

## Initiation of Coverage

July 20<sup>th</sup> 2017

## BioLineRx Ltd.:

**An Opportunity to Invest in the Development of Unique Cancer Treatment Technologies**

Primary exchange: TASE

Secondary exchange (1 ADS = share 1):  
NASDAQ

Symbol: TASE, NASDAQ:BLRX

Sector: Biotechnology

Sub-sector: Drug Development

Stock target price: NIS 4.90

As of July 18<sup>th</sup>, 2017

Closing price: NIS 3.29

Market cap: NIS 315.3 million

# of shares: 95.6 million

Stock performance (YTD): 5.5%

Daily-trading-vol. (12 months):  
NIS 424.9K

## Company overview

BioLineRx Ltd. ("The Company") is an Israeli clinical-stage biopharmaceutical company focused on oncology and immunology. In 2007, the company was listed on the Tel Aviv Stock Exchange (TASE). In July 2011, the company registered American Depositary (ADSs) in the NASDAQ Capital Market. The Company in-licenses compounds, develops them through pre-clinical and/or clinical stages, and then partners with pharmaceutical companies for advanced clinical development and/or commercialization.

BioLineRx's leading therapeutic clinical platform is BL-8040, a cancer therapy platform: a phase IIa study was successfully completed for relapsed/refractory AML; a Phase IIb study as an AML consolidation treatment is ongoing; and a Phase II study in stem cell mobilization for allogeneic transplantation is ongoing. BL-5010, a solution for treatment of skin lesions was out-licensed to Perrigo.

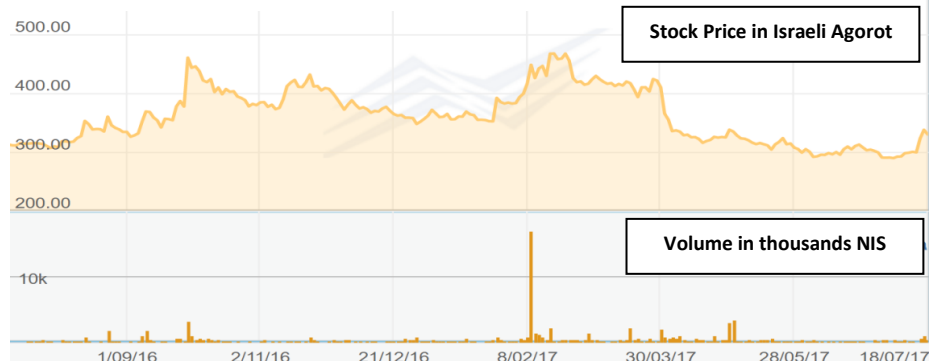
## Highlights

- The company has several strategic agreements:
  - BioLineRx has a strategic collaboration with Novartis for the co-development of selected Israeli-sourced drug candidates such as dry eye syndrome.
  - Collaboration agreement with MSD (known as Merck in the US and Canada), on the basis of which the company has initiated a Phase IIa study in Pancreatic cancer using the combination of BL-8040 and Merck's KEYTRUDA.
  - The company also has a collaboration agreement with Genentech, a member of the Roche Group, to investigate the combination of BL-8040 and Genentech's Atezolizumab in several Phase Ib studies for multiple solid tumor indications and AML.
- BioLineRx recently acquired Agalimmune, a UK-based oncology company, for \$6 million. Agalimmune has a key flagship product, AGI-134, for the treatment of various solid tumors (expected to commence a first-in-man study in patients with solid tumors in the first half of 2018).
- BioLineRx has an experienced management team, Board of Directors and Oncology Scientific Advisory Board with a successful track record at big and small pharma of bringing patented drugs to the market.
- The company had funds of 56 million as of 30<sup>th</sup> April 2017
- We see the company as a long-term investment opportunity in the field of Immuno-Oncology for cancer treatment. In the coming months, several significant events are expected that will impact the company value significantly. While Immuno-Oncology is a promising domain, there significant risks associated with it in the clinical, regulatory and commercialization stages. Albeit, in our view, BiolineRx's market valuation is undervalued, with regards to multiple clinical indications in the company's development pipeline, the company's latest acquisition, and sufficient funds. The aforementioned are expected to support its business strategy until the year 2019.
- We estimate the company's equity value at \$131.5 million / NIS 468.1 million; target price of NIS 4.90 per share (range of NIS 4.76-5.04).**

## Stock overview YTD (Source: TASE website)

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## Executive Summary

### Investment Thesis

BioLineRx Ltd. is an Israeli publicly-traded (NASDAQ: BLRX; TASE: BLRX) specialty biopharmaceutical company focused on the in-licensing and clinical development of therapeutics for oncology and immunology. BioLineRx, headquartered in Modi'in, Israel, was incorporated and commenced operations in April 2003. In 2007, the company was listed on the Tel Aviv Stock Exchange (TASE). In July 2011, the company registered American Depositary (ADSs) in the NASDAQ Capital Market. Investors can view the company as a large clinical “lab” that licenses advanced candidates in pre-clinical phases and transforms them into commercially-ready drugs.

BioLineRx is currently advancing a lead clinical program, BL-8040, in multiple clinical studies: three Phase II programs for consolidation AML, stem-cell mobilization (SCM) and pancreatic cancer; and four Phase I studies for the treatment of maintenance AML, gastric cancer, non-small cell lung cancer and pancreatic cancer. In addition, the Company intends to initiate a Phase III SCM registrational study later this year in preparation for autologous bone-marrow transplantation (BMT). The Company has multiple pre-clinical ongoing studies with AGI-134: an immunotherapy treatment for multiple solid tumors, with clinical studies expected to commence in H1 2018; three programs with Novartis for NASH, liver failure diseases and dry eye syndrome indications; and one program with JHL for type I diabetes. In addition, the Company out-licensed their BL-5010 drug for treatment of skin lesions to Perrigo.

BioLineRx has an experienced management team, Board of Directors and Oncology Scientific Advisory Board with a successful track record at big and small pharma of bringing patented drugs to the market, as well as extensive managerial, financial, and transactional expertise to support its clinical and business progress. Furthermore, the company pipeline is generated by systematically identifying, validating and in-licensing therapeutic candidates. Over 2,000 compounds have already been systematically screened and evaluated, of which over forty commenced development.

However, after a decade of working in the “classic” business model used by many small drug development companies, of in-licensing pre-clinical compounds and out-licensing them during late clinical stages, the company has not yet launched a significant drug into the market. Last year, the Company made some significant changes, replacing the CEO, and adopting a strategy to focus on Oncology and Immunology. This business/clinical shift may hamper the development process as they may lack the needed know-how in bringing advanced clinical programs to the market.

**We see the company as a long-term investment opportunity in the field of Immuno-Oncology for cancer treatment. In the coming months, several significant events are expected that will impact the company significantly. While Immuno-Oncology is a promising domain, there are significant risks associated with it in the clinical, regulatory and commercialization stages. In our view, Bioline’s market valuation is undervalued, due to multiple clinical indications in the company's development pipeline, the company's latest acquisition, and sufficient funds. The aforementioned are expected to support its business strategy until the year 2019.**

## Pipeline Summary

BioLineRx is currently advancing multiple clinical programs. Key programs are:

**BL-8040** - a short cyclic peptide for SCM (initiating Phase III study later in 2017 for autologous bone-marrow transplantation (BMT) and ongoing Phase II for allogeneic BMT), AML (consolidation AML Phase IIb study ongoing and maintenance AML Phase Ib study, in combination with Atezolizumab, expected to be initiated in H2 17), and pancreatic cancer in combination with Merck’s Pembrolizumab (Phase II study ongoing). It is also in Phase I clinical trials in combination with Genentech’s Atezolizumab for the treatment of gastric cancer, non-small cell lung cancer and pancreatic cancer.

**BL-5010** - a proprietary, pen-like applicator containing a novel, acidic, aqueous solution for treatment of skin lesions. The rights to the product in Europe, and a few additional regions, were out-licensed to Perrigo. The BL-5010 received a CE Mark in Q2 2016, and is being commercialized as a medical device in Europe; however, it is not a major driver for the Company.

The diagram below represents the estimated timeline per indication in the pipeline. This is subject to changes in development plans and regulatory requirements/clarifications, including complementary /additional studies.



Source: Bioline

## Upcoming Potential Catalysts

Program	Event	Significance	Timeline
<b>BL-8040</b>	Completion of Phase II (allogenic SCM)	Medium	<b>H2 2017</b>
	Initiation Phase III (autologous SCM)	Medium	<b>H2 2017</b>
	Partial results Phase II (pancreatic cancer)	Medium	<b>H2 2017</b>
	Top-line results Phase II (pancreatic) cancer)	High	<b>H1 2018</b>
	Initiation Phase Ib (AML maintenance)	Medium	<b>H2 2017</b>
	Partial results Phase Ib	Low	<b>H2 2018</b>
	Initiation Phase Ib (multiple solid tumors)	Medium	<b>H2 2017</b>
	Partial results Phase Ib (multiple solid tumors)	Low	<b>H2 2018</b>
<b>AGI-134</b>	Top-line Phase IIb results (AML consolidation)	Medium	<b>H2 2019</b>
	Initiation of Phase I/II (multiple solid tumors)	Low	<b>H1 2018</b>

Upside scenarios	Downside scenarios
Strategic collaborations with three of the leading global pharma companies could lead to major deals.	BioLineRx's business model is the "classic" small drug development company model – in-licensing compounds in pre-clinical stages and out-licensing them in late clinical stages. Albeit, BioLineRx has not yet launched a significant drug in to the market. This may occur again in the future.
BioLineRx's focus is on Oncology and Immunology with 9 ongoing and planned clinical studies over the next 12-18 months. These clinical platforms can boost the company's business. -	If the company does not meet its end-point results in one of the BL-8040 indications, this may delay its clinical development.
The company's cash position as of July 2017 is approximately \$52 million and sufficient until 2019, with a solid capital structure based on key life-sciences investors (e.g., Novartis 5.2%).	

## Valuation Methodology

R&D company valuations are challenging due to a non-cash valuation with a long time to market in most cases. Methods typically used for company valuations, such as asset valuation or multiplier methods, are incompatible with the valuation of R&D companies. In such companies, the current status of business cannot be analyzed by the capital in the balance sheet, and in most cases cannot be compared to similar companies due to their uniqueness, in both technological and financial aspects.

As part of a discounted cash flow (DCF), the accepted method used in financial valuations, there are several modifications to an R&D company's valuation. In general, there are three primary methods within the DCF method:

- **Real Options** - valuation method designated for pre-clinical and early-stage clinical programs/companies where the assessment is binary during the initial phases, and based upon scientific-regulatory assessment only (binomial model with certain adjustments).
- **Pipeline assessment** - valuation method used for programs/companies prior to the market stage. The company's value is the total discounted cash flow plus unallocated costs and assessment of future technological basis. The assessment of the future technological basis is established based on the company's ability to “produce” new clinical and pre-clinical projects and their feed rate potential.
- **DCF valuation** - similar to companies not operating in the life sciences field, this method applies to companies with products that have a positive cash flow from operations.

BioLineRx's valuation was implemented using the “Pipeline” method that is suitable for the development stages of the company's products. The company's valuation is calculated by examining the company as a holding company vis-à-vis existing projects, with Risk-adjusted Net Present Value (rNPV) capitalization to the net present value, including weighting of several scenarios. These primarily include analysis of the company's income, evaluated in accordance with scientific/technological assessment, based on various sources and estimates relating to the market scope, the degree of projected market success, and regulatory risk.

The weighted average of company revenue in the pharmaceutical and medical equipment market is based on the following data:

- Total Market - market potential for the product/product line
- Market Share - company's ability to penetrate the market during the forecast period
- Peak Sales - peak sales of the company/product during the forecast period
- Annual Cost of Treatment – estimated annual cost per patient, based on updated market studies
- Success Rate - chances for success of clinical trials and transition to the next phase in the examined sub-field.

BioLineRx focuses on the identification, in-licensing and development of oncology and immunology therapeutic candidates. Innovative compounds are in-licensed predominantly from academic institutions and biotechnology companies based in Israel. BioLineRx develops drug candidates through pre-clinical and clinical stages, and then partnering with pharmaceutical companies for further clinical development and commercialization. In some cases, where the indication is in a focused therapeutic market, the Company might also consider commercializing some of its projects directly. BioLineRx is currently advancing multiple clinical programs, with BL-8040 being most prominent. BL-8040 is a CXCR4 antagonist that can be used on its own or in combination with various already-marketed checkpoint molecules.

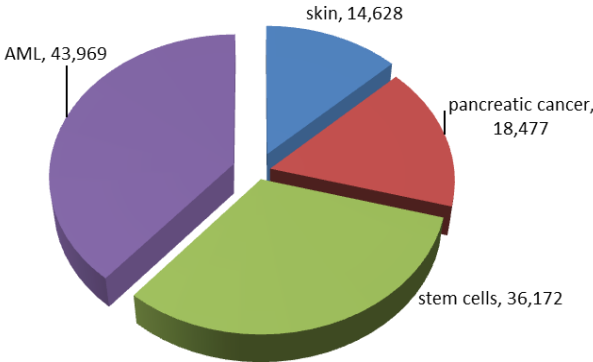
Valuation of BioLineRx's "technological basis" is, in fact, a valuation of the company's "residual value". This valuation was conducted using the Feed Rate methodology that is common in the field of Life Sciences, rather than using the conventional terminal value, normally used by non- Life-Science companies.

