BioCure Technology Inc.

BCP CAR-T cell Therapy Program – BCP401

September, 2020

CSE: CURE | www.biocuretech.com
OTC: BICTF
Superior points of BiocurePharm’s CAR-T cell therapy

1. Front runner of Commercializing of CAR-T cell therapy in Korea

2. Experience of the investigated clinical trial in China
   - Secure the data of efficacy and safety for CAR-T cell therapy

3. Product Cost Competitiveness
   - Empirical cost competitiveness based on manufacturing data

4. Experience of CAR-T therapy in Korea
   - 2 terminal stage ALL patients who being cared in Asan Medical Center transferred to Chinese hospital for operating BCP 401 CAR-T. Those 2 patients show CR (Complete Remission) after 1 month of CAR-T therapy.
   - It is the first case of CAR-T therapy in Korea.

5. Establishment of the bridge into a global market
   - Establishment of CAR-T production factory in South-eastern Asian and Europe

6. Improvement of manufacturing process of CAR-T cell therapy with localization
CAR-T Cell for Acute lymphoblastic leukemia (ALL)

- Competitive treatment individually customized for the blood cancer
- Novartis has shown 83% complete response for the patients who are terminally ill

[Mechanism]

- The treatment: Extracts T-Cells from the patient’s blood and modify the cells with a specific virus
- Then grows the modified cells and inject back in the patient. Now cells kill the cancer
FDA Approved CD19_CAR-T cell therapy

◆ EX.1> Novartis, Kymriah

0.2-5 x 10⁶/kg
Max. 0.1-2.5 x 10⁸

For autologous use only.
For intravenous use only.
At 10 to 20 mL per min injection

KYMRIAH is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

◆ EX.2> Kite Pharma, Yescarta

2 x 10⁶/kg
Max. 2 x 10⁸

For autologous use only.
For intravenous use only.
Approximately 68 mL per patient

YESCARTA is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

$475,000, ALL
$373,000, DLBCL

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The 1st CAR-T Cell therapy Kymriah was launched in late 2017 (USA) and 2020 (EU) by Novartis

The therapy is expected to benefit many leukemia patients – old and young

According to the NIH report, more than 340,000 leukemia patients were reported in 2015 in the U.S. (corresponding to 0.1% of the population)

Annual growth rate is expected to increase steadily to around 53.9% (2017-2028)

The market value for CAR-T cell therapeutics is anticipated to grow significantly
Many bio companies are seeking to enter the market by merging with global companies.

CD19 is still the most powerful antigen of hematologic tumors in clinical trial.

Many new attempts are being made using CAR-T cell therapy to treat solid cancer beyond hematologic cancer.

Finding the specific antigen, combination therapy, safety switch off, engineered (Allogeneic) T cell etc.

### Clinical trials of a competitive CAR-T cell products

<table>
<thead>
<tr>
<th>Therapy Name</th>
<th>Target</th>
<th>Manufacturer</th>
<th>Stage</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tisagenlecleucel, Kymria(CTL019)</td>
<td>CD19</td>
<td>Novartis</td>
<td>FDA Approved</td>
<td>relapsed/refractory ALL</td>
</tr>
<tr>
<td>Axicabtagene ciloleucel, Yescarta (KTE-C19, ZUMA-1)</td>
<td>CD19</td>
<td>Gilead (KITE)</td>
<td>FDA Approved</td>
<td>non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>Lisocabtagene marealeucel (JCAR017)</td>
<td>CD19</td>
<td>BMS (Juno)</td>
<td>Submission</td>
<td>Leukemia, Lymphoma, NHL</td>
</tr>
<tr>
<td>Idecabtagene Ciclucel (BB2121)</td>
<td>BCMA</td>
<td>Celgene</td>
<td>Phase II</td>
<td>multiple myeloma</td>
</tr>
<tr>
<td>AUTO-1</td>
<td>CD19</td>
<td>Autolus Limited</td>
<td>Phase I/II</td>
<td>Leukemia, Lymphoma</td>
</tr>
<tr>
<td>JCAR014</td>
<td>CD19</td>
<td>Juno therapeutics</td>
<td>Phase I</td>
<td>NHL</td>
</tr>
<tr>
<td>UCART1</td>
<td>CD19</td>
<td>Cellectis (Servier/Allogene)</td>
<td>Phase I</td>
<td>Leukemia, Lymphoma</td>
</tr>
</tbody>
</table>
Currently stage of BCP019: Production for Clinical trial

