**SECURITIES AND EXCHANGE COMMISSION**
**WASHINGTON, D.C. 20549**

# FORM 6-K

**REPORT OF FOREIGN PRIVATE ISSUER**
**PURSUANT TO RULE 13a-16 OR 15d-16 OF**
**THE SECURITIES EXCHANGE ACT OF 1934**

***For the month of December 2014***

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# BioLineRx Ltd.

(Translation of Registrant's name into English)

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**P.O. Box 45158**
**19 Hartum Street**
**Jerusalem 91450, Israel**
(Address of Principal Executive Offices)

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Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

**Form 20-F x** **Form 40-F o**

Indicate by check mark whether the registrant by furnishing the information contained in this form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934:

**Yes o** **No x**

On December 12, 2014, at 8:30 am EST, the Registrant will make a presentation to investors and analysts concerning its clinical development plans for BL-8040 over the next 2-3 years. The aforementioned presentation is filed as Exhibit 1 to this Report on Form 6-K.

This Form 6-K, including all exhibits hereto, is hereby incorporated by reference into all effective registration statements filed by the Company under the Securities Act of 1933.

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**BioLineRx Ltd.**

By: /s/ Philip Serlin
Philip Serlin
Chief Financial and Operating Officer

Dated: December 12, 2014

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# BL-8040

## A NOVEL PLATFORM FOR THE TREATMENT OF HEMATOLOGICAL MALIGNANCIES

INVESTOR AND ANALYST BREAKFAST

DECEMBER 12, 2014

# BL-8040 Overview


| | |
|---|---|
| **Indication** | AML & other hematological indications (Orphan designation for AML and SC mobilization) |
| **Mode of Action** | CXCR4 antagonism (CXCR4 over-expressed in >70% of tumors, correlates with disease severity) |
| **Status** | Phase II ongoing (under IND) |
| **Product Highlights** | • Induces apoptosis in cancer cells<br>• Mobilizes cancer cells from bone marrow to peripheral blood<br>• Induces terminal differentiation of immature cancer cells<br>• Sensitizes cancer cells to chemo- and bio-based anti-cancer therapy<br>• Safe and well tolerated at all doses tested to date (up to 1.25mg/kg) |



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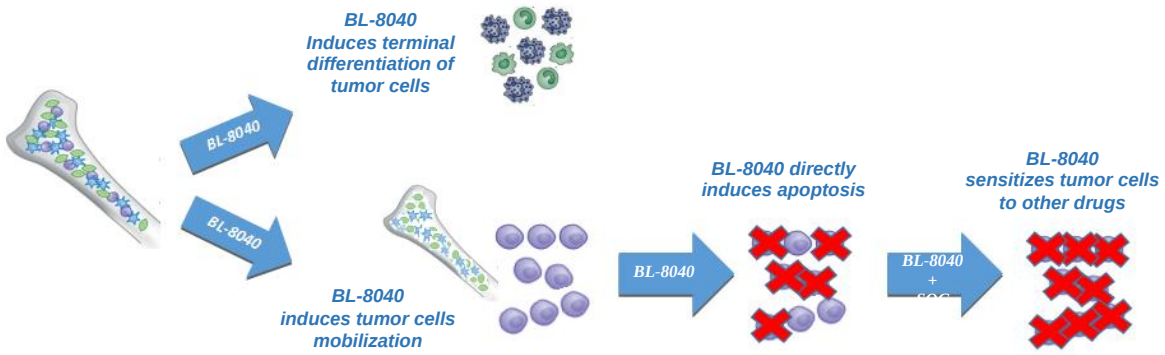
# BL-8040's Unique Mechanism Presents An Opportunity Across Many Hematological Indications

## Results And MOA

- Binds CXCR4 with high affinity (1-2 nM) and works as inverse agonist
- Maintains extended inhibition through long receptor occupancy (>24 hours)
- Induces apoptosis of tumor cells dependent on CXCR4 for survival
- Increases sensitivity to anti-cancer agents by mobilizing tumor cells from the protective microenvironment niche
- Induces terminal differentiation of immature cancer cells