**Valuation Summary**

BioLineRx is currently advancing a lead clinical program, BL-8040, in multiple clinical studies: three Phase II programs for consolidation AML, stem-cell mobilization (SCM) and pancreatic cancer; and four Phase I studies for the treatment of maintenance AML, gastric cancer, non-small cell lung cancer and pancreatic cancer.

The valuation of BL-8040 is a risk-adjusted net present value (rNPV) capitalization to the net present value. The valuation includes weighting of several scenarios, based upon the main assessments described in the valuation section in this report. In addition, we value BL-5010 based on the company’s estimations for future annual net sales of \$2-\$4 million, royalties based on sales by Perrigo. We conclude our pipeline interim analysis with a total value of \$113.2 million. This value is for BioLineRx ’s main indications:

**Pipeline analysis (000K)**

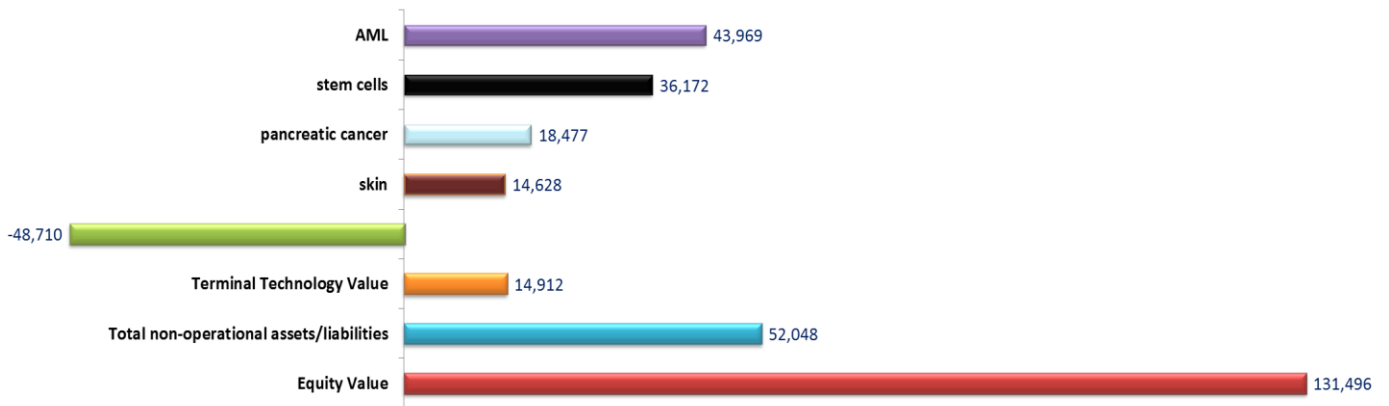


Source: Frost & Sullivan analysis

As of March 31, 2017, the Company has non-operational assets (cash) of approximately \$30 million, with an estimated annual burn rate of \$16-\$17 million based on previous years 2015-2017 (\$1.4 million per month). During April 2017 the company successfully completed an underwritten public offering of its ADSs for net proceeds of \$26.2 million. Thus, the company holds a total of \$56.2 million as of April 2017, less its current burn rate of \$1.4 million per month.

We value the company’s pipeline and its technological platform (equity value) as follows at \$131.5 million:

**BioLineRx pipeline and technology platform value in 000K:**



Given the aforementioned parameters, we estimate BioLineRx’s equity value at \$131.5 million / NIS 468.1 million.

**Sensitivity Analysis**

The table below presents BioLineRx's target price in relation to the capitalization rate. We set a range of 0.5% change from our CAPM model (as presented in Appendix B) as the stock range.

Sensitivity Analysis - /Capitalization rate vs. Target price

Cap. rate	Target Price (NIS)
19.9%	5.20
<b>20.4%</b>	<b>5.04</b>
<b>20.9%</b>	<b>4.90</b>
<b>21.4%</b>	<b>4.76</b>
21.9%	4.63

We estimate the target price to be in the range of NIS 4.76 - NIS 5.04, with a mean of NIS 4.90. Thus, 1 ADS (an ADS represents 1 ordinary share) is equal to \$1.38<sup>1</sup>

<sup>1</sup> Calculation is NIS 4.90 divided by 3.56 NIS/\$ .

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## Clinical Programs

### BL-8040: CXCR4 antagonist for multiple oncology indications and stem cell mobilization

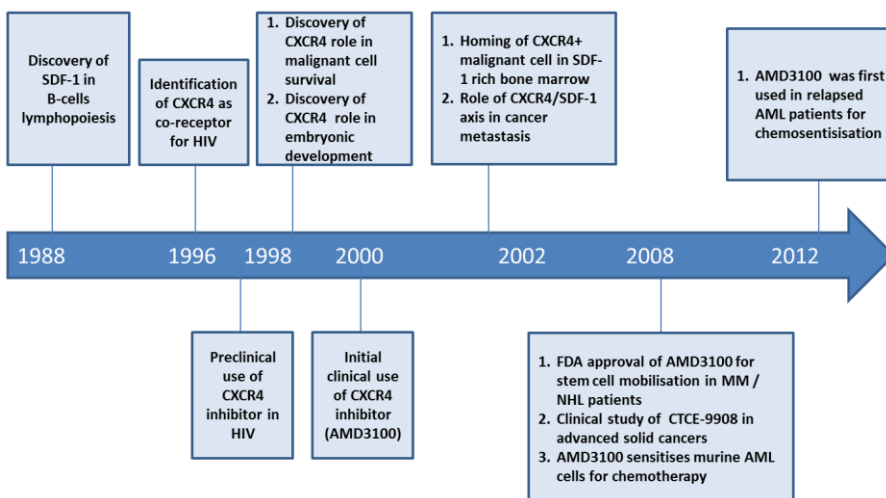
#### Background

##### CXCR4 antagonist

C-X-C chemokine receptor type 4 (CXCR4) is a chemokine receptor that belongs to the family of G-protein-coupled cell surface receptors with seven transmembrane-spanning domains with seven helical regions connected by six extramembrane loops. This receptor is composed of 352-amino acid and displays variable levels of homology to other CXC and CC members of the chemokine receptor family. The CXCR4 receptor is known to be a critical regulator of many biological processes and plays a pivotal role in multiple cellular processes including organogenesis, hematopoiesis, and immunity. CXCR4 is commonly expressed on most hematopoietic cell types as well as on Langerhans cells, vascular endothelial cells, multiple CNS cells and embryonic stem cells (Chatterjee et al.2014; PMID: 25287686). CXCR4-expressing cells respond to and migrate along its ligand - CXC chemokine stromal development factor 1 (SDF-1)<sup>2</sup>.

SDF-1/CXCR4 interaction is essential in early embryonic development as it is involved in vascular, nervous, hematopoietic and cardiac systems formation. This receptor is expressed on progenitor cells, allowing the migration from their place of origin to the final destination where differentiation into organs and tissues will take place. In the adulthood, the SDF-1/CXCR4 axis has been shown to be associated with trafficking and homeostasis of immune cells such as T-lymphocytes, T-cell redistribution within the tumors as well as retention of hematopoietic stem cells within the bone marrow. Initially, CXCR4 involvement in HIV infection of T-cells was demonstrated, and only later its participation in cancer, specifically, involvement in B-cell trafficking and tissue localisation in chronic leukaemia patients was noted.<sup>3</sup>

#### Key discoveries on SDF-1/CXCR4 axis



<sup>2</sup> Burger JA, Kipps TJ. *Blood*. 2006;107(5):1761-1767

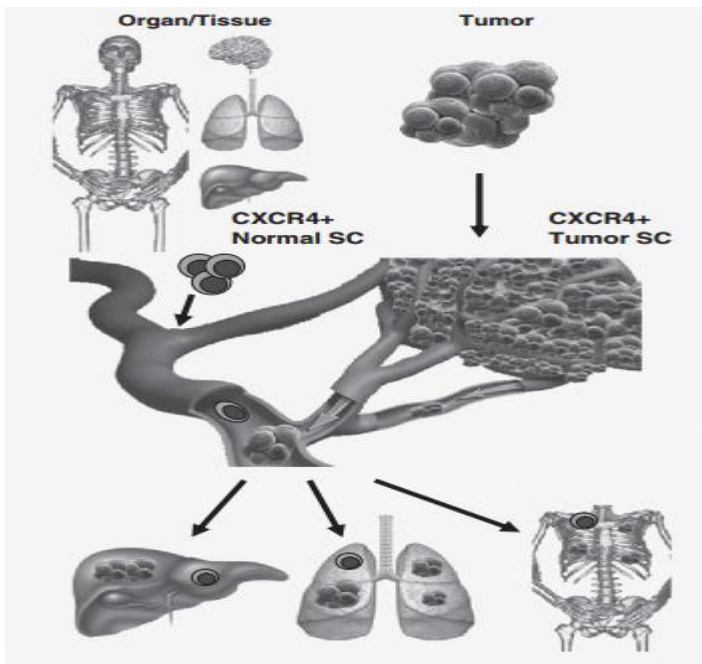
<sup>3</sup> Chatterjee S, Azad BB, Nimmagadda S. The Intricate Role of CXCR4 in Cancer. *Advances in cancer research*. 2014;124:31-82. doi:10.1016/B978-0-12-411638-2.00002-1.   
 myeloma, NHL- non-Hodgkin's lymphoma

CXCR4 has also been shown to be overexpressed in 23 different cancer types including ovarian, prostate, oesophageal, melanoma, neuroblastoma, and renal cell carcinoma as well as within the tumor microenvironment<sup>4</sup>. This overexpression was shown crucial in adding to tumor growth, invasion, angiogenesis, metastasis, relapse, and therapeutic resistance<sup>5</sup>. Several studies have shown that over-expression of CXCR4 in Melanoma<sup>[3]</sup>, breast and lung cancer patients led to worse prognosis compared to patients whose expression of that receptor was not elevated.

In addition, cancer stem cells also express CXCR4. This indicates that the SDF-1/CXCR4 axis may direct the trafficking and metastasis of cancerous stem cells to SDF-1 high expressing organs such as the lymph nodes, lungs, liver, and bone<sup>6</sup>. The migration process occurs in multiple steps including the release of cancer stem cells from their niche into the circulation, redistribution and arrival at the site of homing via the peripheral blood or lymph, adherence to the endothelium, invasion of tissues, and proliferation and expansion at a location that provides a favourable environment.

It has been reported that high expressing CXCR4 cancers were metastasized through the bloodstream in an SDF-1-dependent manner to bones.

#### Involvement of SDF-1/CXCR4 axis in migration/circulation of normal stem cells and metastasis of cancer stem cells



Source: Adapted from Furusato B, et al. CXCR4 and cancer<sup>7</sup>.

Disruption of this interaction of membrane chemokine receptor and the corresponding ligand (SDF-1/CXCR4) is being investigated as a potential therapy for treating haematological and solid tumor patients.

<sup>4</sup> Domanska UM, et al, European Journal of Cancer Volume 49, Issue 1, January 2013, Pages 219–230. A review on CXCR4/CXCL12 axis in oncology: No place to hide

<sup>5</sup> Otsuka S, Bebb G. J Thorac Oncol. 2008;3(12):1379-1383. And Chatterjee S, Azad BB, Nimmagadda S. The Intricate Role of CXCR4 in Cancer. Advances in cancer research. 2014;124:31-82. doi:10.1016/B978-0-12-411638-2.00002-1

<sup>[3]</sup> Domanska UM, et al, European Journal of Cancer Volume 49, Issue 1, January 2013, Pages 219–230. A review on CXCR4/CXCL12 axis in oncology: No place to hide

<sup>6</sup> Furusato B, Mohamed A, Uhlén M, Rhim JS. Pathol Int. 2010 Jul;60(7):497-505. doi: 10.1111/j.1440-1827.2010.02548.x. CXCR4 and cancer.

<sup>7</sup> Furusato B, Mohamed A, Uhlén M, Rhim JS. Pathol Int. 2010 Jul;60(7):497-505. doi: 10.1111/j.1440-1827.2010.02548.x. CXCR4 and cancer.

CXCR4 antagonism has been shown to disrupt SDF-1/CXCR4 interactions leading to sensitization of cancerous cells to cytotoxic drugs, and reduction of tumor growth and metastasis. For instance, several *in vitro* and *in vivo* studies have shown attenuation of breast cancer growth upon exposure of those cells to peptides or small molecule inhibitors of CXCR4. Therefore, CXCR4 is not only ideal therapeutic target but may as well be used as a marker for disease progression<sup>8</sup>.

### Market, Standard of Care and Unmet needs

The three key indications for BL-8040 are **acute myeloid leukaemia, stem cell mobilization and pancreatic cancer**, which we will elaborate on in the following sections:.

#### **Acute Myeloid Leukaemia**

Acute myeloid leukaemia (AML) is an aggressive form of a blood cancer with an unknown aetiology. It begins in the bone marrow when stem cells overproduce immature white blood cells. Those immature white blood cells are called blast cells and they quickly spread into the bloodstream from where they can often metastasize to other organs and tissues.

AML is the most common type of leukaemia in adults (uncommon before the age of 45) and if left untreated it progresses quickly and aggressively and can be fatal. AML continues to have the lowest survival rate of all leukaemias. Some key environmental factors such as chemical and radiation exposure have been shown to increase the risk for AML.