BCP401 IND filing
- Preclinical efficacy / toxicity test completed
- SOP and Specification for manufacturing on GMP facility
- CMC (Chemistry, Manufacturing and Control)

IND review for Clinical trial
Supplementation in progress

Current stage

Nonclinical Toxicity / Distribution
- Single to one toxicity
- Repeat-permeability
- Immunotoxicity
- Carcinogenicity
- Reproductive-toxicity
- Genetic-toxicity
- Distribution test

Nonclinical Efficacy / CMC
- Physical Chemistry and Biological properties
  - Viability
  - Expansion fold
  - Phenotype
  - CAR expression
  - Gene copy number
- In vitro Efficacy
  - Cytokine release
  - Cytotoxicity
- In vivo Efficacy
  - Tumor regression
  - Survival rate

Manufacturing in GMP / Specification and Assay
- Lenti virus
  - Genetic verification for Vector
  - Construction of cell bank
  - Establishment of manufacturing process
  - Stability test
  - Establishment of Specification and Assay
- CAR-T cell Manufacturing
  - Establishment of manufacturing process
  - Stability test
  - Establishment of Specification and Assay

IND Filing
- Application
- Plan to clinical trial
- GMP documentation
- Self criteria and Test method
- Document of Stability and Efficacy
  - Development plan
  - Introduction
  - CMC assay for clinical sample
  - Document of nonclinical results
  - Document for clinical trial applicant
Manufacturing Process and QC Management

Release QC
- Sterility
- Mycoplasma
- Endotoxin
- Adventitious viruses
- RCL
- Viability
- Quantity
- Identity
- Purity
- Impurity
- Potency

IPC
- Cell counting
- Cell Viability

CAR-T cell culture and expansion

Transduction of T cell by Lentivirus

T cell Activation

Formulation

PBMC Isolation

Fill & Finish into transfer bag

Patient Blood

Freeze

Harvest of CAR-T cell

Blood Collection

Isolation & Activation

Gene Engineering

Cell Expansion

Infusion

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# Safety Test for BCP401 in a Non-Clinical Efficacy Distribution

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Distribution</th>
<th>Single to toxicity</th>
<th>Repeat to toxicity</th>
<th>Genetic toxicity</th>
<th>Carcinogenicity</th>
<th>Reproductive toxicity</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>O</td>
<td>O</td>
<td>X</td>
<td>X</td>
<td>△</td>
<td>X</td>
<td>△ (Local)</td>
</tr>
</tbody>
</table>

### Single to toxicity
- Single administration
- Test Model: Nude mice
  - (6 males and females per a test)
- How to inject: intravenous
- Dosing: Low, middle, High
  → maximum dose considering safety
- Period: 28 days

### Distribution
- Single administration
- Test Model: Nude mice
  - (5 males and females per a test)
- How to inject: intravenous
- Dosing: maximum dose considering safety
- Test organs: Inguinal LNs, Lung, Heart, Kidney, BM, Liver, Gut, Skin, Blood, Spleen, Gonads, Brain
- Detection for BD: qPCR by validated protocol

### Results:
The test results indicate that the foreign substance, BCP401 will be completely eliminated on 7th and 28th days after administrating it to the immunodeficient animal Balb/c nu/nu mouse. That means there will be little toxic effects that remain to affect other organs.