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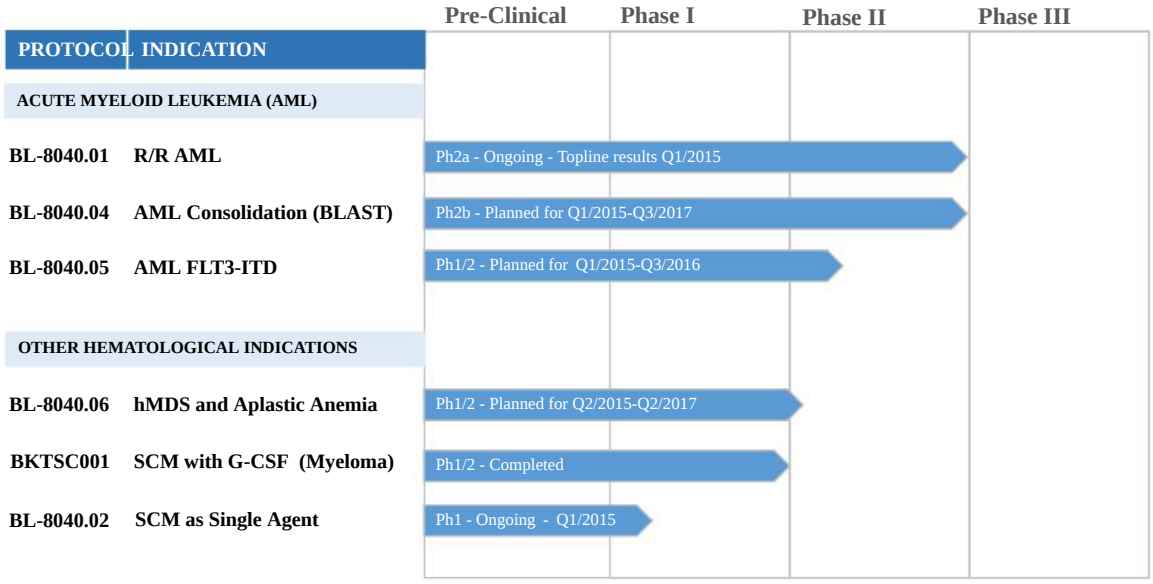
# Clinical Program

December 2014

# Projected Clinical Program Targets Several Hematological Indications With High Unmet Need



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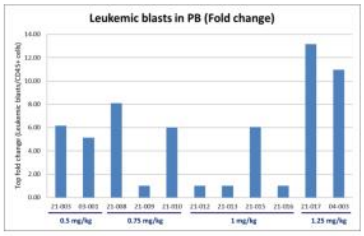
# rrAML

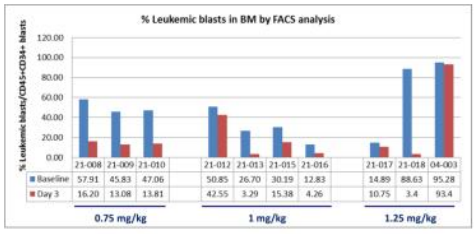
BL-8040.01 study

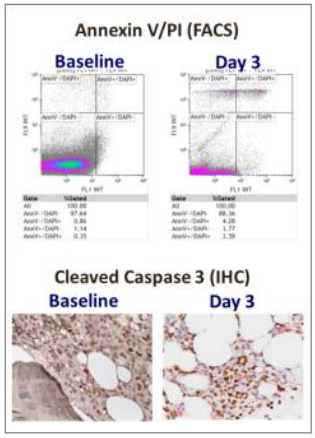
Ongoing Ph2a study

# Results From Ongoing Study

- First four cohorts were completed (0.5, 0.75, 1 and 1.25 mg/kg)
- There were no BL-8040 related SAEs and none of the AEs were considered DLTs
- Robust leukemic blast mobilization was observed (median of 6-fold increase)
- Two days of BL-8040 monotherapy decreased amount of leukemic cells in BM by median of approx. 70%
- Two days of BL-8040 monotherapy induced cancer cell death (apoptosis)
- Topline results are expected during H2/2015