The highest rates of AML are observed in the United States, Australia and Europe. AML predominantly affects elderly people, and it has been estimated by the American Cancer Society that there will be approximately 21,380 new cases and 10,590 deaths from AML in the United States in 2017<sup>9</sup>. The annual incidence rate of AML in Europe is estimated to be 1/33,000 - 1/25,000<sup>10</sup>. The 2011 global AML disease therapeutics market was estimated at \$ 239.3 million. Over the coming years, this market is predicted to expand at a CAGR of 28.4% (2015-2020) and reach \$ 1.67 billion by 2020.<sup>11</sup>

Treatment for AML is primarily determined by a patient's age, performance status and cytogenetics. The current standard of care for AML includes intensive chemotherapy, radiation therapy, and stem cell transplant.

After receiving remission induction chemotherapy, over 90% of patients will have a recurrence of the disease. To prevent this from happening, consolidation therapy follows immediately after a patient recovers from the remission induction therapy. Not all patients would be eligible for the intensive therapy due to debilitating side effects of this treatment. In most cases, only patients younger than 60 years old qualify for this therapy. According to BioLineRx

<sup>8</sup> Furusato B, Mohamed A, Uhlén M, Rhim JS. *Pathol Int.* 2010 Jul;60(7):497-505. doi: 10.1111/j.1440-1827.2010.02548.x. CXCR4 and cancer.

<sup>9</sup> <https://www.cancer.org/cancer/acute-myeloid-leukemia/about/key-statistics.html>. Accessed on 20th of April 2017

<sup>10</sup> OrphaNet (2014). "Acute myeloid leukemia." [http://www.orpha.net/consor4.01/www/cgi-bin/OC\\_Exp.php?lng=EN&Expert=519](http://www.orpha.net/consor4.01/www/cgi-bin/OC_Exp.php?lng=EN&Expert=519) Accessed January 27, 2016.

<sup>11</sup> <https://www.thepharmaletter.com/article/acute-myeloid-leukemia-market-to-be-worth-1-67-billion-by-2020>

management, the majority of patients achieving complete remission at the induction treatment will continue to consolidation treatment. CR rates at induction are estimated at 60%-70%.

The most commonly used chemotherapy drugs for treating AML are cytarabine (cytosine arabinoside or ara-C) and the anthracycline drugs (such as daunorubicin (daunomycin), idarubicin, and mitoxantrone). Other chemotherapy drugs used are: Cladribine (Leustatin<sup>®</sup>, 2-CdA) Fludarabine (Fludara<sup>®</sup>); Topotecan; Etoposide (VP-16); 6-thioguanine (6-TG), Hydroxyurea (Hydrea<sup>®</sup>); corticosteroid drugs, such as prednisone or dexamethasone (Decadron<sup>®</sup>), methotrexate (MTX), 6-mercaptopurine (6-MP, Azacitidine (Vidaza<sup>®</sup>); and Decitabine (Dacogen<sup>®</sup>) to name a few.

Current treatment guidelines of AML have not changed dramatically over the past years<sup>12</sup>. With increased knowledge about the underlying causes of the AML, one would expect to observe new viable treatments to enter the market. It has been observed that one in three people diagnosed with AML has a mutation in the *FLT3* gene. There were no new drugs approved during the last 25 years, until April 2017, when Novartis announced FDA approval of their Rydapt<sup>®</sup> for newly diagnosed patients who are FMS-like tyrosine kinase 3 mutation-positive (FLT3+), hence opening new treatment options for approximately 30% of diagnosed patients. There are some AML cases that can be explained by changes in the c-KIT gene. Alternative treatments that are being evaluated in clinical trials for the treatment of AML are categorized as targeted therapies, such as small molecule inhibitors of serine-threonine proteins kinases, immunological agents against tumor-associated antigens/genes, and antagonists against cell-surface receptors as well as monoclonal antibodies.

The pipeline is very extensive (100+ drug candidates) and only several promising drug candidates in late clinical trials are shown below.

#### **Drug Pipeline for AML (adapted from new drugs in acute myeloid leukaemia<sup>13,14</sup>)**

Agent	Company	Mode of action	Clinical trial	Notes
<b>Bisantre</b>	Race Oncology	RNA synthesis inhibitor/DNA inhibitor	Registered	Anthracycline-related cytostatic
<b>Vyxeos (CPX-351)</b>	Jazz Pharmaceuticals	Cytotoxic; liposomal formulation of cytarabine and daunorubicin in 5:1 molar ratio	Phase II Study	CPX-351 versus 7 + 3 exhibited improved outcomes in patients with secondary AML
<b>Volasertib</b>	Boehringer Ingelheim	Polo-like kinase 1 inhibitor/Protein kinase inhibitor/Apoptosis stimulant/Cell cycle inhibitor	Phase III Study	2nd-generation dihydropteridinone polo-like kinase 1 inhibitor. Volasertib combined with LDAC demonstrated improved outcomes over LDAC.
<b>Sapacitabine</b>	Sankyo	Cytotoxic; orally bioavailable novel	Phase III Study	Sapacitabine had outcomes similar to low-dose cytarabine

<sup>12</sup> T. M. Kadia, F. Ravandi, J. Cortes, H. Kantarjian; New drugs in acute myeloid leukemia. *Ann Oncol* 2016; 27 (5): 770-778. doi: 10.1093/annonc/mdw015

<sup>13</sup> T. M. Kadia, F. Ravandi, J. Cortes, H. Kantarjian; New drugs in acute myeloid leukemia. *Ann Oncol* 2016; 27 (5): 770-778. doi: 10.1093/annonc/mdw015

<sup>14</sup> Evaluate Pharma

SGI-110		nucleoside analog		(LDAC), but sequential combination study with decitabine showed promising results.
	Astex Pharmaceuticals	Cytotoxic; longer acting hypomethylating agent	Phase III Study	Single-agent activity in AML and myelodysplastic syndrome seems promising.
AG-221	Agios Pharmaceuticals	Small-molecule inhibitor of isocitrate dehydrogenase (IDH)-2 enzyme	NDA filing	Single-agent studies demonstrated significant activity in patients with IDH2-mutated AML. Combination studies with conventional chemotherapy have been planned.
Gilteritinib ASP2215	Kotobuki Pharmaceutical in collaboration with Astellas	Small molecule both FLT3 and AXL kinases	Phase III Study	Single-agent studies are just underway, with preliminary data anticipated.
Midostaurin		Small-molecule multikinase inhibitor with activity against mutant FLT (FLT-ITD) in AML	FDA approved	7 + 3 with our without midostaurin in newly diagnosed patients with FLT3-mutated AML demonstrated significant improvement in event-free- and overall survival among younger patients (median age 48 years) in the midostaurin treated arm.
Quizartinib	Ambit Biosciences (Acquired by Daiichi-Sankyo )	Small-molecule multikinase inhibitor with potent activity against FLT3-ITD	Phase III Study	Single-agent dose-finding studies have demonstrated efficacy, but DLT is QT prolongation. Lower doses of quizartinib have demonstrated similar activity but less toxicity. These are now being studied in combination studies.
SGN-CD33A	Seattle Genetics	Monoclonal antibody-drug conjugate directed at CD33, carrying a pyrrolobenzodiazepine dimer (toxin)	Phase III Study	Single-agent and combination studies are underway in several clinical settings. Preliminary experience is positive, demonstrating good safety profile and efficacy in clearing bone marrow blasts.
Idasanutlin	Roche	MDM2 inhibitor	Phase III Study	Small molecule that activates the p53 pathway by preventing the binding between the p53 and its inhibitor MDM2

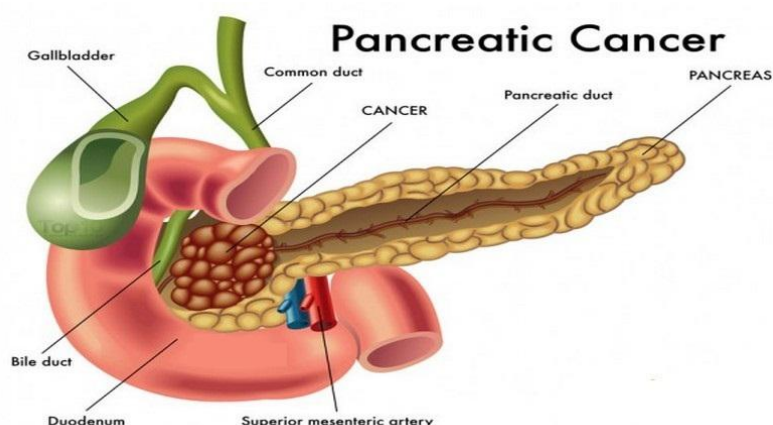
The major unmet needs in current AML disease management include treatment of older patients. The 5-year overall survival (OS) among patients over the age of 60 years is in the range of 10%–20%, highlighting the clear need for newer therapies to address those patients.

AML has the lowest survival rates and, as previously mentioned, while one in nine patients require intensive therapy, they will not necessarily qualify for it. Companies are looking at alternative treatments that are less invasive and have fewer side effects. Based on the company's understanding, physicians are very concerned about remission durations and rates. The understanding in this field is that minimal-residual disease (MRD) is a critical factor in determining the duration of response, and this specifically where we assume BL-8040 can contribute.

### **Pancreatic Cancer**

Pancreatic cancer is caused by the uncontrolled and abnormal growth of cells in the pancreas. Depending on the origin of the cancerous cells it can be classified as:

- Ductal adenocarcinoma, which starts from cells in the lining of the pancreatic ducts (95% of all cases);
- Ampullary cancer, which starts from cells in the hepatopancreatic duct;
- Cystic tumors, with cancerous cells being found in the cysts in the pancreas;
- Acinar cell carcinomas, which starts from the cells that make pancreatic juice;
- Neuroendocrine tumors, which starts from the endocrine cells;
- Lymphoma, which starts from the lymphatic tissue in the pancreas.



### **Diagram of the pancreas and pancreatic cancer<sup>15</sup>**

Pancreatic cancer is a major cause of cancer-associated mortality and it is the 10<sup>th</sup> most common cancer, excluding non-melanoma skin cancer. The highest rates of pancreatic cancer are observed in the United States, Australia and Europe.<sup>16</sup>

Pancreatic cancer is more common in older people, with 50% of all new cases diagnosed in people aged 75 or over. Statistics show that 1 in 71 people will be diagnosed with pancreatic cancer during their lifetime<sup>17</sup>. It has been estimated by the American Cancer Society that there will be approximately 53,670 new cases and 43,090 deaths from pancreatic cancer in the United States in 2017<sup>18</sup>.

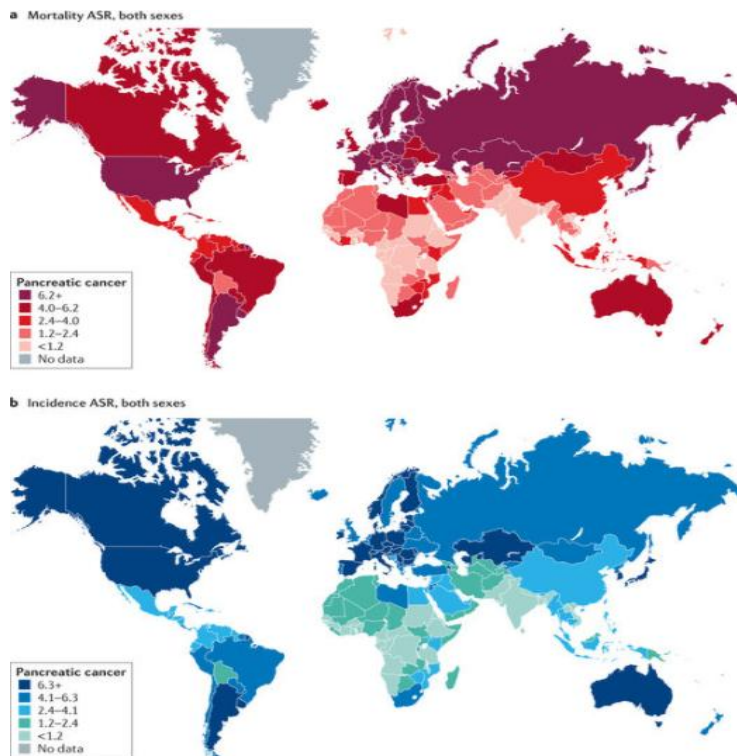
<sup>15</sup> <http://surgicalgastro.com/>. Accessed on 22nd of May 2017.

<sup>16</sup> Kleeff, J, Korc, M, Apte, M et al. Pancreatic cancer. *Nat Rev Dis Primers*. 2016; 2: 16022

<sup>17</sup> <http://www.macmillan.org.uk>

<sup>18</sup> <https://www.cancer.org/cancer/pancreatic-cancer/about/key-statistics.html> Accessed on 19th of June 2017

Some risk factors can increase the chance of getting pancreatic cancer. Smoking was shown to increase that chance by 50%, with approximately 20-30% of all cases being caused solely by cigarette smoking. Obesity is additional risk factor, with overweight people being 20% more likely to develop that form of cancer. In addition, age, gender, race, family history as well as pre-existing conditions may also increase the likelihood of developing this disease.



**Global mortality and incidence rates of pancreatic cancer. Source:** Kleeff, J, et al. Pancreatic cancer. Nat Rev Dis Primers. 2016.