### Efficacy
- Efficacy for anti-cancer
- Test Model: NPG mice that injected Burkitt’s lymphoma Raji cell, NOD-Prkdc<sup>scid</sup> IL2 Yg<sup>null</sup>)
- How to inject: intravenous
- Dosing: Low, middle, high
- Period: 49 days
- QC Items: Adverse reaction, Weight, Survival rate,

Efficacy evaluation with the level of luciferase expression on tissues and mice

### Results:
Using IVIS, the results of the measurement of the mice that injected for each dose, the expression of luciferase showed about 56% for G2, 22.8% for G3, and 4.8% for G4 compared with a reference. And the expression of luciferase on each organ tissue was confirmed. The survival rate confirms that the group of G4 survives for more than 49 days.

BIOCURE TECHNOLOGY Inc. @ 2020 – Strictly Confidential and Proprietary
# Development of Clinical Trial protocol for BCP401 (Draft)

<table>
<thead>
<tr>
<th>Title</th>
<th>Open phase 1 clinical trial for evaluation of safety for an Autologous T cell which transduced ANTI-CD19 scFv with CD3-ζ and 4-1BB domain from CD19 positive patient who has tolerance drug or non-response for an anti-cancer drug.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance</td>
<td>Autologous T cells introduced with lentiviral vectors expressing ANTI-CD19 scFv with CD3-ζ and 4-1BB signaling domains attached</td>
</tr>
</tbody>
</table>
| Purpose | **Primary:**
Evaluate the safety and efficacy of Autologous T cells (BCP401) in patients and establish the recommended doses for a clinical trial.

**Secondary:**
Evaluate of the tumor reactions after administration of BCP401
Comparison of cytokine changes after administration of BCP401
Confirmation of Pharmacokinetics after administration of BCP401
Check the immunogenicity after administration of BCP401 |
| Number of Tester | 9-12 patients |
| Target Group for Patient | Patients with CD19-positive B-cell tumors and no useful curative treatment options (eg, autologous or other stem cell transplantation) and have a limited prognosis (currently months to less than 2 years) with current treatment. |
| Dosage and Administration | Single dose, IV
- Initial dose : 0.2 to 1 x 10^6 CAR-T cell(BCP401) / kg
- Second stage : 1 to 2.5 x 10^6 CAR-T cell(BCP401) / kg
- Third stage : 2.5 to 5 x 10^6 CAR-T cell(BCP401) / kg
The maximum dose is within 2.5 x 10^8 CAR-T cell(BCP401) |
| Indication | CD19 positive leukemia, Acute Lymphoblastic Leukemia |
Plan for Clinical trial of BCP401

- Clinical hospital or institute
  - Korea: Asan Medical Center, Catholic University of Korea Seoul St. Mary’s Hospital (In discussion and to be determined upon IND approval)
  - Europe: German and/or Bulgarian parties (In discussion)

- Korea IND submission
  - 4Q 2020

- Expected date for clinical trial
  - Korea: 1Q 2021
  - Europe: 4Q 2021 (Korean IND documents to be submitted to EMEA)
### 63 Subjects with relapse/refractory ALL (1~25 age)

### Primary Endpoint for the Efficacy Analysis

7 of 63 are not allowed to be evaluated the efficacy (ND_Not Determine),

**ORR** (overall response rate) was $55/56(98.21\%)$ as a result of the evaluated 56 subjects: CR$_{53}(94.64\%)$, CRi$_2(3.57\%)$, NR$_1(1.79\%)$

### Secondary Endpoint for the Efficacy Analysis

35(62.5\%) of 56 subjects were carried out by HSCT and 21(37.5\%) did not undergo HSCT.

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#### Conclusion

To treat r/r B cell ALL with CD19 positive, CAR-T program has good response with a single dose.

**Evaluation Index**: ORR

It was confirmed through peripheral blood, bone marrow, cerebrospinal fluid analysis, and physical examination. Initial evaluation of CR or CRi was assessed from 28 days.