# BL-8040.01 Currently Taking Place at Multiple Leading Medical Centers in the US and Israel

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

**Dr. Gautam Borthakur**

**Dr. Jessica Altman**

**Dr. Martin Tallman**

MAYO CLINIC

**Dr. James Foran**

Shaare Zedek Medical Center in Jerusalem
Affiliated with the Hebrew University School of Medicine

**Dr. Jacob Rowe**

RAMBAM MEDICAL CENTER

**Dr. Yishai Ofran**

Tel-Aviv Sourasky Medical Center

**Dr. Nadav Sarid**

**Dr. Arnon Nagler**

**Dr. Dina Ben-Yehuda**

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# AML Consolidation

BL-8040.01 - the BLAST study

In Collaboration with German
Study Alliance Leukemia Group

# Phase 2b - Consolidation Treatment for AML Patients

## Rationale

- BL-8040 will deepen response by eliminating minimal residual disease left in BM after induction therapy
- Safety of combination with high dose Ara-C is well established by data from r/r AML study encouraging use of BL-8040 as part of the consolidation therapy
- Single agent high dose Ara-C is standard of care worldwide for consolidation treatment

## Advantages

- BL-8040 dose selected from r/r AML study
- Unmet need with no current direct competition
- Earlier line in AML treatment
- Treatment line found interesting by potential partners

# Phase 2b - Consolidation Treatment for AML Patients

**A Phase 2, double-blind, placebo-controlled, randomized, multicenter study to assess efficacy of BL-8040 on top of Ara-C for AML patients in first complete remission, compared to placebo on top of Ara-C**

**Study Design**

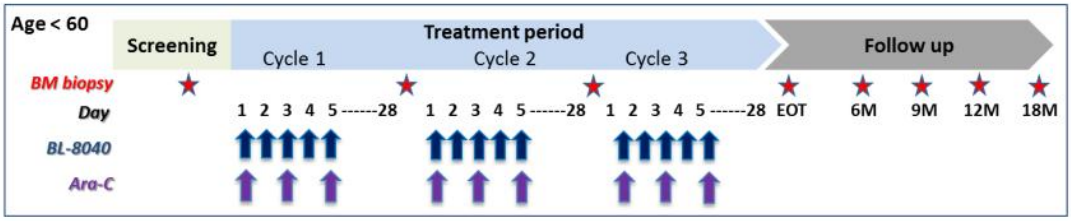
- Double-blind, placebo-controlled, repeated administrations, multiple treatment cycles
- Sample size - ~200 patients
- 20-25 sites in Germany

**Endpoints**

- Relapse Free Survival (RFS) at 3, 6, 9, 12 and 18 months after randomization
- Toxicity, safety and tolerability of BL-8040 in combination with high-dose Ara-C as part of consolidation treatment
- MRD (by FACS) at time of enrollment and during follow-up period (at 3, 6, 9, 12 and 18 months)
- Overall survival (OS) as an open label extension

**Timelines**

- Topline results expected by end of 2017



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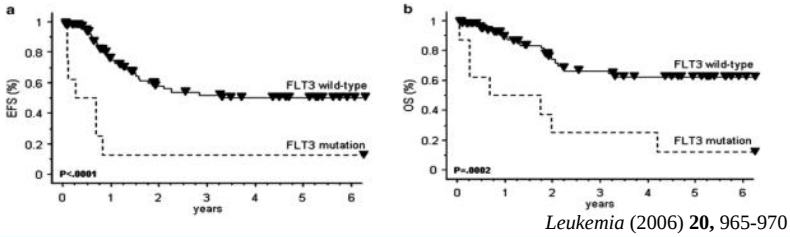
# AML FLT3-ITD

In Collaboration with
MD Anderson Cancer Center

# FLT3 Mutations in AML

- FLT3 is a member of class III receptor tyrosine kinase family, mainly expressed by early myeloid and lymphoid progenitor cells
- FLT3 has important role in proliferation, survival, and differentiation of progenitor cells
- FLT3 mutations present in 30-35% of AML patients & are associated with adverse prognosis
- Internal tandem duplications (ITD) in FLT3 are associated with abnormal leukocytosis and increased marrow blast percentage
- FLT3-ITD confers poor response to chemotherapy, high relapse rates and only transient response to FLT3 inhibitors