Pancreatic cancer survival rates have been improving from decade to decade. However, this type of cancer is still considered to be largely incurable, due to the fact that there are no symptoms at the early stages of the disease, and hence it is often not detected until the cancer has advanced. It is also highly difficult to diagnose early, as pancreatic cancer does not display sensitive and specific markers to aid detection.

The 2016 global pancreatic cancer therapeutics market was estimated at \$2.08 billion. Over the coming years, this market is predicted to expand at a CAGR of 7.54% (2016-2021) and reach \$2.99 billion by 2021<sup>19</sup>.

The treatment for pancreatic cancer is mostly determined by type and location of cancer, as well as how advanced it is and whether it has metastasized. The current standard of care for pancreatic cancer includes surgery that aims at complete removal of the tumor and any other cancerous cells. Approximately 17% of patients will have an operable form of cancer; however for the remaining 83% of the patients, the cancer is unresectable and their prognosis is extremely poor. Chemotherapy or chemoradiotherapy for non-operable patients are two available treatment options that aim at slowing down the growth of cancer and relieving symptoms. It may also be used before the surgery to

<sup>19</sup> Market Data Forecast: "Pancreatic Cancer Therapeutics Market By Treatment Type (Surgery, Chemotherapy, Radiation Therapy, Others), By Type (Exocrine Pancreas Cancer, Endocrine Pancreas Cancer), By End Users (Hospitals, Clinics, Research Institutes, Others), by Region – Global Industry Analysis, Size, Share, Growth, Trends, and Forecasts (2016–2021)"

shrink the cancerous mass and hence facilitate removal. For chemotherapy, the most commonly used first-line treatment is Gemcitabine (Gemzar®), FOLFIRINOX, Tarceva, Nab-paclitaxel (Abraxane®), Fluorouracil (5-FU) and Gemcitabine given with Capecitabine (GemCap). A patient often becomes resistant to chemotherapy treatment; thus, second-line chemotherapy is prescribed to extend the patient's life. ONIVYDE has been recently approved and can be used for patients with metastatic pancreatic cancer that have been previously treated with Gemcitabine.

Current treatment guidelines for pancreatic cancer have not changed dramatically in the past years and progress in drug development is hindered due to the complex genomic, epigenetic and metabolic underlying causes of the disease<sup>20</sup>. Alternative treatments being evaluated in clinical trials for the treatment of pancreatic cancer primarily focus on testing out new combinations of existing drugs or adding new drugs to standard chemotherapy treatments. There are several promising therapeutic targets in Phase III clinical trials however single-agent use of checkpoint inhibitors has not yielded any efficacy in this indication.

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<sup>20</sup> Kleeff, J, Korc, M, Apte, M et al. Pancreatic cancer. Nat Rev Dis Primers. 2016; 2: 16022



**Drug pipeline for pancreatic cancer<sup>21,22</sup>**

Agent	Company	Mode of action	Notes
TS-1 + leucovorin	Taiho	Thymidylate synthase inhibitor/ Orotate phosphoribosyltransferase inhibitor	Fixed-dose combination of TS-1 (tegafur + CDHP + oxonic acid) and calcium folinate (leucovorin)
Trabedersen	Autotelic	Transforming growth factor beta 2 antagonist	An antisense therapy targeted to transforming growth factor (TGF)-β2
Rigosertib	Onconova	Polo-like kinase 1 inhibitor/ Cell cycle inhibitor/ Mcl-1 antagonist	Novel, small molecule, tumor specific PI-3K (phosphoinositide-3 kinase) and PLK (Polo-like kinase) inhibitor targeting the Ras binding domain
Pegylated interleukin-10	ARMO BioSciences	Interleukin 10 agonist	PEGylated form of recombinant human interleukin-10 (IL-10)
PEGPH20	Halozyme	Hyaluronidase stimulant	Pegylated recombinant human hyaluronidase for use in combination with chemotherapeutics as an anticancer agent
Novaferon	Genova Biotech	Angiogenesis inhibitor/ Apoptosis stimulant/ Immunostimulant	Interferon-like protein. It inhibits tumor cell proliferation and revascularization, induces apoptosis and stimulates antitumor activity of the immune system
Napabucasin	Boston Biomedical	STAT transcription factor 3 inhibitor/ Apoptosis stimulant	Orally-administered agent targeting STAT3
Glufosfamide	Baxter Oncology	DNA inhibitor	Alkylating agent with a structure similar to that of the oxazaphosphorines
Gastrimmune	Cancer Advances	Gastrin inhibitor/ Immunostimulant/ Apoptosis stimulant	Synthetic version of the 9 amino acid residues from the N-terminus of gastrin-17 (G17) linked to a diphtheria toxoid (DT) via a peptide spacer
Dendritic cell vaccine	Tella	Immunostimulant	Dendritic cells are extracted from the blood of patients and pulsed with cancer associated antigens such as WT1 or MUC1 peptides before being readministered to the patient, where they stimulate a specific immune response to the cancer antigen
Cisplatin	NanoCarrier	DNA inhibitor	Medicelle formulation of cisplatin
Algenpantucel-L	NewLink Genetics	Immunostimulant	Polyvalent HyperAcute-Pancreatic cancer vaccine

<sup>21</sup> EvaluatePharma

<sup>22</sup> Frost & Sullivan Analysis

Pancreatic cancer still remains one of the most difficult cancers to treat and, in fact, to date the only curative therapy is a surgical resection. Only 17% of pancreatic cancers are operable (median survival for patients is 24 months) and 83% of patients do not qualify for operation (median survival of 6 months) and hence require alternative therapies.

Currently available chemotherapies are not curative but primarily aimed at improving the quality of life and easing symptoms. There are no targeted therapies or immune-oncology therapies being developed for pancreatic cancer. There is still a clear need to identify new therapeutic targets, as the four key genes identified to be involved in pancreatic cancer, namely TP53, KRAS, SMAD4 and CDKN2A, do not have developed targets against them. Therefore, there is a clear need for newer therapies to improve the survival rate for pancreatic cancer patients.

**According to BioLineRx management, evidence of efficacy in this tumor will lead to rapid expansion of studies in other tumor types such as NSCLC, gastric, ovarian and others (in combination with checkpoint inhibitors).**

### **Stem Cell Mobilization (SCM)**

Bone marrow contains hematopoietic stem cells that mature into white blood cells (leukocytes), red blood cells (erythrocytes), and platelets (thrombocytes). Limited amounts of those hematopoietic stem cells are naturally released from the bone marrow into the bloodstream and are called peripheral blood stem cells (PBSCs).

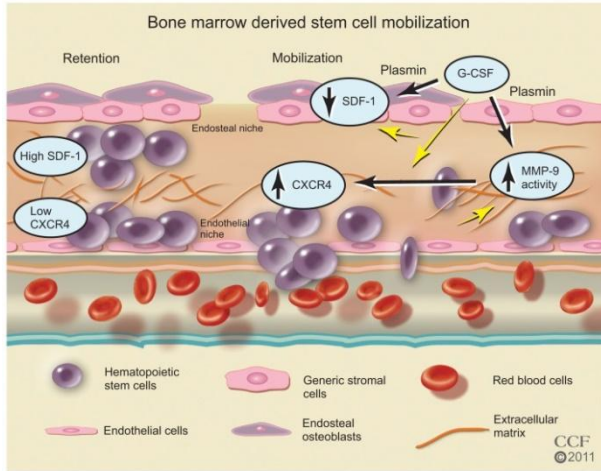
Patients with malignant and non-malignant disorders of the blood and the immune system can often be treated with high doses of chemotherapy and/or radiation therapy. This frequently results in complete depletion of hematopoietic stem cells and hence it is vital to restore them. One of the methods to treat haematological cancer patients is to perform stem cell transplant. This therapy is based on infusing healthy blood-forming stem cells into the body and hence restoring the healthy bone marrow.

As previously mentioned PBSCs in the peripheral blood are present in very low quantities, which are not sufficient to treat patients.

Previously, the only way to collect stem cells for a transplant was through the bone marrow harvest which involved a surgical procedure. Nowadays, the stem cells for transplantation are collected from placental and umbilical cord blood but most often from peripheral blood. There are two types of peripheral blood stem cell transplants, namely autologous (donor is also a recipient) and allogeneic (recipient obtains cells from matched or mismatched donor).

The process in which the cells from the bone marrow are stimulated to migrate into the bloodstream, from where they can be collected, is called stem cell mobilization. In order to achieve that, a donor takes white cell growth factor, such as granulocyte-colony stimulating factor (G-CSF) drug. G-CSF treatment increases MMP-9 which in turns affects the SDF-1/CXCR4 pathway. As a result, the levels of SDF-1 are reduced and the stem cell receptor CXCR4 levels are increased leading to the creation of the chemotactic gradient with the peripheral blood and mobilization of those cells.

Bone marrow-derived stem cell mobilization<sup>23</sup>



Source: Vascular Health and Risk Management Journal

The blood is firstly removed from the donor and the cells collected using a process called apheresis. This process allows to separate red cells, plasma, white cells and platelets. Stem cells are collected from the white cells and platelets, while the red cells and plasma are transfused back to the donor. Normally it takes one to two cycles of apheresis to collect sufficient blood from a matched unrelated donor. Those cells are then preserved, frozen, stored and used later for transplantation<sup>24</sup>.

Stem cell transplantation process<sup>25</sup>.



Source: International Waldenstrom's Macroglobulinemia Foundation

<sup>23</sup> Hoover-Plow J, Gong Y. Challenges for heart disease stem cell therapy. Vascular Health and Risk Management. 2012;8:99-113. doi:10.2147/VHRM.S25665.

<sup>24</sup> <http://www.iwmf.com>. Haematopoietic Stem Cell Mobilisation and Apheresis. A Practical Guide for Nurses and Other Allied Health Care Professionals Accessed on 25/05/2017

<sup>25</sup> <http://www.iwmf.com>. Haematopoietic Stem Cell Mobilisation and Apheresis. A Practical Guide for Nurses and Other Allied Health Care Professionals Accessed on 25/05/2017

## Competitive Landscape

There are only a few agents that can mobilize stem cells. The only one indicated is Mozobil (plerixafor injection), which is always given in combination with granulocyte-colony stimulating factor (G-CSF). Mozobil is injected four to six times a day and is mostly used for autologous transplantation in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM). It is not intended for patients with leukaemia. Filgrastim (Neupogen) is a Granulocyte Colony Stimulating Factor that is used most frequently as mobilization agent.

For allogeneic transplants, only Neupogen (with or without plerixafor) is used since it is relatively safe and produces positive results in most patients. There is also a pegfilgrastim (Neulasta) which is a colony-stimulating factor that was shown to be effective in stem cell mobilization. Other approved agents for hematopoietic progenitor cell mobilization include granulocyte-macrophage-colony-stimulating factor - Sargramostim and a stem cell factor – Ancestim<sup>26</sup>. Most drug candidates are in the early stages of clinical trials. Thus, only PolyPhor, Noxxon and Taigen are in direct competition with BL-8040. The Table below summarizes the leading drug candidates in the pipeline.

### Leading drug candidates in the stem cell mobilization pipeline<sup>20</sup>

Specific Agent	Company	Drugs/Pathways	Mode of action	Clinical Trials
POL6326	Polyphor	CXCL12/CXCR4 modulators	CXCR4 antagonists	Phase I/II
BKT-140	BioLineRx (BL-8040)	CXCL12/CXCR4 modulators	CXCR4 antagonists	Phase I/II
TG-0054	Taigen Biotechnology	CXCL12/CXCR4 modulators	CXCR4 antagonists	Phase II
NOX-A12	NOXXON Pharma	CXCL12/CXCR4 modulators	Neutralisation of CXCL12	Phase II
SEW2871	NA	phingosine-1-phosphate Agonists	Alteration of S1P gradient between PB and BM, which may counteract HSC retention in the BM	Animal Studies
BIO 5192	NA	VCAM/VLA-4 (vascular cell adhesion molecule-1/Very Late Antigen 4)Inhibitors	Inhibition of VLA-4 mediated HSC adhesion to VCAM-1 within the bone marrow stroma	Animal Studies
Bortezomib	Celgene	Proteasome Inhibitors	Possible alteration of the VLA-4/VCAM-1 pathway	Phase III
SB-251353	NA	Groß	Release of proteases that alter HSC adhesion to the BM niche	Animal Studies
FG-4497	NA	Stabilisation of hypoxia-inducible factor	Expression of VEGF-A in the BM sinusoids, leading to vasodilatation	Animal Studies

<sup>26</sup> Hopman RK, DiPersio JF. Advances in Stem Cell Mobilization. Blood reviews. 2014;28(1):31-40. doi:10.1016/j.blre.2014.01.001.

There are also some investigational agents such as parathyroid hormone, antibodies against VLA-4, human growth hormone, TPO-receptor agonists and retinoic acid receptor- $\alpha$  agonists drugs that are being tested in early clinical trials<sup>27</sup>.

