

# Bio-Path Holdings

An Oncology-Focused  
Biotechnology Company

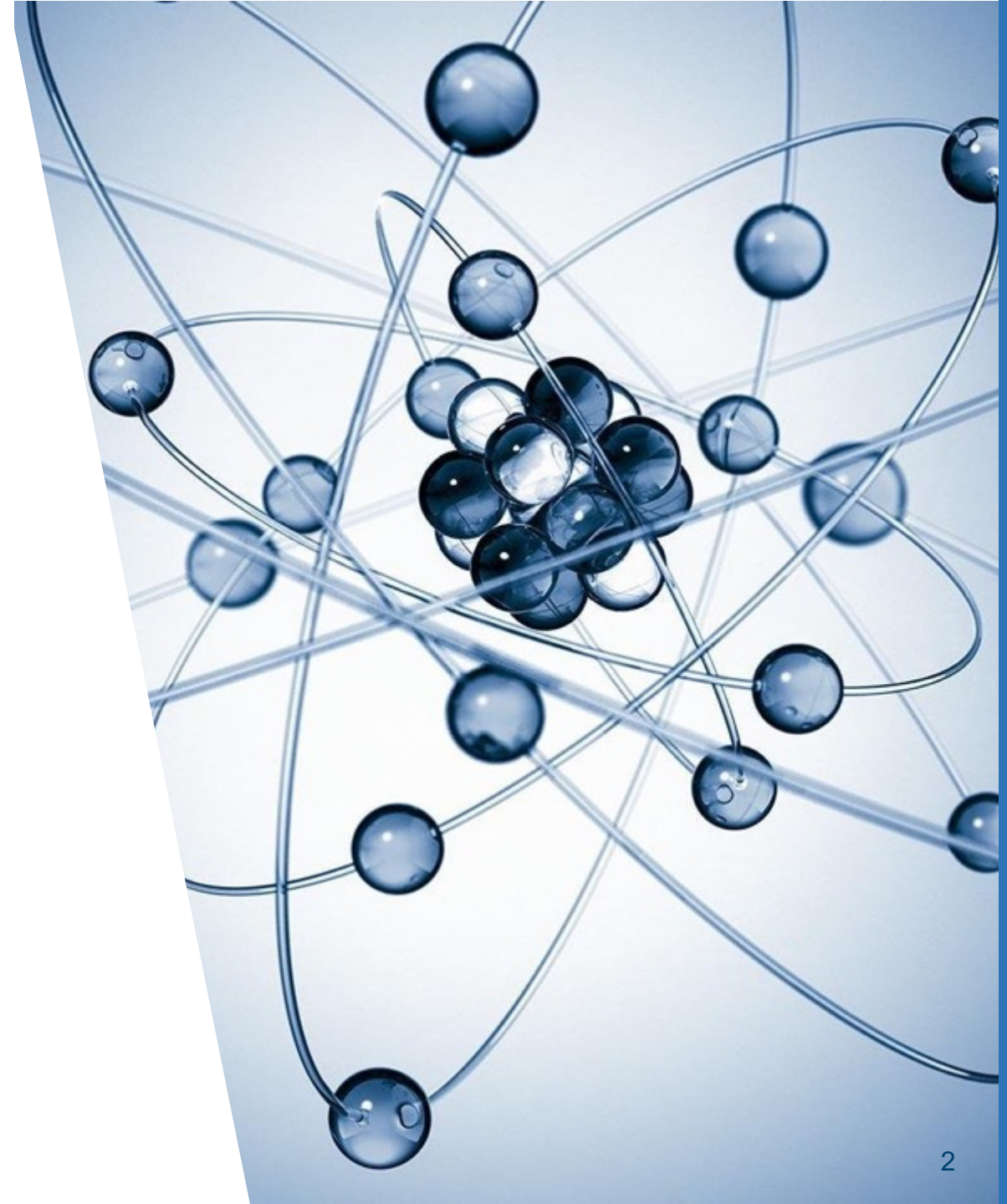
September 2019



# Forward looking statements

This Presentation contains forward-looking statements with respect to business conducted by Bio-Path Holdings, Inc. By their nature, forward-looking statements and forecasts involve risks and uncertainties because they relate to events and depend on circumstances that will occur in the future.