**Prognostic impact of FLT3 mutation in AML patients**




*Leukemia* (2006) **20,** 965-970



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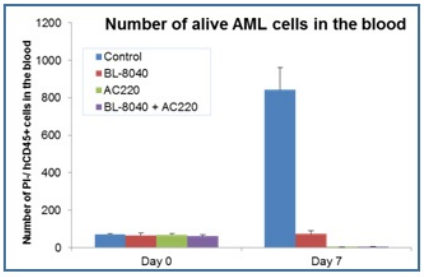
# FLT3 and CXCR4 in AML

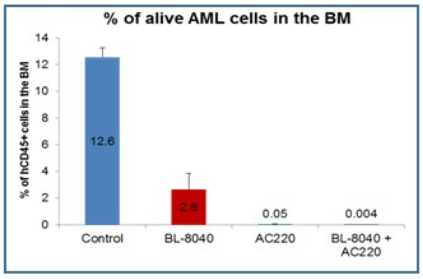
- Emerging data highlight the importance of the bone marrow (BM) niche for the survival of FLT3-mutated AML
- Through CXCL12/CXCR4 interaction, leukemia cells retained in microscopic niches within the BM leading to increased proliferation and survival
- CXCR4 expression is significantly higher in FLT-ITD AML than in FLT3 wild-type AML
- FLT3-ITD mutation activates CXCR4 signaling
- Disruption of the CXCL12/CXCR4 axis with a highly potent CXCR4 antagonist may augment the anti-leukemic effect of FLT3 inhibitors:
  - CXCR4 inhibition enhances the sensitivity of FLT3-mutated leukemic cells to the apoptogenic effects of the FLT3 inhibitor sorafenib (Zeng Z, Blood 2009)
  - CXCR4 inhibition in combination with sorafenib leads to mobilization and elimination of FLT3-ITD AML in a phase 1 trial in relapsed/refractory AML patients (Andreeff M, Blood 2012)

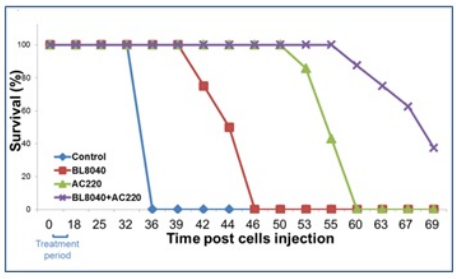
# BL-8040 Affects AML Survival *In-Vivo* (Pre-Clinical Data)

- *In-vivo* FLT3-ITD AML model in NSG mice. Mice are treated with BL-8040 for 7 days after which they are scarified and blood, BM and spleen are collected and analyzed
- Multiple BL-8040 injections reduces the number of AML cells in blood, BM and spleen
- Combination of BL-8040 with FLT3 inhibitor (AC220) is superior to the single agent activity
- Combination of BL-8040 with AC220 eliminated the disease in 4/8 mice and extended survival

| | | Treatment | | | | | | | End of Exp. |
|---|---|---|---|---|---|---|---|---|---|
| Day (-1) | Day 0 | Day 17-23 | | | | | | | Day 24 |
| Irradiation 200 rad | Cells transplantation | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Mice sacrifice Blood, BM and Spleen Collected |
| BL-8040 (SC- 400 ug/mouse) | | + | + | + | + | + | + | + | |
| AC220 (oral – 10 mg/Kg) | | + | + | + | + | + | + | + | |



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# Phase 1/2 - BL-8040 in Combination with Sorafenib for the Treatment of FLT3-ITD AML Patients

## Rationale

- CXCR4 expression is significantly higher in FLT-ITD AML than in FLT3 wild-type AML
- CXCR4 inhibition enhances the sensitivity of FLT3-mutated leukemic cells to the apoptogenic effects of Sorafenib
- Although a good response can be achieved with FLT3 inhibitors, the durability of the response in these patients with a single agent is still very poor

## Advantages

- Well-defined, high-risk patient population - strong reimbursement incentive
- Supported by strong MOA and preclinical data
- PoC can be achieved with small sample size and short-term follow up

# Phase 1/2 - BL-8040 in Combination with Sorafenib for the Treatment of Patients with FLT3-ITD AML

**An Open-label Phase 1/2 Study of BL-8040 in Combination with Sorafenib for Treatment of Patients with FLT3-ITD Mutated AML**