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The product of 4 patients(#23, #32, #35, #48) was produced by PBMCs derived from sister, brother, and father.
Adverse Events (Safety) by CAR-T-19 during research purpose clinical trial

- Adverse events were immune responses related to CAR-T cell proliferation and cytokines release such as IFN gamma, IL-6, IL-10 etc..
- It was possible to control with IL-6 inhibitor and corticosteroid according to the level of IL-6 and CRP
- Evaluated with CTCAE (Common Adverse Event Terminology Standard) 4.03 of NCI.

**Comparison with a Kymriah (Tisagenlecleucel)**

- ORR at 3 months for primary efficacy evaluation is 52/63 (82.5%) in Kymriah, while results of BIOCURE is 55/63 (87.3%).

<table>
<thead>
<tr>
<th>ORR at 3 Month</th>
<th>Kymriah</th>
<th>BIOCURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>*ORR in Total group</td>
<td>52/63 (82.5%)</td>
<td>55/63 (87.3%)</td>
</tr>
</tbody>
</table>

ORR, overall response rate

- Results of OS at 3 months, Kymriah is 57/63 (90.5%), versus BIOCURE is 63/63 (100%).
- The rate of overall survival are 82.5% (52/63) in Kymriah and 93.7% (59/63) in BIOCURE.

<table>
<thead>
<tr>
<th>OS</th>
<th>Kymriah</th>
<th>BIOCURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>*OS at 3 Month</td>
<td>57/63 (90.5%)</td>
<td>63/63 (100%)</td>
</tr>
<tr>
<td>*OS (Total Period)</td>
<td>52/63 (82.5%)</td>
<td>59/63 (93.7%)</td>
</tr>
</tbody>
</table>

OS, overall survival

Reference Data (Kymriah)
- ORR Results for the Efficacy Analysis

<table>
<thead>
<tr>
<th>primary endpoint (n=63) at 3 month</th>
<th>Efficacy Analysis CR/CRI on D28</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>52 (82.5%)</td>
</tr>
<tr>
<td>CR</td>
<td>40 (63%)</td>
</tr>
<tr>
<td>CRI</td>
<td>12 (19%)</td>
</tr>
<tr>
<td>NR/UNK</td>
<td>11 (17.5%)</td>
</tr>
</tbody>
</table>

Source: FDA Statistical Reviewer
Hurdles of CAR-T cell therapy in Solid tumor

2nd CAR-T cell therapy showed outstanding response rate in hematological malignancies. The results of treatment for non-hematological malignancies, especially solid tumors, seems to be restricted. A lot of researchers are studying various try on the basis of hypothesis and mechanisms.

Major challenges followed as:

- Target antigen heterogeneity
- Trafficking
- Hostile Tumor microenvironments
  - physical barriers, low pH, low oxygen, low nutrient
  - Immunosuppressive immune cells
- Intrinsic regulatory mechanisms of T cells
Overcoming Solid cancer with CAR-T cell therapy

Specificity and Cytotoxicity
- Screening optimal antigen, Increase of cytotoxicity with costimulatory molecules, chemokines

 Trafficking, Infiltration
- Chemokine, signaling receptor (IL-7, CCL2, TGFβ etc.), CARs that degrade the extracellular matrix

 Immune-suppression
- Combination blockage: PD-1/CTLA-4, IL-10/TGF-β, IDO inhibitor etc., stimulating Treg by IL-7 and IL-21

 Others
- CAR design, T cell phenotype, pre-conditioning of patients, manufacturing etc..

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**Immunotherapy** (2016) 8(12), 1355–1361
InterLeukin-7

Proliferation of immature T cell stimulated by IL-7 results in expansion.

IL-7 guides more CTLs and other immune effectors cells infiltration with better survival and upregulated killing activities. It fights against the immunosuppressive network to improve immune function on cancer cells.
PRIME CAR-T cell (IL-7 x CCL19)

- NOILE Immune tech. (Japan) cooperates with LEGEND BIO. (China) and J&J

PRIME (proliferation-inducing and migration-enhancing): IL-7 and CCL19 secretion with proliferation of CAR-T cell

IL-7 and CCL19 helps to infiltration and survival on T-zone fibroblastic reticular cell of tumor

IL-7 increases T cell proliferation and CCL19 induces T cell and DC as a chemoattractant
Combination therapy with Hyleukin-7

- Interleukin-7 enhances T cell trafficking and infiltration into tumors.
- Antagonizes T cell exhaustion

Possible to be more positive results of treatment for solid cancers by the combination of BCP-CAR-T and safety Hyleukin-7 that could use a high dose than others.