#### The SCM Market:

The stem cells mobilization market is based on current marketable agents that are used to mobilize stem cells from a donor's bone marrow into the peripheral blood circulation. Granulocyte-colony stimulating factor (G-CSF) analogs such as Neupogen and Neulasta, which generate billions of dollars in sales annually, are the most intensively used for stem cell mobilization for autologous and allogeneic transplantations, but as off-label drugs; they are intended and approved for other indications such as slow white blood cell recovery following chemotherapy. Therefore, they do not entirely reflect the potential BL-8040 market for this indication. Mozobil (plerixafor), on the other hand, is specifically labeled for stem cell mobilization, primarily used for autologous transplantation, and is given to 40-50% of patients in which the use of G-CSF alone did not produce sufficient stem cell mobilization to the bloodstream. Thus, we used it as a benchmark to estimate the economic potential for BL-8040. Nevertheless, BL-8040 is investigated as a candidate drug for allogeneic as well as autologous transplantations, in which it will be given solely, or in addition to G-CSF.

The following table provides the primary sales of drugs and forecasts, upon which we based our market valuation:

Product	Company	2016	2017	2018	2019	2020	2021	2022	CAGR
Mozobil	Sanofi	168	173	178	184	190	195	201	+3%
Neulasta+Kyowa Hakko Kirin	Amgen	4,791	4,613	4,390	3,902	3,495	3,117	2,795	-9%
Neupogen	Amgen	765	561	491	433	392	362	331	-13%

Source: EvaluatePharma, WW Sales. All Financial Data in US \$ (million)

### BL-8040

BL-8040 is a 14 amino acid synthetic peptide which is a high-affinity antagonist of CXCR4. Its composition is covered by patents granted in the US, EU and Japan through 2023, not including patent-term extension. CXCR4 antagonist mode of action is relevant to multiple different cancer types and it was shown in a broad range of *in vitro* and *in vivo* studies that BL-8040 can induce apoptosis of cancerous cells, sensitize cancerous cells to chemo- and bio-based anti-cancer therapy, and can facilitate mobilization of stem cells from bone marrow<sup>28,29,30,31,32</sup>.

BL-8040 inhibits the ligand CXCL12 (also called SDF-1) from binding to its CXCR4 receptor expressed in tumortumor cells and hence impacting a magnitude of tumorigenic processes. This blockage promotes the release of tumortumor

<sup>27</sup> Bakanay SM, Demirer T. Novel agents and approaches for stem cell mobilization in normal donors and patients. Bone marrow transplantation. 2012 Sep 9;47:1154–63.

<sup>28</sup> Peled A, Abraham M, Avivi I, Rowe JM, Beider K, Wald H, Tiomkin L, Ribakovsky L, Riback Y, Ramati Y, et al. The high-affinity CXCR4 antagonist BKT140 is safe and induces a robust mobilization of human CD34+ cells in patients with multiple myeloma. Clin Cancer Res. 2014;20(2):469–79.

<sup>29</sup> Beider, K, Darash-Yahana, M, Blaier, O, Koren-Michowitz, M, Abraham, M, Wald, H, Wald, O, Galun, E, Eizenberg, O, Peled, A & Nagler, A 2014, 'Combination of imatinib with CXCR4 Antagonist BKT140 overcomes the protective effect of stroma and targets CML in vitro and in vivo' Molecular Cancer Therapeutics, vol 13, no. 5, pp. 1155-1169. DOI: 10.1158/1535-7163.MCT-13-0410

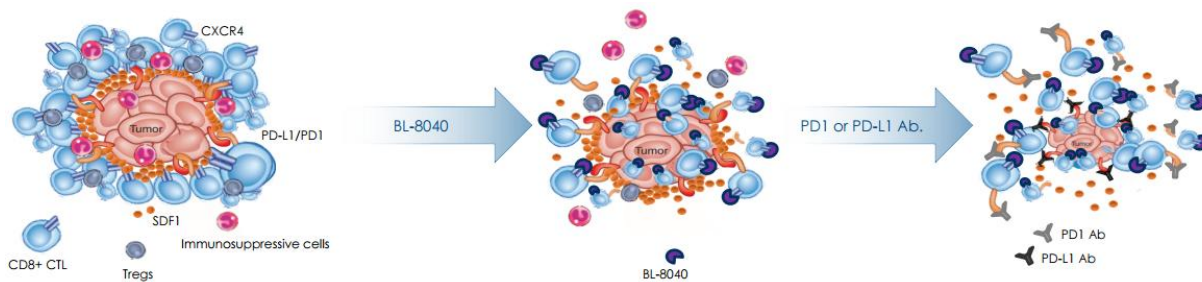
<sup>30</sup> Fahham D, Weiss ID, Abraham M, et al. In vitro and in vivo therapeutic efficacy of CXCR4 antagonist BKT140 against human non-small cell lung cancer. J Thorac Cardiovasc Surg. 2012;144(1167–1175):e1.

<sup>31</sup> Burger JA, Stewart DJ, Wald O, Peled A. Potential of CXCR4 antagonists for the treatment of metastatic lung cancer. Expert Rev Anticancer Ther. 2011;11:621–630. doi: 10.1586/era.11.11.

<sup>32</sup> Burger J. A., Peled A. (2009). Cxcr4 antagonists: targeting the microenvironment in leukemia and other cancers. Leukemia 23 43–52. 10.1038/leu.2008.299

cells from the bone marrow into the bloodstream and hence increases the sensitivity of tumor cells to various chemotherapy treatments. BL-8040 was also found to induce apoptosis of tumor cells and, together with checkpoint inhibitors, significantly impacts tumor microenvironment.

### BL-8040 mode of action in cancer immunotherapy



Source: BioLineRx May 2017 Presentation

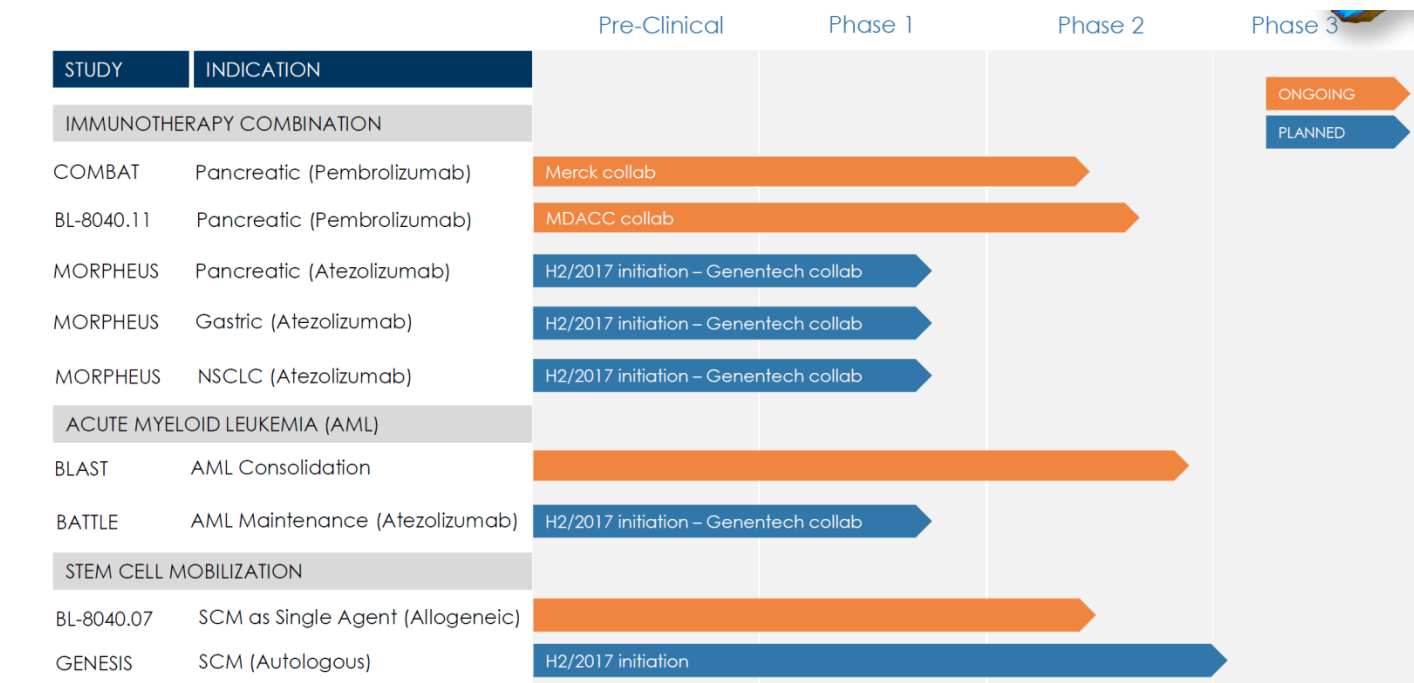
BL-8040 has three key modes of action. It works as an immunostimulant (mobilizes immune cells from bone marrow and lymph nodes), a potentiator (facilitates immune cells infiltrations into the tumors), and as a microenvironment modifier (decrease CXCR4-mediated migration of immune suppressor cells). In addition, BL-8040 induces apoptosis in AML, and facilitates mobilization of stem cells.

It is worth noting that caution should be taken when inhibition of the SDF-1/CXCR4 signalling pathway is applied in human subjects. Inhibition of CXCR4 signalling attenuates the immune responses, therefore moderate activation of CXCR4 pathway contributes to depression of inflammation and is beneficial for the cancer patients. On the other hand, excessive activation of CXCR4 pathway might dampen the hosts' immune responses and decrease anticancer ability.

BL-8040 has received the Orphan Drug Designation from the FDA for the treatment of AML and SCM. The drug is being investigated as a combination therapy with multiple partners including Merck, MDACC and Genentech (described in the following "Clinical Development" section).

## Clinical Development

BL-8040 is in Phase II clinical trials for three main indications: AML, pancreatic cancer and SCM as a single agent for allogeneic transplants. A Phase III study is expected to be initiated in SCM in combination with G-CSF in late 2017.



Source: BioLineRx data

### Pancreatic Cancer Clinical Trials

The Phase IIa study was designed to examine the combination of BL-8040 with Merck’s Keytruda (anti-PD1 immune checkpoint inhibitor). The study will recruit approximately 30 patients with metastatic pancreatic adenocarcinoma. This open-label, single-arm trial is being conducted in the US, Israel and South Korea. The primary endpoint of the study is to assess clinical response (objective response rate), safety and tolerability of this drug combination as well as multiple pharmacodynamic parameters, including the ability to improve infiltration of T-cells into the tumor and their reactivity. The study commenced at the end of Q3 2016 and partial results are expected in H2 2017, while top-line results are expected in H2 2018.

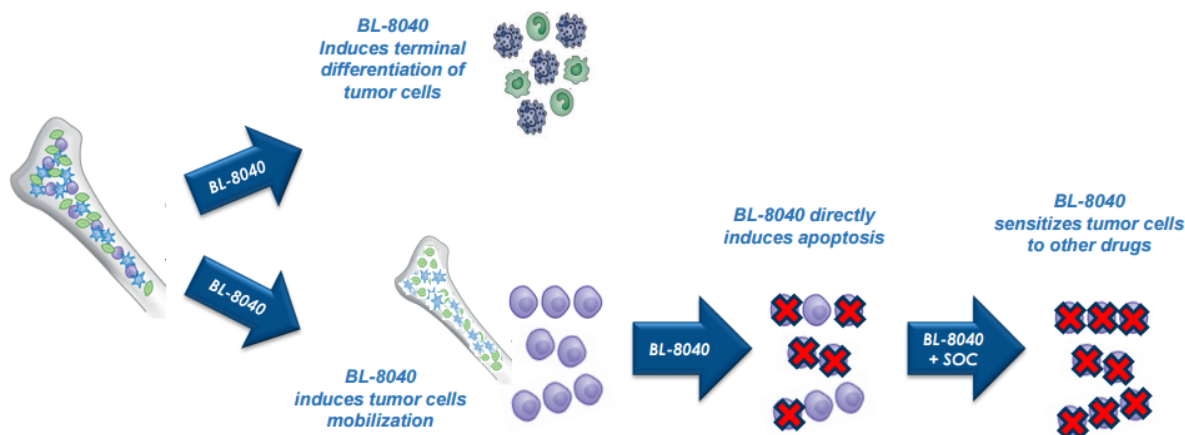
BioLineRx is running an additional study in collaboration with Merck and MD Anderson Cancer Center. This Phase II study was initiated in Q1 2017 and aims at testing BL-8040 with Keytruda in gastrointestinal cancers. Similarly to the other study, the primary endpoint is to measure efficacy, and also to monitor various biological markers of the anti-tumor response.

### AML Clinical Trials

BioLineRx has also conducted a successful proof-of-concept Phase IIa study in relapsed/refractory AML evaluating safety and efficacy of BL-8040 in combination with cytarabine (Ara-C). The study recruited 42 patients and examined

safety and tolerability, as well as clinical efficacy. The results indicated robust bone marrow clearance, apoptotic effect and terminal differentiation of AML cells as expected.

### BL-8040 mode of action in AML



Source: BioLineRx May 2017 Presentation

The final successful results of this study accelerated development in the AML space and highlighted the potential for elimination of the minimal residual disease (MRD).

Additionally, a consolidation AML Phase IIb study commenced in September 2015 that aims to evaluate the addition of BL-8040 to the standard consolidation therapy with cytarabine in adults. Half of the participants will receive BL-8040 and cytarabine in combination, while the other half will receive placebo and cytarabine. The study will recruit a total of 194 patients at 25 different sites in Germany. The primary endpoint of the study is to assess relapse-free survival [Time Frame: 18 months], while the secondary endpoints are to evaluate overall survival, time to relapse, relapse-free survival [Time Frame: 6, 9, 12 and 18 months], minimal residual disease and toxicity. The study's partial results are expected in H2 2018 while top-line results are expected in H2 2019.