**Study Design**

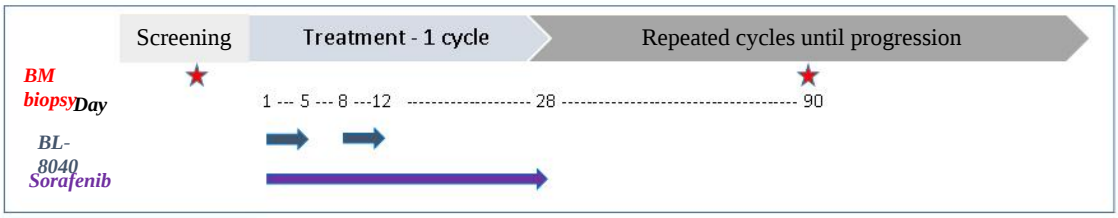
- Open label, two parts, repeated administrations, multiple treatment cycles
- Part I: Assessment of MTD of Sorafinib in combination with BL-8040; dose selection for Part II
- Part II: Safety and efficacy of the combination in different FLT3-ITD patients populations

**Endpoints**

- Composite response rate (CRc = CR + CRp + CRi) within 3 months of treatment initiation
- Duration of response, event-free survival (EFS) and overall survival (OS)
- Safety of BL-8040 in combination with Sorafenib

**Timelines**

- Topline results expected by Q1/2017



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# hMDS and Aplastic Anemia

In Collaboration with

MD Anderson Cancer Center

# Hypoplastic Myelodysplastic Syndrome (hMDS)

- MDS is an heterogeneous group of malignant clonal disorders characterized by bone marrow dysplasia, ineffective hematopoiesis, cytopenias, and the potential to transform into acute myelogenous leukemia (AML)
- Hypoplastic MDS is a subtype of MDS where the bone marrow cellularity is low (< 30%)
- Studies have shown that in this subset of MDS patients the cytopenias respond to immunosuppressive treatment with hATG and cyclosporine

*Leukemia* (2006) **20,** 965-970



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# Aplastic Anemia (AA)

- Deficiency of red cells, neutrophils, monocytes, and platelets without morphological evidence of another marrow disorder. Examination of bone marrow reveals a near absence of hematopoietic precursors and fatty replacement.
- Anemia leads to fatigue, dyspnea, and cardiac symptoms; thrombocytopenia to bruising and bleeding; and neutropenia to increased susceptibility to infection. Treatment with transfusions and antibiotics alone result in limited survival rates.
- Treatments depends on severity of the disease. Supportive treatments include: RBC and platelet transfusion, antibiotics and antivirals. Further treatments are directed against the T-cell mediated autoimmune response and combine horse antithymocyte globulin (hATG) with cyclosporine.
- Hematologic responses occur in 65% of patients treated with hATG and cyclosporine (3-6 months to achieve response); such patients no longer require transfusions and are less susceptible to infection.
- 25-33% of patients do not respond to hATG and cyclosporine.

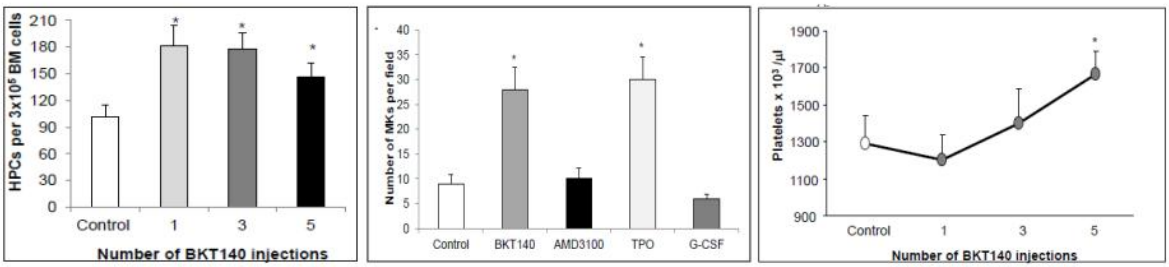
*Leukemia* (2006) **20,** 965-970

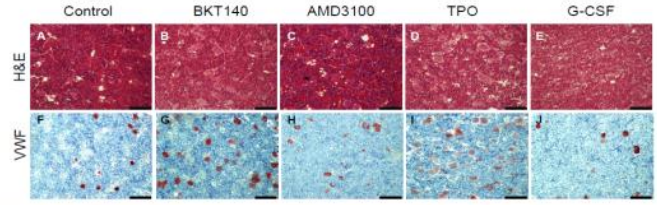
# CXCR4 Involvement in Hypoplastic MDS (hMDS) and Aplastic Anemia (AA)