The Company does not undertake to update any forward-looking statements. There are a number of factors that could cause actual results and developments to differ materially and investors should use their own judgment to evaluate risks.



# Introducing Bio-Path Holdings

Advanced Oligonucleotide Therapeutics with  
High Efficiency Systemic Delivery

Publicly traded  
NASDAQ  
BPTH

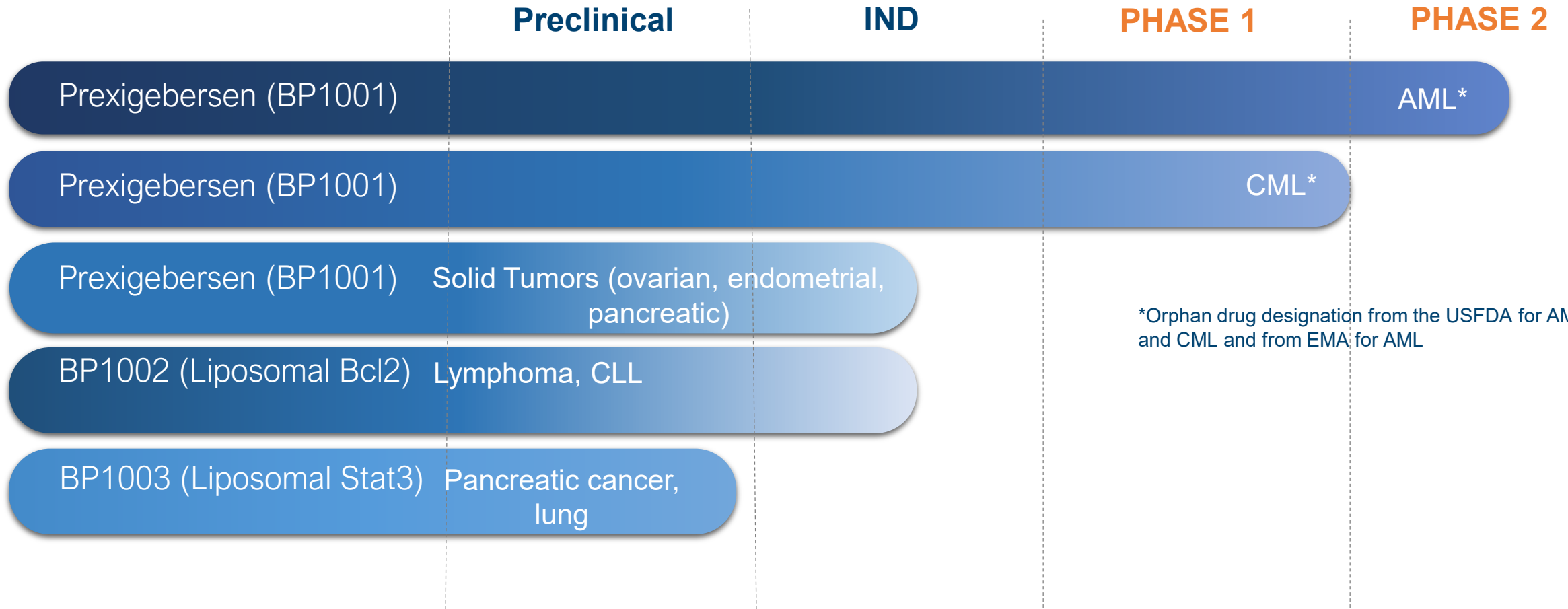
Employees,  
Contract &  
Consultants  
13

Established  
Houston, TX  
2007

**DNAbilize<sup>®</sup> Technology**, next generation single-stranded DNA antisense  
**Robust** clinical pipeline with novel oncology targets



# Robust Oncology Pipeline



\*Orphan drug designation from the USFDA for AML and CML and from EMA for AML

# DNAbilize<sup>®</sup> Technology

Proven As Safe, Robust and Targeted Method for Treating Disease

## No Toxicity

With human patients to date in prexigebersen clinical trial.

- DNAbilize<sup>™</sup> liposome structure is similar to the cellular membrane
- P-ethoxy DNA does not induce hepatotoxicity or thrombocytopenia

## Systemic Treatment

I.V. delivery to the main organs via blood flow.