Source: NeoImmue Tech
Anti PD-1 Mono Clone Antibody YBL-006 & Anti-CD-19 CAR-T Combined Therapy Development

The purpose of this agreement is to research the effectiveness of combined treatment of Immune Checkpoint Inhibitor PD-1 (Programmed Cell Death Protein-1) developed by YB and anti-CD19 CAR T-Cell Therapy developed by BPK.

Next Generation Anticancer Treatment for Solid Tumors.

Reported by Jong Won Chang at Biospecdata on January 8, 2019
Plan for production: GMP facility and advance for Global Market

<table>
<thead>
<tr>
<th>Area</th>
<th>Plan</th>
<th>Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>It will be established in a Science business belt in Daejeon city on a site already owned by Biocure Pharm</td>
<td>Design in 2020, Completed in 2021</td>
</tr>
<tr>
<td>Germany</td>
<td>Using the existing GMP facility</td>
<td>In progress with interested parties in Germany</td>
</tr>
<tr>
<td>Bugaria</td>
<td>JV to be set up for clinical trial and local GMP facility.</td>
<td>MOU has been executed</td>
</tr>
<tr>
<td>Asia</td>
<td>Compassionate clinical trial in Malaysia with Univ. of Malaya</td>
<td>MOU has been executed</td>
</tr>
</tbody>
</table>

- Compassionate clinical trial with Malaysian Hospital may start in 2020 subject to fund availability.
Further R&D planning on basis of the CAR-T therapy

➢ **Targetable to Solid tumor**

  : Pancreatic cancer, Lung cancer, Ovarian cancer

① Development of new treatment for solid cancers using antibody technology of Y biologics that have various libraries of antibody and developing techniques

② Development of treatment for solid cancers using combination injection with IL-2 and IL-7

➢ **The possibility of solid cancer target treatments using CAR-T cell is seen as likely and important**

   No CAR-T Cell treatment for solid tumor has been approved by the FDA yet

   Several early clinical studies have indicated in roads to successful treatment in solid cancers
# Company Roadmap

<table>
<thead>
<tr>
<th>Classification</th>
<th>Project</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
<th>2024</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immuno-Therapy</strong></td>
<td>CAR-T for ALL</td>
<td></td>
<td></td>
<td>Clinical trial</td>
<td>Launching</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Advanced CAR-T for solid tumor</td>
<td></td>
<td></td>
<td>Pre-clinical</td>
<td>Clinical trial</td>
<td></td>
</tr>
<tr>
<td><strong>Biosimilar</strong></td>
<td>Interferon-β</td>
<td></td>
<td></td>
<td>Clinical</td>
<td>Launching</td>
<td></td>
</tr>
<tr>
<td><strong>Classification</strong></td>
<td><strong>Product</strong></td>
<td>2020</td>
<td>2021</td>
<td>2022</td>
<td>2023</td>
<td></td>
</tr>
<tr>
<td>Overseas network</td>
<td></td>
<td>Malaysia</td>
<td>Germany, Bulgaria</td>
<td>Italy, France, UK and EU</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Main Business Category

- Ongoing - to commercialize the first CAR-T cell therapy in Korea
  - CAR-T Cell therapy preclinical completed in 2020
  - Clinical trial Scheduled for late-2020 / early 2021

- Development of human growth factors as cosmetic ingredient
  - RCHG, RCAW, RCPW launched

- Foot and Mouth Disease Vaccine
  - Using recombinant protein as opposed to cell culture

- Biosimilar and biopharmaceuticals development

- Join Venture Project (in the field of technology support)
  - Interferon-β preclinical in progress to be completed in 2021.