- hMDS and AA are hematological disorders characterized by bone marrow dysplasia, ineffective hematopoiesis and cytopenias
- In AA and hMDS, an autoimmune microenvironment within the bone marrow niche has been implicated in the depletion of hematopoietic precursors
- This effect is mediated by both soluble factors such as TNF-α, IFN-γ, and TGF-β as well as direct contact with effector cytotoxic T-lymphocytes.
- Disrupting this close interaction and displacing hematopoietic progenitors (and immune cells) from the bone marrow niche may mitigate the autoimmune depletion of hematopoietic precursors and allow recovery of hematopoiesis

# Effect of BL-8040 on BM Regeneration (Preclinical Data)

- Repeated doses of BL-8040 led to marked increase in the number of hematopoietic progenitor cells (HPCs) and hematopoietic stem cells (HSCs) in the bone marrow and peripheral blood of mice
- BL-8040 also promoted increased megakaryopoiesis in the bone marrow, leading to increased platelet production with prolonged effect




Stem Cells. 2007 Sep;25(9):2158-66
Leukemia. 2009 Aug;23(8):1378-88
Br J Haematol. 2013 Oct;163(2):248-59



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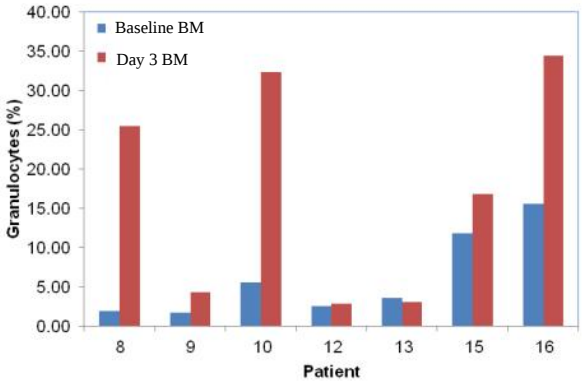
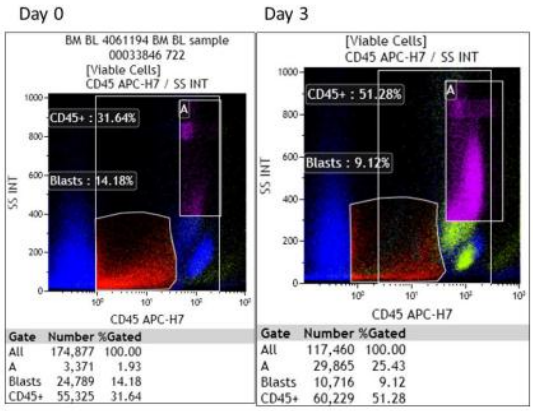
# Effect of BL-8040 on BM Regeneration - Granulocytes (Clinical Data)

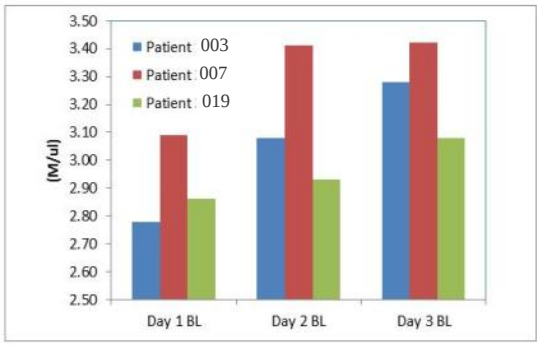
- Preliminary data from BL-8040.01 trial suggest that BL-8040 induces the differentiation of BM leukemic cells into mature cells