BioLineRx is also planning to initiate a Phase Ib/II study in maintenance AML, combining BL-8040 with Genentech's atezolizumab. This open label study is planned to be initiated in H2 2017.

### Stem Cell Mobilization Clinical Trials

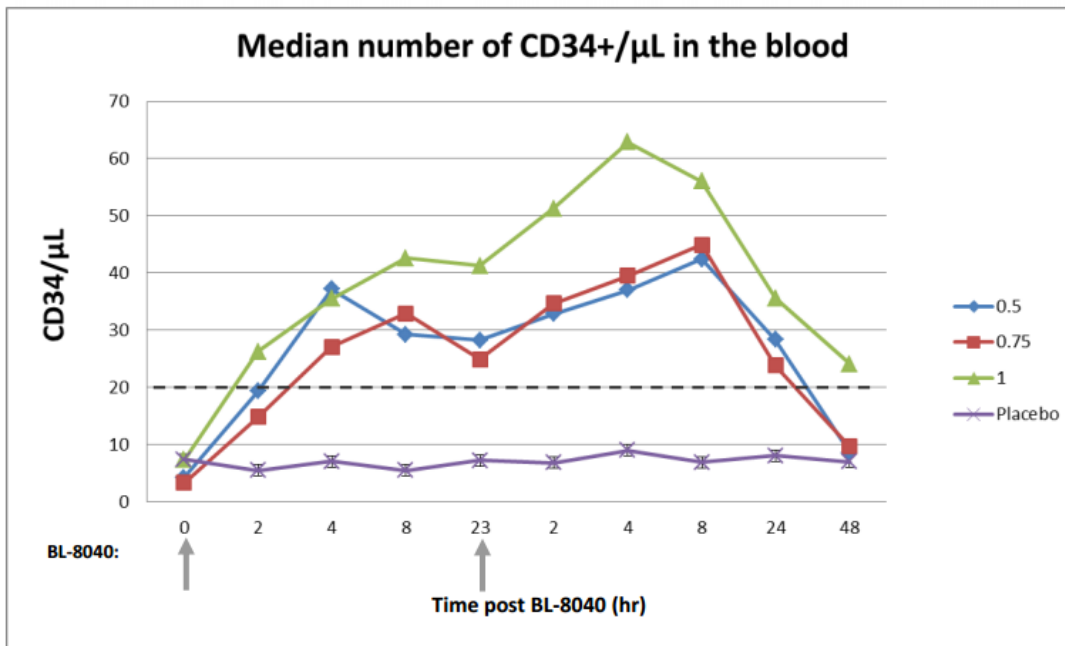
#### SCM for Allogeneic BMT

BioLineRx has completed a successful proof-of-concept Phase I study in 2015. The aim of the study was to determine whether BL-8040 is safe, tolerable and effective in the mobilization of Hematopoietic Stem Cells (HSC) in healthy volunteers.

This study showed substantial HSC mobilization (CD34+ cells) from bone marrow to peripheral blood, compared to the placebo treated group after a single administration of BL-8040. Single apheresis resulted in the robust collection of stem cells; the yield exceeded the required amounts to support a transplant.



## HSC mobilization (CD34+ cells) from bone marrow to peripheral blood



Source: BioLineRx May 2017 Presentation

In addition, the study indicated that BL-8040 was safe and well tolerated by healthy volunteers; as a result of those positive findings, the Phase IIa study was launched. This ongoing Phase IIa study aims at evaluating the number of donors who are able to mobilize more than  $2 \times 10^6$  CD34+ cells per kg (weight of patient) after a single administration of BL-8040. Successful partial results were announced stating that a single injection of BL-8040 mobilized sufficient amounts of cells without the need for G-CSF. In addition, all transplant recipients experienced successful neutrophil engraftment. The secondary endpoints that are also being investigated include safety and tolerability, but also the incidence of any acute and chronic graft versus host disease (GVHD) events. The top line results are expected by the end of 2017.

### SCM for Autologous BMT

BL-8040 was tested in a Phase I study in multiple myeloma patients undergoing an autologous bone-marrow transplant and demonstrated strong efficacy results. Based on this data, BioLineRx plans to initiate the Phase III registrational study in autologous SCM for H2 2017. This study will be designed based on the understanding reached with the FDA during a meeting held during April 2017, and could potentially serve as a registrational study for BL-8040 in this indication in the US.

### Future Developments

BioLineRx also has four Phase Ib studies planned in collaboration with Genentech. They are planned to be initiated in H2 2017, and will aim at investigating the combination of BL-8040 with Genentech's Tecentriq™ (Atezolizumab - anti-PDL1 immune checkpoint inhibitor) for multiple indications including pancreatic cancer, gastric cancer and non-small cell lung cancer (NSCLC). The agreement with Genentech mandates they will sponsor and conduct three Phase Ib

studies in multiple solid tumors while BioLineRx will be responsible for sponsoring and conducting a single Phase Ib study in (maintenance) AML. All of them will be open-label, repeated administration studies conducted on a group of up to 60 patients. The primary endpoint for those studies is to assess clinical response, safety and tolerability as well as to investigate multiple pharmacodynamic parameters. The studies are expected to commence in H2 2017 with partial results expected in H2 2018.

### Pipeline Competition

Since CXCR4 signalling was shown to be involved in a range of pathological processes, small-molecule antagonists directed against CXCR4 are of great interest as potential therapeutic use. A large number of drug candidates targeting CXCR4 have been discovered, however so far only one, plerixafor, has been approved by the FDA for the mobilization of HSPCs for autologous transplantation in patients with non-Hodgkin's lymphoma. A few therapeutic drugs that are in the clinical pipeline and directly competing with BL-8040's mechanism of action are presented in the table below.

#### CXCR4 competitive landscape

Drug	Company	Development stage (Indication)	Remarks
X4P-001	X4 Pharmaceuticals	Phase II/III (WHIM) Phase I/II (refractory clear cell renal cell carcinoma (ccRCC), melanoma, and other solid tumors)	Low-dose formulation of X4P-001, an oral, small molecule inhibitor of CXCR4, or C-X-C receptor type 4
Mozobil	Genzyme/Sanofi	Launched for SCM, being tested in multiple clinical trials for various indications	Mozobil (plerixafor injection) is approved by FDA to be used with another agent, granulocyte-colony stimulating factor (G-CSF)
POL6326	Polyphor	Phase I (mobilise and collect hematopoietic stem cells) Phase II (tissue repair in acute myocardial infarction-Terminated)	Orally bioavailable inhibitor of CXC chemokine receptor 4 (CXCR4) with receptor binding and hematopoietic stem cell mobilization activities
PF-06747143	Pfizer	Phase I (Acute Myeloid Leukemia (Biologic))	Novel-humanized IgG1 CXCR4 antagonist antibody
USL-311	Proximagen	Phase I/II	USL-311 is a CXCR4 inhibitor, under development by Proximagen for the treatment of glioblastoma and solid tumors
GMI-1359	GlycoMimetics	Phase I (hematologic malignancies)	GMI-1359 is a lead compound targeting both E-Selectin and CXCR4

### Summary of competitive analysis

The BL-8040 is a platform that can be used in multiple indications as shown above. It has a very distinct mechanism of action combining the ability to impact tumor microenvironment, induce apoptosis and facilitate mobilization of stem cells, immune cells and malignant cells from bone marrow.

It is believed to have the greatest potential when used in combination with checkpoint inhibitors and therefore collaboration with Genentech and Merck are crucial for the success of this platform in the oncology field.

BL-8040 has also been shown as a potent therapeutic candidate for the treatment of AML. The competition in the AML field is fierce and there are hundreds of drugs under development. The direct competitor would be an Ulocuplumab-a fully human IgG4 anti-CXCR4 antibody that induces cell death in chronic lymphocytic leukaemia. Unlike BL-8040, Ulocuplumab has significantly lower mobilization properties, milder apoptotic effect, and there are no published data on T-cell infiltration into tumors.

In the stem cell mobilization field, there is a scarcity of approved therapies that offer sufficient standard of care. BL-8040 does not have much competition and offers an advantage over current standard of care. Mozobil injections are administered four to six times a day and on average one to four apheresis are required to collect a sufficient number of cells for transplant. In addition, Mozobil was shown to have a lower affinity for CXCR4, lower mobilization properties, and has no effect on cancer cell apoptosis and hence it is inferior in comparison to BL-8040. There are a couple of drugs in the pipeline positioned at a similar developmental stage that aim at modulating CXCL12/CXCR4 pathway. Hence, should BL-8040 reach the market, its sales could be hampered by those investigational agents.

## Pre-Clinical Programs

### [AGI-134: alpha-Gal immunotherapy for multiple solid tumor indications](#)

BioLineRx acquired Agalimmune, a UK-based oncology company, for \$6 million in cash and stock in H1 2017. Agalimmune has a key flagship product for the treatment of various solid tumors. This AGI-134 product is a synthetic  $\alpha$ Gal immunotherapy. Abundantly and naturally present, anti- $\alpha$ Gal (anti-Gal) antibodies can be recruited to the sites on tumors so that the body's natural immune response is stimulated to attack cancerous cells.

AGI-134 is injected into the tumor, where it coats the tumor cell membrane and hence presents  $\alpha$ Gal antigen on the surface. Anti-Gal antibodies bind to the  $\alpha$ Gal part of AGI-134 to induce an initial immune response that activates certain pathways of cellular cytotoxicity, or cell death. This cytotoxicity generates immune-tagged tumor cells and cellular debris that generate a follow-on systemic immune response by activation and expansion of T-cells to the patient's own neo-antigens.

This approach not only targets the primary injectable tumor, but has also demonstrated efficacy against existing distant secondary tumors and metastases. The mechanism of action also suggests the potential of long-term protection against future metastases.

AGI-134 has completed multiple pre-clinical studies. Upon single injection tested on a model of melanoma, robust protection against secondary cancer was demonstrated for over 90 days. In addition, AGI-134 was also tested in combination with PD-1 immune checkpoint inhibitor and showed positive results. With regards to the latter, it was found that checkpoint drugs work best in highly mutated tumors that are highly infiltrated with immune cells, known as "hot tumors". Unfortunately, the overwhelming majority of human tumors are "cold" tumors, without immune cells. Therefore, transforming a cold tumor into a hot tumor is a major objective in cancer treatment.

With AGI-134, which harnesses naturally occurring, pre-existing antibodies to elicit a tumor-specific immune response, the resulting activation and clonal expansion of T-cells to the patient's own neo-antigens has the potential to transform cold tumors to hot tumors, thereby significantly expanding treatment potential

**The AGI-134 is likely to commence a first-in-man study in patients with solid tumors in H1 2018.**

### [BL-9020 Collaboration with JHL](#)

BioLineRx has an agreement with JHL to collaborate in the development and commercialization of BL-9020. JHL has global manufacturing rights to BL-9020, along with development and commercialization rights in China and Southeast Asia. BioLineRx has those rights in the rest of the world.

The BL-9020 product is a novel antibody that slows down the destruction of insulin-producing pancreatic cells in early stages of Type 1 diabetes patients and hence preventing full maturation of the disease. BL-9020 targets the Natural Killer (NK) receptor NKp46, which has been shown to specifically recognize pancreatic beta cells, leading to their destruction and hence contributing to the development of Type 1 diabetes. BL-9020 has completed pre-clinical studies

in a mouse model of Type 1 diabetes. The results were promising and demonstrated that BL-9020 can delay the onset of diabetes.

### **BL-1210/BL1220/BL-1230 Collaboration with Novartis**

BioLineRx has a number of collaborations with Novartis for joint development of innovative drug candidates.

BL-1210 is a therapeutic candidate for the treatment of liver fibrosis. Professor Rifaat Safadi, from the Department of Medicine at Hadassah Medical Center, Jerusalem, Israel, developed a novel method to reduce liver fibrogenesis and subsequently minimize scarring through modulation of the immune system. By modulating natural killer cell activity through inhibition of NGn4 expression, NK cell's anti-fibrotic propensity are stimulated. This mechanism of action can be used with nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver disease (NAFLD) patients as BL-1210 has a potential to halt liver fibrosis progression and NASH aggravation.

Orally-administered BL-1220 is a drug candidate for the treatment of numerous liver failure conditions such as end-stage liver disease (ESLD) and for conditions potentially leading to liver failure such as NASH. BL-1220 is a novel composition of sodium alginate developed by Professor Smadar Cohen (Ben-Gurion University of the Negev, Israel) and Professor Yaron Ilan (Hadassah Medical Center, Jerusalem, Israel). Pre-clinical studies of BL-1220 have been completed in animal models of liver impairment. The results were promising and demonstrated that BL-1220 has hepatoprotective properties with the ability to restore liver function.