## High Cellular Uptake

Liposome structure is similar to the cellular membrane enhancing cellular uptake.

## Nanoparticle Liposomes

Enable penetration into tumors for delivery of drug.

## Proven Target Inhibition

Demonstrated that DNAbilize<sup>®</sup> method inhibits target protein, proving delivery technology works.



No Toxicity



Systemic Treatment



High Cellular uptake



Nanoparticle liposomes



Proven target inhibition

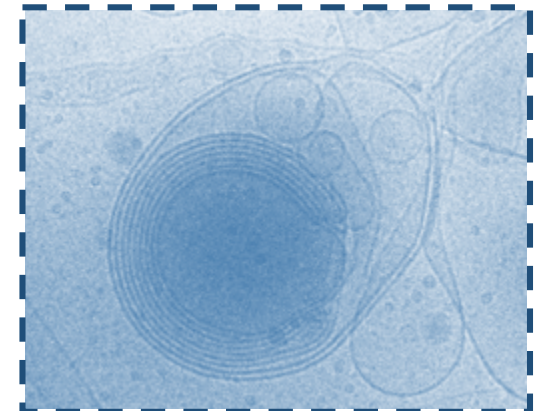
# DNAbilize<sup>®</sup> Technology

Nanoparticle Delivery Ensures Stabilization *In Vivo*

- **Lack of surface charge** on lipid nanoparticle means avoidance of steric hindrance and **ensures cellular uptake**.
- **Slight hydrophobic nature** allows the oligonucleotide to incorporate readily into the lipid bilayers of a **neutral, uncharged lipid nanoparticle** forming **tight association and enabling safe delivery** throughout the body.
- **Nanoparticles are endocytosed** into the cells where the oligonucleotide is released.



Neutral liposome nanoparticle  
drives efficient cell delivery



# DNAbilize<sup>®</sup> Technology

Compared to other Antisense

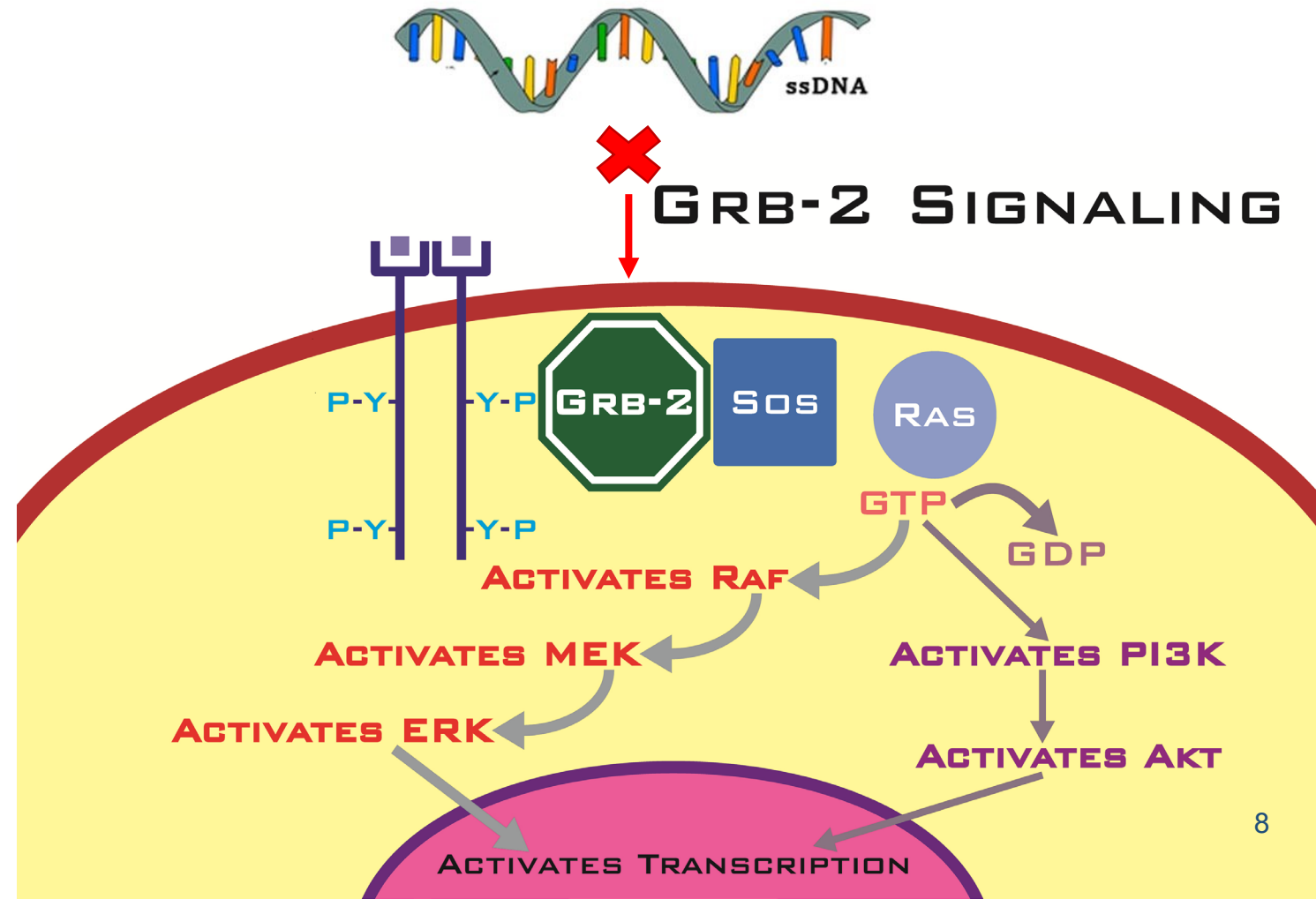
	1 <sup>st</sup> Generation	2 <sup>nd</sup> Generation	DNAbilize <sup>®</sup>
No toxicity			✓ ✓
Systemic Delivery			✓ ✓
Target Specific	✓	✓	✓ ✓
Effectiveness	✓	✓	✓ ✓
High Cellular Uptake			✓ ✓
Neutral charged stabilizing DNA backbone			✓ ✓