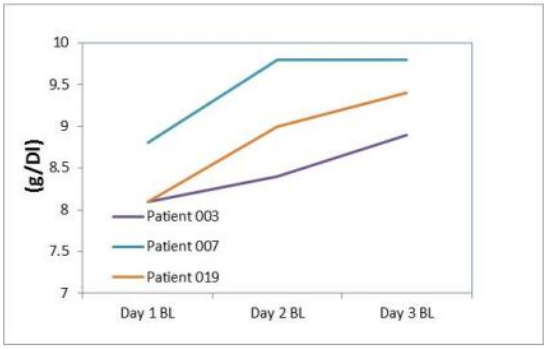



# Effect of BL-8040 on RBC Production (Clinical Data)

- Preliminary data from BL-8040.01 trial suggest that BL-8040 induces the production of mature red blood cells
- The effect was more dramatic in patients where the AML was secondary to MDS




**RBC**




**Hemoglobin**

# Phase 1/2 - Combination of BL-8040 with Immunosuppressive Therapy in Patients with AA or hMDS

## Rationale

- Dual targeted strategy to improve response rates and outcomes
  - hATG and cyclosporine: Target autoimmune attack on hematopoietic precursors with standard immunosuppressive therapy
  - BL-8040: Address the severe depletion of hematopoietic stem cells in the autoimmune bone marrow niche by disrupting this interaction and simultaneously promoting HSC proliferation

## Advantages

- Orphan designation with unmet need
- BL-8040 promotes proliferation of **all** blood cells lines
- Relies on completely different MOA than cancer treatment – BL-8040's effect on SC proliferation and differentiation

# Phase 1/2 - Combination of BL-8040 with Immunosuppressive Therapy in Patients with AA or hMDS

**Phase 1/2 Study of the Combination of BL-8040 with Immunosuppressive Therapy in Patients with Aplastic Anemia (AA) or Hypoplastic Myelodysplastic Syndrome (hMDS)**

**Study Design**

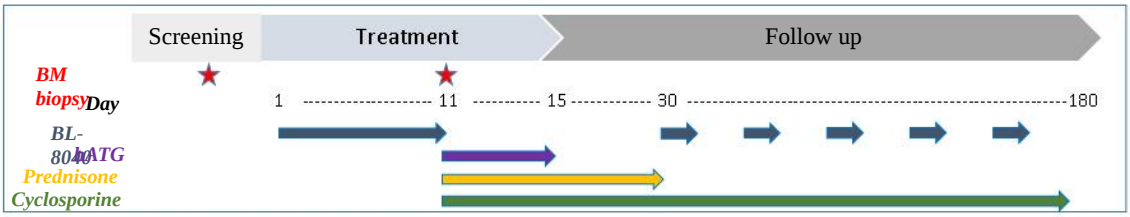
- Open label, repeated administrations, single treatment cycle

**Endpoints**

- Safety, tolerability, and toxicities of the combination of BL-8040, hATG, cyclosporine and prednisone
- Response rate following BL-8040 single agent treatment followed by its combination with hATG, cyclosporine and prednisone
- Time to response, response duration, and overall survival in patients with AA and hMDS treated with the combination of BL-8040, hATG, cyclosporine and prednisone

**Timelines**

- Topline results expected by Q3/2017



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# Stem Cell Mobilization

BL-8040.02 study

Ongoing Ph1 study

# Phase 1 - Single Agent Stem Cell Mobilization

**A Phase 1, Two-Part Study Exploring the Safety, Tolerability, Pharmacodynamic and Pharmacokinetic Effect of Ascending Doses of BL-8040 in Healthy Subjects**

**Study design:**

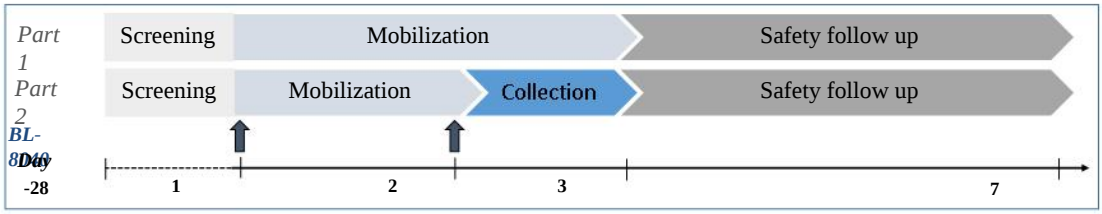
- Part 1 - Dose escalation, randomized, placebo controlled - up to 4 escalating doses (0.5-1.25 mg/kg)
- Part 2 - Dose expansion of safe and efficacious dose group