BL-1230, developed by Professor Raphael Mechoulam (Medicine of the Hebrew University) for the treatment of dry eye syndrome (DES), is an additional drug candidate. The BL-1230 is a selective cannabinoid receptor type 2 (CB2R) agonist. CB2R has been shown to be involved in the immune modulation tempering inflammation associated with DES but also may induce analgesic effects. The eye drops with BL-1230 have been shown to have significant anti-inflammatory effects in three ocular inflammatory models

## Valuation

### Pipeline Analysis Summary

BioLineRx is currently advancing a lead clinical program, BL-8040, in multiple clinical studies: three Phase II programs for consolidation AML, stem-cell mobilization (SCM) and pancreatic cancer; and four Phase I studies for the treatment of maintenance AML, gastric cancer, non-small cell lung cancer and pancreatic cancer. In addition, the Company intends to initiate a Phase III registrational study later this year in SCM in preparation for autologous bone-marrow transplant (BMT). The Company has multiple pre-clinical ongoing studies with AGI-134: an immunotherapy treatment for multiple solid tumors, with clinical studies expected to commence in H1 2018; three programs with Novartis for NASH, liver failure diseases and dry eye syndrome indications; and one program with JHL for type I diabetes. In addition, the Company out-licensed their BL-5010 drug for treatment of skin lesions to Perrigo.

**We commenced our pipeline valuation with the evaluation of BL-8040 focusing on the company's three leading clinical programs, and, in addition, the evaluation of the BL-5010 drug for treatment of skin lesions.**

**8040-AML** - In the first quarter of 2016, BioLineRx completed a Phase IIa trial for the treatment of relapsed or refractory AML which was conducted at six cancer research centers in the US and at five sites in Israel. In March 2016, BioLineRx announced positive top-line results from this study. BioLineRx is currently running a significant Phase IIb trial in Germany, in collaboration with the German Study Alliance Leukemia Group. The Phase IIb trial is a double-blind, placebo-controlled, randomized, multi-center study aimed at assessing the efficacy of BL-8040 in addition to standard consolidation therapy in AML patients. According to the company, up to 194 patients will be enrolled in the trial. The primary endpoint of the study is to compare the relapse-free survival (RFS) time in AML subjects in their first remission during a minimum follow-up time of 18 months after randomization. BioLineRx is considering performing an interim analysis of this study in 2018, with top-line results expected in 2019. We assume Phase III will commence in 2020 and, upon successful outcomes, go-to-market will likely be in 2024.

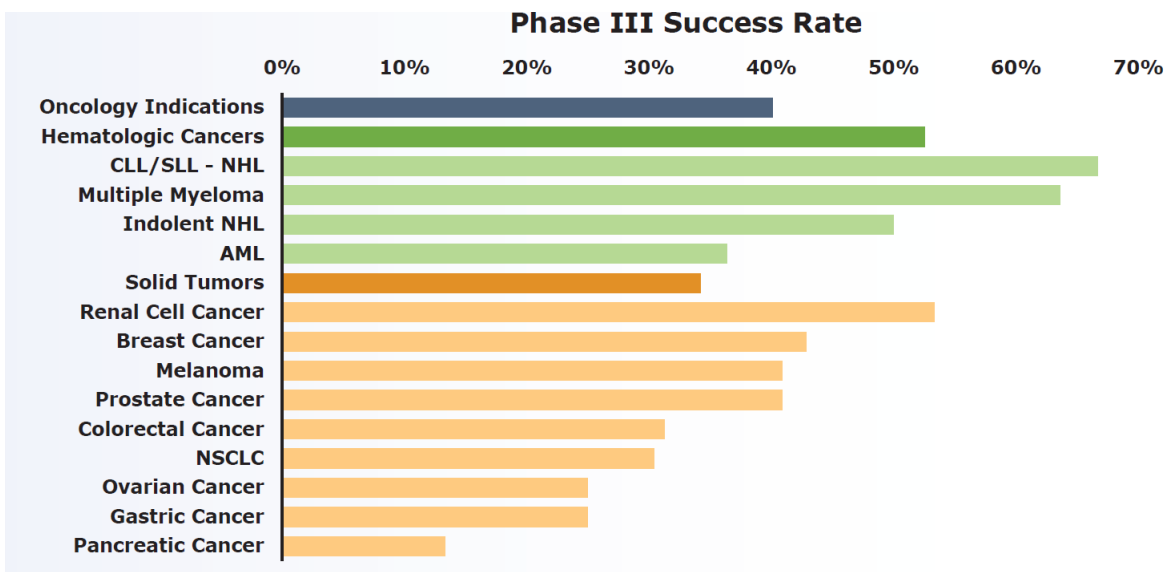
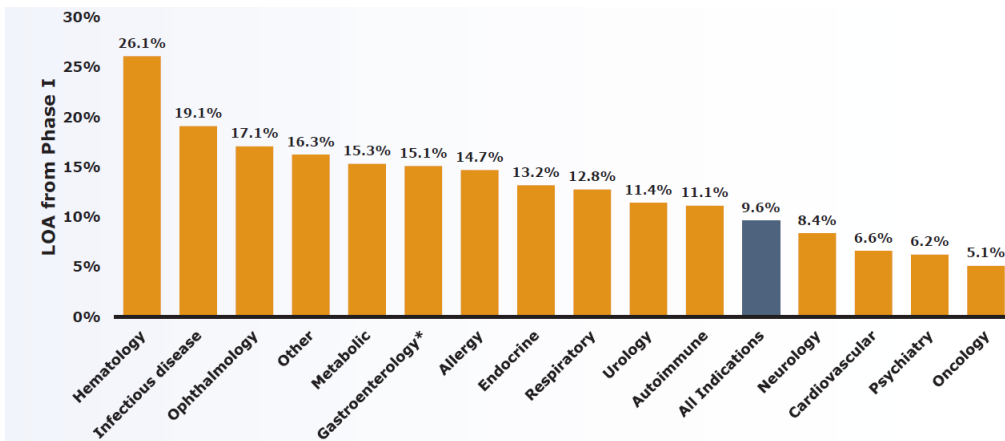
**Stem Cell Mobilization (SCM)** - BioLineRx completed a successful proof-of-concept Phase I study in 2015 in SCM, where SCM acted as Single Agent (Allogeneic); this may provide future economic potential. The aim of the study was to determine whether BL-8040 is safe, tolerable and effective in the mobilization of Hematopoietic Stem Cells (HSC) in healthy volunteers. Initiation of a phase III registrational study in autologous SCM is planned for H2 2017; this is a direct regulatory path, with a possible FDA submission in 2021, and go-to-market - one year later.

**Pancreatic cancer** - In the Immunotherapy combination indication of Pancreatic cancer, BioLineRx is in a Phase IIa study designed to examine the combination of BL-8040 with Merck's Keytruda. The trial is being conducted in the US, Israel and South Korea. The primary endpoint of the study is to assess clinical response (objective response rate), safety and tolerability of this drug combination as well as multiple pharmacodynamics parameters, including the ability to improve infiltration of T-cells into the tumor and their reactivity. The study commenced at the end of Q3 2016 and partial results are expected in H2 2017, while top-line results are expected in H2 2018. We assume Phase III will commence in 2020 and, upon successful outcomes, go-to-market will be in 2024. We also assume that evidence of

efficacy in this tumor will lead to rapid expansion of studies in other tumor types such as NSCLC, gastric, ovarian and others (in combination with checkpoint inhibitors).

**Distribution agreement:** The Company will develop these indications through clinical phase II, and then partner with pharmaceutical companies for advanced clinical development and commercialization. We consider out-licensing deals for the 8040 with the three indications upon success in phase II, i.e. until 2020. We assume deal structure will be in the range of \$400 - \$600 million with royalties in the range of 10%-15%.

**Success rates** – the company engages in a high-risk therapeutic area, primarily with pancreatic cancer. Success rate data indicates lower success rates for oncology (5.1%) in comparison to the total average of all indications (9.6%) from phase I until FDA approval. Moreover, when we explore oncology in depth by phase III success rates, AML has less than a 40% success rate, while pancreatic cancer has a 15% success rate to move from phase III to FDA regulatory stage; 25% success rates are seen in phase II for all BL-8040 indications. We address these clinical risks in our rNPV valuation of each indication.



Source: Clinical Development Success Rates, 2006-2015. Biomedtracker 2016.

Capitalization rate: We calculate our discount rate at 20.9%, based on our CAPM model (See Appendix B).

Other parameters: We agree with BioLineRx’s assumption that its patents related to BL-8040 processes and methods will remain active until 2034. R&D expenses in our analysis will be similar to those during 2015-2016 of \$11-\$12 million, until the go-to-market stage. The company has several agreements in place with its in-licensee, in which BioLineRx is obligated to pay a 40% share of future royalties (but not from milestones payments. We assume current carry-forward-tax; thus, BioLineRx will not pay any taxes until the end of the patent period.

Valuation of BL-8040 is a risk-adjusted net present value (rNPV) capitalization to the net present value. The valuation includes weighting of several scenarios, based upon the main assessments described above. The valuation parameters are summarized in the following table.

Main valuation parameters for BL-8040

Indications	Current development stage	Success Rate Phase II	Success Rate Phase III	Regulatory approval success rate	Launch	Patent period
AML	2b	25%	40%	90%	2024	2034
SCM	2	25%	40%	90%	2024	2034
P. cancer	2a	25%	15%	90%	2024	2034

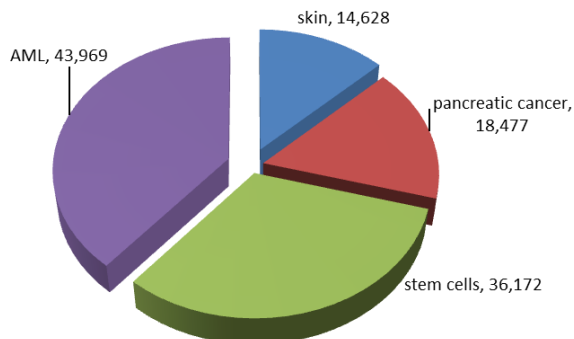
Parameters/Indications	AML	SCM	pancreatic cancer
Total market per product (000K)	800	2,200	5,500 (incl. Autologous)
Market Growth (CAGR)	7.5%	7.5%	7.5%
Company share from Market (Peak Sales)	30.0%	50.0%	20.0%
Royalties to BioLineRx	12.5%	12.5%	12.5%
Royalties to original developer	40.0%	40.0%	40.0%

We value BL-5010 based on the company’s estimations for future annual net sales of \$2 -\$4 million, royalty-based sales from Perrigo. This is based on an international 20-year patent application that covers the BL-5010P applicator, and that will expire in 2033.



We conclude our pipeline interim analysis with a total value of \$113.2 million for BioLineRx's primary indications.

### Pipeline analysis (000K)



### Technological Platform Valuation

BioLineRx's product pipeline is supported by the company's broad business and technological base. Valuation of BioLineRx's "technological basis" is in fact a valuation of the company's "residual value". This valuation was conducted using the Feed Rate methodology that is common in the field of life sciences, rather than using the conventional terminal value, normally used by non-life science companies, for the following reasons:

- The terminal value reflects a type of steady state in the BioLineRx's sales with a certain fixed growth rate (g) based upon past data. This is not the case for life science companies, where the terminal value is derived from projects in development.
- The terminal value for a given company usually constitutes between 70-80% of its worth. In contrast, the main share of the value of a life science company is attributed to income generated during several years following product launch (for the most part, approximately 6-10 years), after which a certain decline occurs (for example, expiration of a patent, and the emergence of competing products).

The technological platform valuation is based on the average number of new projects that a company can yield annually. Estimating the capitalization value of future projects is based on pre-clinical and clinical development aspects, assessment of unallocated costs, and a higher capitalization rate than the one used during the forecast years, due to the uncertainty of the company's future projects<sup>33</sup>.

Our valuation includes early clinical stage indications within the company's pipeline such as AGI-134, an immunotherapy treatment in development for multiple solid tumors, for which a first-in-man study is expected to be initiated during H1 2018. In addition, BioLineRx has a strategic collaboration with Novartis for the co-development of selected Israeli-sourced novel drug candidates; a collaboration agreement with MSD; and a collaboration agreement with Genentech, a member of the Roche Group, to investigate the combination of BL-8040 and Genentech's Atezolizumab in several Phase 1b studies for multiple solid tumor indications and AML. To wit, in BioLineRx, we see the company's technological platform as management's ability to produce additional worthy technology acquisitions, and incorporating them into the company's product pipeline in advanced clinical phases.

<sup>33</sup> Bogdan & Villiger, "Valuation in Life Science - Practical Guide", 2008, Second Edition.

Main technology platform valuation points:

- We assume one new project every three years with an average value of \$32.9 million (equal to the average value of the current pipeline programs)
- Unallocated costs are mainly G&A and sales costs, with a similar share from the project's value as in the current pipeline programs
- We estimate unexpected costs to be 10% of the average value
- Statutory tax rate of 23%
- The capitalization rate is higher than the one used in the pipeline valuation, reflecting increased uncertainty
- It is assumed that the "platform" generates projects for n years: in our valuation, and based on the average patent period, n=18 years. We therefore subtract from the technological platform value all projects generated after n years (the exceeding projects).

The following formula reflects the value of the technology:

$$V(\text{tech}) = \frac{(fV_{\text{project}} - (1+r)\text{costs})}{r} * 1 - \frac{1}{(1+r)^n}$$

Main valuation parameters of the technological platform

<b>Average # of New Projects per Year</b>	0.3
<b>Project Value (000K)</b>	<b>32,873</b>
<b>Unallocated Costs (000K)</b>	-14,139
<b>Unexpected Costs (000K)</b>	-3,287
<b>Tax</b>	23%
<b>Capitalization</b>	25.9%
<b>Terminal Technology Value (000K)</b>	<b>15,152</b>
Technology Value - 2017-2034 (000K)	<b>240</b>
<b>Technology Value (000K)</b>	<b>14,912</b>

## Equity Value

Non-operational assets/liabilities and unallocated costs

As of March 31, 2017, BioLineRx has non-operational assets (cash) of approximately \$30 million with an estimated annual burn rate of \$16-\$17 million for 2015-2017 (\$1.4 million per month). During April 2017, the company successfully completed an underwritten public offering of its ADSs for net proceeds of \$26.2 million. Thus, BioLineRx holds a total of \$56.2 million as of April 2017, less its current burn rate of \$1.4 million per month.