Unlike other antisense technologies that demonstrate toxicities and poor cellular delivery, DNAbilize<sup>®</sup> technology enables the development and delivery of **systemic** antisense RNAi nanoparticle treatments for a **broad spectrum** of cancers and other diseases.

# DNAbilize® Lead Target and Indications: Grb2 and Myeloid Leukemia

Prexigebersen is an antisense RNAi nanoparticle targeting Grb2

- Ideal target for myeloid leukemia because it shuts down the Ras pathway in receptor activated myeloid cells without exerting adverse effects on Ras signaling through other channels
- Antisense strategy to inhibit Grb2 because Grb2 is an intracellular protein with no enzymatic activity

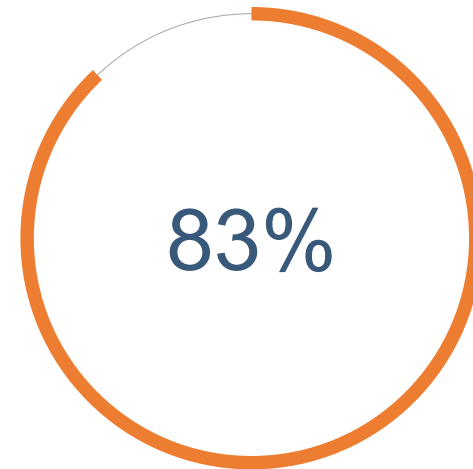




# Summary of Phase 1 Monotherapy Clinical Trial Results for Prexigebersen

- N=39, AML, CML, & MDS Patients Refractory or Resistant to Current Therapies
  - Patients averaged 6 prior therapies
- Dose escalating treatment cycle, 8 doses over 4 weeks, up to 90 mg/m<sup>2</sup>
- **NO ADVERSE EVENTS RELATED TO DRUG/DRUG WAS WELL TOLERATED**  
One mucositis DLT occurred at the lowest dose (5 mg/m<sup>2</sup>) on the study in a patient with a history of prior exposure to hydroxyurea (hydroxyurea treatment continued during the study)