BiocurePharm’s therapy is based on genetic recombinant protein technology, and developed with collaborators in various fields.
The Team

• **Sang-Mok Lee,  CEO & President, Director**
  Dr. Lee has been a President and CEO since the inception in 2005. Dr. Lee holds a PhD in microbiology from Busan National University in Korea and is currently an adjunct professor in microbiology at Chungnam National University. Dr. Lee is a committee member for the hi-tech medical complex city in Daejeon, Korea and a committee member of KOFST (the Korean Federation of Science and Technology Societies).

• **Konstantin Lichtenwald, CFO, Director**
  Mr. Lichtenwald has over ten years of finance and accounting experience, including corporate compliance, accounting and financial management and IPO, RTO services. Mr. Lichtenwald offers extensive knowledge and know-how for companies in two key financial jurisdictions, North America and German speaking parts of Europe. His accounting, financial skills offer a multi-faceted hands on approach to strategic management and problem solving. Mr. Lichtenwald earned his bachelor of business administration degree from Pforzheim University, Germany, and holds the professional designation of Chartered Professional Accountant (CPA, CGA) and Chartered Certified Accountant (ACCA), where he is a member of Chartered Professional Accountants of B.C. and Canada as well as a member of the Association of Chartered Certified Accountants of United Kingdom.

• **Collin (Sang-Goo) Kim, Director**
  Mr. Kim holds a bachelor degree of business administration from Korea University, Seoul, Korea. Mr. Kim came to Vancouver, Canada in 2006 after working for Hanwha Corp., one of Korean business conglomerates for 16 years, where he was dedicated to International trading business for various industrial products. He has been working as a Vice President for Columbia Capital since 2008 and a director of ArcPacific Resources Corp., a public Canadian junior exploration company, since 2015. He is imperative in the communication between Korean management and Canadian management cross the border with his vast knowledge and work experience.
The Team

• **Hans Frykman – Director**
  Dr. Hans Frykman is the current medical director of Neurocode Labs in Vancouver and UBC Diagnostic Services Lab. Neurocode is world leading in the field of neurogenetics accepting difficult adult and pediatric neurology cases from Asia, North America and Europe. It is Canada’s first and only clinical whole exome sequencing laboratory. Also, Neurocode has a best in class software product linking genotype to phenotype in the area of neurogenetics. UBC Diagnostic Services Lab is Canada’s leading clinical Neuroimmunology laboratory servicing all provinces with this highly complex testing. Under Dr. Frykman’s guidance, the UBC Diagnostic Services lab has expanded fourfold. Dr. Frykman has a medical degree from Karolinska Institute in Stockholm, a PhD in Biocatalysis at Royal Institute of Technology, and post graduate medical training from Karolinska University Hospital Solna Campus, Mayo Clinic, University of Minnesota, Memorial Sloan Kettering and University of British Columbia in the areas of internal medicine, oncology, clinical pathology, molecular genetics and medical biochemistry. Dr. Frykman held research positions with the US Government, Astra Zeneca, Akzo Nobel and Novo Nordisk. Early in his career he was part of the discovery teams around Victoza and Losec(Prilosec). He is licensed to practice medicine in Sweden and British Columbia.

• **Danny Joh – Director**
  After completing a PhD in Biochemistry at Texas A&M university and an MBA at Rice University, Danny Joh moved to the San Francisco area to build a career in the biopharma industry. For twenty years, he has expanded his biopharma product development and cross-functional program management experiences while working for major biopharma companies, including Chiron, Genentech, Biomarin, Sangamo and other biotech companies in the San Francisco area. His experience spans from early to late stage product development in various platforms, including biologics, small molecules, and gene therapy across many therapeutic areas, including cancer and rare genetic disorders. He joins the Board of Directors of Biocure Technologies in March, 2019.

• **The Company also has a very strong Advisory Board comprised of Medical Professionals that have key industry contacts and alliances. For their full Bio’s and Summary of expertise please refer to our website.**
Thank you.

Revision – Sep. 2020