**Endpoints:**

- Safety and tolerability of escalating repeated (2 days QD) doses of BL-8040 in healthy subjects
- Effect of BL-8040 on mobilization of Hematopoietic Stem Cells (HSC) to peripheral blood (PB)
- Pharmacokinetic profile of BL-8040
- Yields of hematopoietic progenitor cells, immune cells, and other cellular subsets collected by leukapheresis
- Viability, biological activity and repopulating capacity of the cells collected by leukapheresis

**Timelines**

- Topline results expected by end of Q1/2015



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# Thank you!


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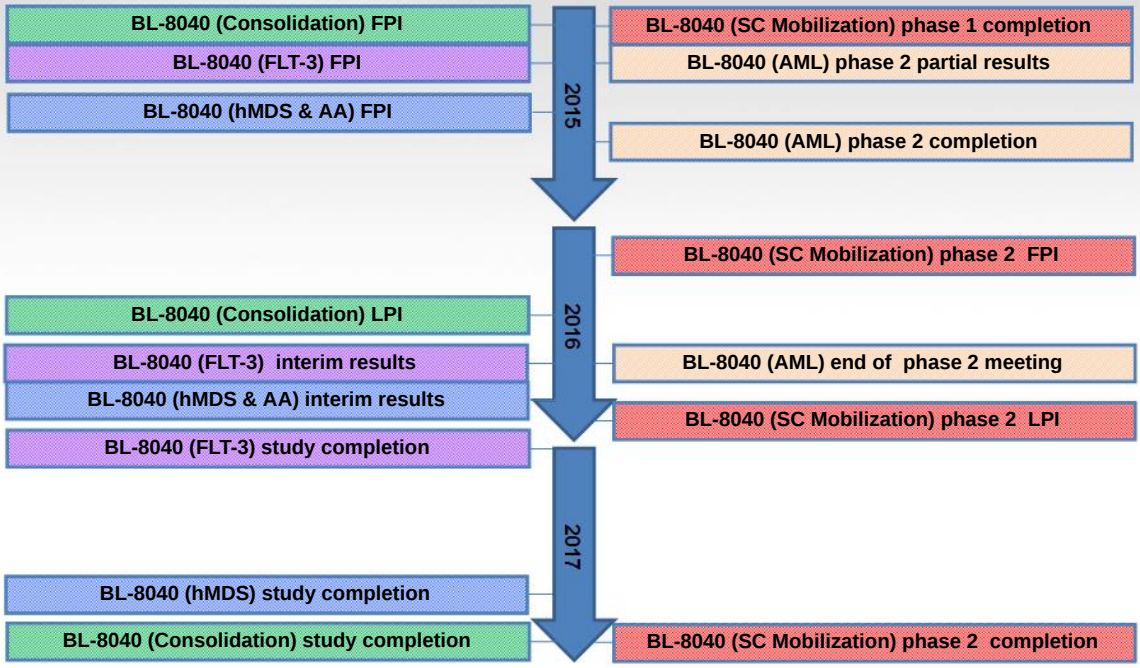
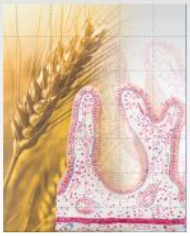
Closing Remarks
Investor/Analyst Breakfast
December 12, 2014
Dr. Kinneret Savitsky

# Major BL-8040 Development Milestones (Next 3 Years)



# Lead Program Update



**BL-7010:**

- Announced Phase 1/2 topline results
- Dose was selected
- Pivotal study for EU to start in H2 2015

**BL-1040:**

- Enrolled over 280 patients out of ~300
- Enrollment to be completed for year-end
- Study completion in mid-2015

# Bench to Bedside to Partner

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