**Of the 18 evaluable patients with circulating blasts, 83% had a reduction in circulating blasts**



# Phase 1 Conclusions

## Results support that Grb2 is a potential therapeutic target for haematological malignancies

- Favorable safety profile strongly suggests that prexigebersen has a very different toxicity profile than other antisense oligonucleotide analogues, which have been associated with serum transaminase activation, thrombocytopenia, and activated partial thrombin time prolongation.
- The tolerability of BP1001 may prove useful in clinical combination settings
- Results published in The Lancet Haematology with Expert Commentary

### The Lancet Haematology

*“Liposomal Grb2 antisense oligodeoxynucleotide (BP1001) in patients with refractory or relapsed haematological malignancies: a single-centre, open-label, dose-escalation, phase 1/1b trial;”*

Volume 5, No. 4, e136–e146, April 2018

# Stage 1 of the Phase 2 Efficacy Trial Design for AML Prexigebersen Combination Therapy

- Treatment of untreated AML patients who are induction therapy ineligible and unfit for stem cell transplant
- Efficacy trial conducted at 6 leading cancer centers in the U.S., including the MD Anderson Cancer Center
- Primary Endpoint: # patients who achieve CR, (accepted surrogate endpoint)



With this Phase 2 design, plans for a pivotal trial would be discussed with FDA if the Interim Analysis significantly exceed current therapy

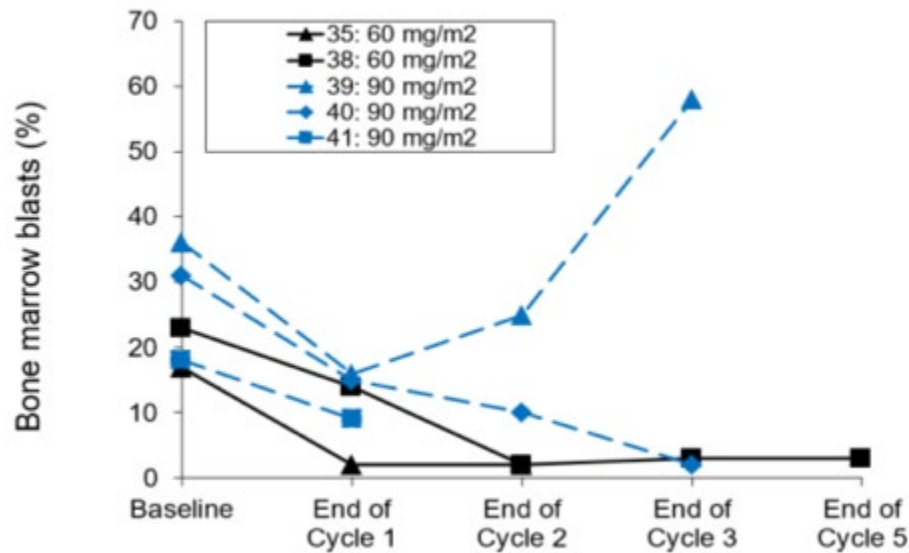
# Safety Segment Phase 2 Prexigebersen + LDAC Combination Therapy Showed Excellent Results

## Relapsed/refractory AML patients

- 3 evaluable patients per cohort, 2 cohorts, n=6
- Dose 60 mg/m<sup>2</sup> and 90 mg/m<sup>2</sup> respectively
- Received drug 2x week for 4 weeks per treatment cycle

## Results

- 3 patients achieved **CR** (and 2 were eligible for bone marrow transplant)
- 2 patients achieved **50% or greater bone marrow blast reduction with stable disease**
- Average age of Patients was 73.5 years old
- No Adverse Effects attributed to prexigebersen
- No MTD reached