The equity valuation elements are presented in the table below:

### Equity value

Pipeline Analysis		rNPV (000K)
<b>8040</b>	AML	43,969
<b>8040</b>	pancreatic cancer	18,477
<b>8040</b>	stem cells	36,172
<b>5010</b>	skin	14,628
<b>Total rNPV Pipeline</b>		<b>113,246</b>
<b>Unallocated Costs</b>		-48,710
Terminal Technology Value		<b>14,912</b>
Enterprise Value		<b>79,448</b>
<b>Non-operational assets/liabilities</b>		52,048
<b>Equity Value</b>		<b>131,496</b>

### Sensitivity Analysis

The table below presents BioLineRx's target price in relation to the capitalization rate. We set a range of 0.5% change from our CAPM model (as presented in Appendix B) as the stock range.

#### Sensitivity Analysis - Capitalization rate vs. Target price

Cap. rate	Target Price (NIS)
19.9%	5.20
<b>20.4%</b>	<b>5.04</b>
<b>20.9%</b>	<b>4.90</b>
<b>21.4%</b>	<b>4.76</b>
21.9%	4.63

We estimate the target price to be in the range of NIS 4.76 - NIS 5.04, with a mean of NIS 4.90. Thus, 1 ADS (an ADS represents 1 ordinary share) is equal to \$1.38<sup>34</sup>

<sup>34</sup> Calculation is NIS 4.90 divided by 3.56 NIS/\$ = \$ 1.38

## Relative Advantages

### Investment Thesis and Price Forecast Risks

Biotech companies, particularly those in the research and development stage, are relatively high-risk companies. Key risks that may affect BioLineRx include:

#### **Delay/postponement of marketing regulatory approval decisions**

In order for BioLineRx to market or out-license its products, it is necessary for them to receive marketing approval from regulatory agencies, such as the FDA (US) and EMA (EU). Our estimates regarding time to market are based on the assumption that these products will successfully complete Phase II- and III clinical trials without significant delays. Failure to fulfill the clinical endpoints of these experiments will force the Company to conduct additional clinical trials or abandon the development of certain projects. We consider this to be the main risk factor for the Company's activity at this stage.

#### **Risks involved in obtaining sources of financing, and stock trading**

As a biotech company in the research and development stage, without minimal revenue from sales, BioLineRx will be required to conduct fundraising prior to becoming profitable, unless early licensing deals are made. Failure to raise funds, or fundraising under conditions that are not beneficial to the Company, may affect its worth. In addition, the low level of tradability may deter some investors from buying BioLineRx stock.

#### **General risks related to similar companies**

The value of small companies in the biotech field could, to a relatively high degree, be affected by publications not related directly to their activities. Such publications may refer, for example, to competitors, macro trends in the healthcare sector, and political events.

## BioLineRx Contact Details & Management

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**Fax:** +972-8-642-9101

Email: [info@BioLineRx.com](mailto:info@BioLineRx.com)

### **Management:**<sup>35</sup>

#### **PHILIP A. SERLIN, CPA, MBA**

##### **Chief Executive Officer**

Mr. Serlin has served as our Chief Executive Officer since October 2016. From May 2009 to October 2016, Mr. Serlin served as our Chief Financial and Operating Officer. From January 2008 to August 2008, Mr. Serlin served as the Chief Financial Officer and Chief Operating Officer of Kayote Networks Inc. From January 2006 to December 2007, he served as the Chief Financial Officer of Tescom Software Systems Testing Ltd., an IT services company publicly traded in both Tel Aviv and London. His background also includes senior positions at Chiaro Networks Ltd. and at Deloitte, where he was head of the SEC and U.S. Accounting Department at the National Office in Tel Aviv, as well as seven years at the SEC at its Washington, D.C., headquarters. Mr. Serlin currently serves as an external director at Vascular Biogenics Ltd. (Nasdaq:VBLT). Mr. Serlin is a CPA and holds a B.Sc. in accounting from Yeshiva University and a Master's degree in economics and public policy from The George Washington University.

#### **MALI ZEEVI, CPA**

##### **Chief Financial Officer**

Ms. Zeevi has served as our Chief Financial Officer since October 2016. Prior to becoming Chief Financial Officer, Ms. Zeevi served as our Senior Director of Finance and Reporting beginning in 2011 and as our Director of Finance and Reporting beginning in 2009. Before joining BioLineRx, Ms. Zeevi was employed by Tescom Software Systems Testing Ltd., her last position there being Vice President Finance. Ms. Zeevi also served as a CPA at Kesselman & Kesselman, a member firm of PricewaterhouseCoopers International Limited. She holds a B.A. in business and accountancy from the College of Management Academic Studies in Israel.

#### **DAVID MALEK**

##### **Chief Business Officer**

David Malek has served as our Chief Business Officer since January 2016. From October 2011 through December 2015, Mr. Malek served as of Vice President of Business Development. Prior to joining the Company, from 2006 to 2011 Mr. Malek served at Sanofi-Aventis in a number of management positions, including Marketing, Finance and Business Development. Most recently, he served as Director of Oncology - New Products and Business Development. Mr. Malek received an MBA from the Tuck Business School at Dartmouth University and a B.A. in statistics and political science from the University of Haifa.

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<sup>35</sup> <http://www.biolinerx.com/>

**ABI VAINSTEIN-HARAS, MD****Vice President Clinical and Medical Affairs**

Abi Vainstein-Haras, M.D., has served as our Vice President Clinical and Medical Affairs since January 2017. From June 2014 to January 2017, Dr. Vainstein-Haras served as our Senior Medical Director responsible for the clinical development of all our clinical phase projects. Prior to joining the Company, from 2012 to 2014, she served as the Director and Clinical Program Leader for COPAXONE® at Teva, and from 2007 to 2012, she served in several medical positions in Innovative R&D at Teva. Dr. Vainstein-Haras holds an M.D. from University of Buenos Aires and is licensed to practice medicine in Israel.

**ELLA SORANI, PhD****Vice President Development**

Ella Sorani, Ph.D., has served as our Vice President Development since February 2017. Before joining BioLineRx, from 2000 through 2016, Dr. Sorani served in a number of management positions in the global R&D division at Teva Pharmaceutical Industries Ltd. In her most recent position as Senior Director and Global Project Leader, Dr. Sorani led the development of one of Teva's leading innovative late stage compounds. Dr. Sorani holds a B.Sc. in chemistry and an M.Sc. and Ph.D. in pharmacology, all from Tel Aviv University.

## Appendices

### Appendix A - Financial Reports

Profit and Loss Statement		USD 000s				
Reporting Year	2013	2014	2015	2016	31.3.2016	31.3.2017
RESEARCH AND DEVELOPMENT EXPENSES, NET	12,208	11,866	11,489	11,177	2,539	3,590
SALES AND MARKETING EXPENSES	1,136	1,589	1,003	1,352	248	681
GENERAL AND ADMINISTRATIVE EXPENSES	3,664	3,800	3,704	3,984	989	1,030
OPERATING LOSS	17,008	17,255	16,196	16,513	3,776	5,301
NON-OPERATING INCOME, NET	1,161	3,061	1,445	214	148	5
FINANCIAL INCOME	720	3,566	457	480	143	457
FINANCIAL EXPENSES	1,897	448	106	22	4	6
NET LOSS	17,024	11,076	14,400	15,841	3,489	4,855
CURRENCY TRANSLATION DIFFERENCES	1,097	2,834	0	0	0	0
COMPREHENSIVE LOSS	15,927	13,910	14,400	15,841	3,489	4,855

Balance Sheet (USD 000s)	2013	2014	2015	2016	31.3.2017
<b>CURRENT ASSETS</b>					
Cash and cash equivalents	8,899	5,790	5,544	2,469	2,201
Short-term bank deposits	9,319	28,890	42,119	33,154	28,167
Prepaid expenses	258	221	229	255	700
Other receivables	360	257	291	223	580
<i>Total current assets</i>	18,836	35,158	48,183	36,101	31,648
<b>NON-CURRENT ASSETS</b>					
Restricted deposits	165	166	0	0	0
Long-term prepaid expenses	49	49	58	52	55
Net PPE	712	721	2,909	2,605	2,540
Intangible assets, net	253	117	152	181	6,875
<i>Total non-current assets</i>	1,179	1,053	3,119	2,838	9,470
<b>Total assets</b>	<b>20,015</b>	<b>36,211</b>	<b>51,302</b>	<b>38,939</b>	<b>41,118</b>
<b>CURRENT LIABILITIES</b>					
Current maturities of long-term bank loan	0	0	93	93	93
Accounts payable and accruals: Trade	2,289	1,654	1,910	2,590	3,450
Other Accounts payable and accruals	764	1,252	1,137	978	1,631
<i>Total current liabilities</i>	3,053	2,906	3,140	3,661	5,174
<b>NON-CURRENT LIABILITIES</b>					
Long-term bank loan, net of current maturities	0	0	344	250	227
Warrants	5,240	1,500	208	1	1
<i>Total non-current liabilities</i>	5,240	1,500	552	251	228
<b>Total Liabilities</b>	<b>8,293</b>	<b>4,406</b>	<b>3,692</b>	<b>3,912</b>	<b>5,402</b>
<b>Total equity</b>	<b>11,722</b>	<b>31,805</b>	<b>47,610</b>	<b>35,027</b>	<b>35,716</b>
<b>Total liabilities and equity</b>	<b>20,015</b>	<b>36,211</b>	<b>51,302</b>	<b>38,939</b>	<b>41,118</b>

## Appendix B - Capitalization Rate

Cost of equity capital ( $k_e$ ) represents the return required by investors. The capitalization rate is calculated using the CAPM (Capital Asset Pricing Model). It is based on a long-term 20-year T-bond with a market risk premium, and based on Professor Aswath Damodaran's (NY University) commonly used sample ([www.damodaran.com](http://www.damodaran.com)). As of December 31, 2016, the Israeli market risk is estimated at 6.69%.

A three-year market regression Beta is 1.19, according to a sample of 411 companies representing the US biotechnology sector. BioLineRx has insignificant loans or any other rate-carrying liabilities, which are considered non-operational liabilities. In order to reach the relative CAPM, we used an unleveraged beta of this sample, which is higher than a leveraged beta, due to high rate of cash versus debt. The implied CAPM is 10.7%.

CAPM model ( $k_e$ ) is estimated as follows:

$$k_e = r_f + \beta(r_m - r_f) + P$$

BioLineRx is a small cap company, in which marketability and size premiums need to be considered. Duff and Phelps data research in the years 1963-2012 indicates that a 10.24% premium needs to be added to the CAPM for small cap companies. We therefore estimate the company's CAPM to be 20.9%.

CAPM Model		Value	Source
Long-term (20 years) T-bond	R(f)	2.67%	US Department of the Treasury (20Y)
Market risk premium	R(m)- R(f)	6.69%	based on Professor Damodaran's sample (1/17)
Beta unleveraged	$\beta$	1.19	Beta sample of 411 Drugs (Biotechnology) firms (1/17)
Cost of Capital	$k_e$	10.7%	
Size Premium		10.24%	Duff and Phelps data
<b>CAPM</b>	<b>CAPM</b>	<b>20.9%</b>	



## Appendix C - Team Bios

**Kobi Hazan** is the Lead Analyst at Frost & Sullivan Research & Consulting Ltd., a subsidiary of Frost & Sullivan in Israel. He has over 14 years of experience in capital markets, including research, analysis, investment advisory, and management. Mr. Hazan served as a Fund Manager for provident and mutual funds at Analyst Ltd. and, since 2012, he owns and manages the Amida Israel Fund, a hedge fund specializing in Israeli equities. Kobi holds an Economics and Management degree from The College of Management Academic Studies. He is licensed as an Investment Advisor in Israel.

**Dr. Anna Cirmirakis** joined Frost & Sullivan Transformational Healthcare team as a Healthcare consultant in February 2015. She works primarily with biotech, pharma and diagnostics companies on a wide range of strategic projects including product evaluation, market analysis as well as competitive intelligence. Prior to her role as a consultant she studied Human Genetics and she holds a PhD in biotechnology from University College London. Anna is a specialist in the field of monoclonal antibody production with keen interest in regenerative medicine, immunotherapies and biologics.

**Dr. Tiran Rothman** is an Analyst and Consultant at Frost & Sullivan Research & Consulting Ltd., a subsidiary of Frost & Sullivan in Israel. He has over 10 years of experience in research and economic analysis of capital and private markets, obtained through positions at a boutique office for economic valuations, as chief economist at the AMPAL group, and as co-founder and analyst at Bioassociate Biotech Consulting. Dr. Rothman also serves as the Economics & Management School Head at Wizo Academic College (Haifa). Tiran holds a PhD in Economics, MBA (finance), and was a visiting scholar at Stern Business School, NYU.

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