treat prostate cancer now has FDA authorization to proceed with its Phase 2 study investigating the effectiveness and safety of aspirin and Ampligen with or without interferon-alpha 2b (Intron A) compared to no drug treatments in a randomized three-arm study of patients with prostate cancer before undergoing radical prostatectomy Aiming to open at the end of the month (June). See the full study at ClinicalTrials.gov.
- First patient treated in a 45-patient clinical study in ovarian cancer at University of Pittsburgh Medical Center combining Ampligen, cisplatin and pembrolizumab, data expected by 2021. See full details of the study at ClinicalTrials.gov.

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Supplemental Data

Publications Demonstrating the Immunological Activity of Ampligen in Oncology

Immunological Activity	Reference(s)*
Only TLR3 agonist to promote selective attraction of CTLs (Teff) with concomitant increase in Teff/Treg ratio in the TME	Theodorika, et al. (2018)
Ampligen induces desirable chemokines in the TME, while other TLR3 agonists, such as poly IC, by activating helicases, induce tumor-promoting signals	Theodorika, et al. (2017)
Phase I/II colorectal cancer trial of Ampligen plus rIFNα-2b and celecoxib showed increase ratio of CXCL10 (CTL-attractant) to CCL22 (Treg-attractant) and increase ratio of CTL/Treg markers	Kalinski, et al. (2016)
Induces epitope spreading and cross-reactive IgA antibody formation in humans	Overton, et al. (2014)
dsRNA/Ampligen increased activity (synergistically) of anti-PD1/PD-L1 drugs	Nagato, et al. (2014); Celis Unpub Data
↑ Teff-attracting chemokine (CXCL10) in the tumor microenvironment (TME)	Muthuswamy, et al. (2012); Kalinski Unpub. Data

* Full reference citations available upon request

Publications Demonstrating the Immunological Activity of Ampligen – *cont'd*

Immunological Activity	Reference(s)*
Induces dendritic cell maturation: Enhances bioactivity of cancer immunotherapy	Nicodemus, et al. (2010)
Promotes optimal dendritic cell maturation and Th1-type responses of healthy donors and cancer patients *in vivo*	Navabi, et al. (2009)
Induces epitope spreading and cross-protective immunity in mice	Ichinohe, et al. (2007)
Increases Delayed Type Hypersensitivity (DTH) response in HIV disease	Thompson, et al. (1996)
Increases LAK cytotoxicity	Hubbell, et al. (1992b)
Increases antitumor immune mechanisms and survival in animal models of renal cell carcinoma and melanoma	Hubbell, et al. (1992a); Hubbell, et al. (1990)
Induction of macrophage tumoricidal activity	Pinto, et al. (1988)
Increases Natural Killer (NK) cell activity	Zarling, et al. (1980)

* Full reference citations available upon request

Publications Demonstrating Activity of Ampligen in ME/CFS and Antiviral Indications

Activity	References
Ampligen increases exercise performance in ME/CFS in Phase III, placebo-controlled trial	Strayer, et al. (2012)
Review of Ampligen clinical activity in ME/CFS	Mitchell (2016)
Low NK cell activity in ME/CFS increased by Ampligen (*in vitro*)	Strayer, et al. (2015)
Antiviral activity of Ampligen in MERS/SARS	Strayer, et al. (2014)
Protection against Venezuelan and Western Equine Encephalitis Virus (*in vivo*, mouse)	Pinto, et al. (1988) Julander, et al. (2009)
Increased survival in Ebola virus disease (*in vivo*, mouse)	Strayer, et al. (2015)

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