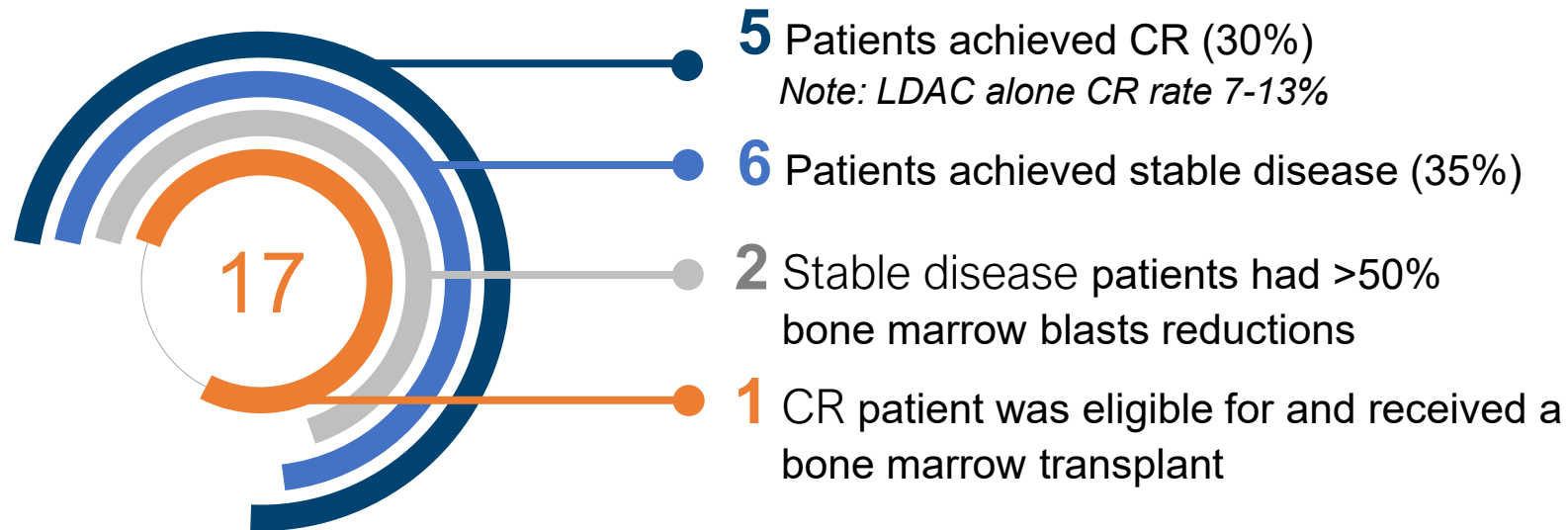


Patient	BP1001 (mg/m <sup>2</sup> )	BM Blasts % Reduction	Cycles completed	Response
35	60	88	1	CR
37	60	0	1	PD
38	60	91	5	CR
39	90	56	3	SD w/ ≥50% bmb reduction
40	90	68	3	CR
41	90	50	3	SD w/ ≥50% bmb reduction

**71% average reduction bone marrow blasts in responding patients**

# Results of Stage 1 Interim Analysis

## Patient evaluation summary



### **Importantly no toxicity associated with prexigebersen**

Based on the recommendations of the study PIs, protocol amendments are being made for Stage 2 in the ongoing study

- A cohort of refractory/resistant AML patients will be added
- High risk Myelodysplastic Syndrome (MDS) patients will be added
- LDAC cohort to be discontinued
- Result is 2 cohort trial with untreated AML/high risk MDS & refractory/resistant AML/MDS
- Triple combination treatment of prexigebersen/decitabine/venetoclax

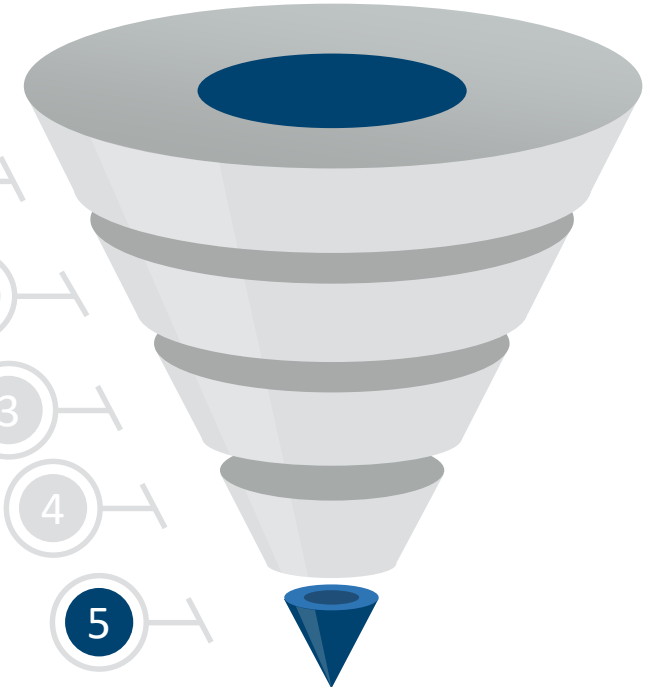


Of the evaluable patients 65% showed some form of response, including CR and stable disease, to the combination treatment

# Prexigebersen (BP1001): A Promising Treatment of Myeloid Leukemia

Prexigebersen in combination with LDAC was well-tolerated and showed early anti-leukemic activity in nearly 65% of evaluable AML patients in Stage 1 of our Phase 2 studies

- 1 PK: 30 hour half life in plasma
- 2 No adverse effects attributed to Prexigebersen were observed
- 3 MTD was not reached as expected
- 4 71% average reduction of bone marrow blasts in responding patients
- 5



Newly planned protocol amendments for Stage 2 of the Phase 2 may provide for pivotal study outcome data and potential approvals in the US and Europe. Two cohorts planned.

# Prexigebersen Phase 1b/2a CML Study

## Potential to treat the 33% of CML patients who are Gleevec resistant

- Phase 1b prexigebersen + dasatinib study
  - Determine safety of the combination in accelerated and blast crisis CML patients
  - 2 cohorts of 3 evaluable patients at 60 mg/m<sup>2</sup> and 90 mg/m<sup>2</sup>
  - Compare the efficacy of the combination to historical response rates in accelerated and blast phase CML patients
- Issues – no enrollment to date
  - Not many accelerated and blast crisis CML patients
  - Add Ph+ AML and Ph+ MDS patients in Amendment 8
- Amendment 9
  - Open enrollment to CML chronic phase patients who are resistant to tyrosine kinase inhibitor therapy
- Current Status
  - Performing market assessment of adding additional sites to increase patient enrollment



# Prexigebersen-A Phase 1 Study in Solid Tumors

- Prexigebersen efficacy against ovarian tumors enhanced when combined with paclitaxel
- Prexigebersen in combination with gemcitabine efficacious against pancreatic tumors
- Clinical Plans
  - First, open a Phase 1a study of prexigebersen in solid tumor patients with recurrent ovarian or endometrial tumors, pancreatic and other solid tumors
    - ❑ Phase 1a allows clinical testing to move quickly through lower dose due to prexigebersen safety record and potentially add an efficacy profile of prexigebersen monotherapy in solid tumors
  - Second - open Phase 1b studies of prexigebersen + paclitaxel in recurrent ovarian or endometrial tumors and prexigebersen + gemcitabine in patients with metastatic pancreatic tumors
- Bio-Path re-engineered the oligo drug product in prexigebersen with the intent to reduce nanoparticle size for use in solid tumors
- This product is referred as prexigebersen-A or BP1001-A
- A new IND was required for solid tumors
  - Currently expects to open a Phase 1 clinical trial in the fourth quarter 2019



## BP1002 – A Phase 1 Study in Lymphoma and CLL

- BP1002 is an RNAi antisense nanoparticle targeting Bcl-2
- BP1002 decreased viability of lymphoma cells (11 of 15 lymphoma cell lines)
- By blocking Bcl-2 protein expression, BP1002 allows chemotherapy and radiation to activate apoptosis
- BP1002 extended survival of mice bearing lymphoma xenografts
- Completed IND-enabling studies (pharmacokinetics, toxicology, genotoxicity), expected IND submission 3Q19
- Launch Phase 1 in lymphoma and CLL at MD Anderson, the plan is to add additional sites
- Focus in CLL will be on patients who have relapsed on venetoclax treatment



# BP1003 Targeting STAT3

- BP1003 has efficacy against non-small cell lung cancer, AML, and pancreatic cancer cells
- BP1003 + gemcitabine combination is efficacious in pancreatic cancer-derived tumors
- IND enabling studies during 2019
- Conduct a Phase 1 study of BP1003 in patients with refractory/metastatic solid tumors (pancreatic, non-small cell lung cancer, colorectal)
- Submit a new IND in 2020

# Experienced Leadership Team



**Peter Nielsen**

**Co-Founder, President,  
Chief Executive Officer  
and Chief Financial  
Officer**

**Officer and Director  
since founding  
Company in 2007**

Manufacturing  
development and  
evolution of engineered  
product design



**Michael Hickey**

**Director Clinical  
Program Management**

**20+ years experience across  
all phases of drug  
development**

**Point of escalation Amgen  
for South East regional CRO  
monitoring**



**Ana Tari Ashizawa,  
PhD, MBA**

**Sr Vice President,  
Research, Development  
& Clinical Design**

**Key member of the  
research team that  
developed our  
liposomal delivery  
technology**



**Anthony Price,  
MBA**

**Sr Vice President,  
Finance, Accounting  
& Administration**

**Former Associate Director  
of Accounting and Finance  
at Lexicon Pharmaceuticals**

# Scientific Advisory Board



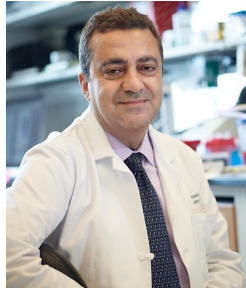
**Jorge Cortes, M.D.**  
Chairman

- Director, Cancer Center at Augusta University
- Georgia Research Alliance Eminent Scholar in Cancer
- Formerly, Jane and John Justin Distinguished Chair in Leukemia Research, Chief of the AML and CML sections, and Deputy Chair of the Department of Leukemia at The University of Texas MD Anderson Cancer Center



**D. Craig Hooper,**  
Ph.D.

- Professor of Cancer Biology and Neurological Surgery and the Section Chief for Translational Research, Tumor Division, in the Department of Neurological Surgery at Thomas Jefferson University
- His work has led to novel immune therapies for rabies infection, neuro-inflammation, and cancer with 10 issued U.S. patents and 19 international patents that have been licensed to five companies in the U.S. and abroad
- He is the founding president of the Jefferson Chapter of the National Academy of Inventors and a fellow of the National Academy of Inventors.



**Anas Younes, M.D.**

- Professor and chief of the Memorial Sloan Kettering's Lymphoma Service. He has an extensive background in translational scientific research with a particular interest in targeted therapies.
- More than 20 years career at M.D. Anderson Cancer Center, most recently as director of clinical and translational medicine in the Department of Lymphoma and Myeloma.
- Medical degree from the University of Damascus School of Medicine. He completed his internal medicine residency training at SUNY Downstate Medical Center and his pathology residency at the Medical College of Ohio. He completed his hematology fellowship training at Memorial Sloan Kettering.



**Jason B. Fleming,**  
M.D., F.A.C.S.

- Newly appointed Chair of the Department of Gastroenterology at H. Lee Moffitt Cancer Center and Research Institute.
- Professor with tenure in the Department of Surgical Oncology at the University of Texas MD Anderson Cancer Center in Houston.
- Served as as chief of Pancreas Surgery and executive director of Perioperative Services and created the first xenograft program in gastrointestinal cancer.
- Received the Castle Connolly Top Doctor award every year since 2013
- President's Faculty Recognition Award for Outstanding Contribution to the University of Texas MD Anderson Cancer Center in 2016.

# IP and Financial Snapshot

## Intellectual Property

- Original patents licensed from MD Anderson
- New composition and methods of use patent issued covers DNAbilize<sup>®</sup> technology, solely owned by Bio-Path
  - Second patent issued for composition and methods with additional claims granted
  - Four additional patents pending

## Financial Snapshot

- **Ticker:** NASDAQ: BPTH
- **Cash:** \$17.1 million as of June 30, 2019
- **Market Cap:** Approximately \$35 – 40 million
- **Burn rate:**
  - Approximately \$2 million per quarter

# Bio-Path Holdings

Thank you

Bio-Path Holdings, Inc.

4710 Bellaire Blvd Suite 210 Bellaire, TX 77401

Web: [www.biopathholdings.com](http://www.biopathholdings.com)

Mail: [partnering@biopathholdings.com](mailto:partnering@biopathholdings.com)

Tel: (832) 742-1369