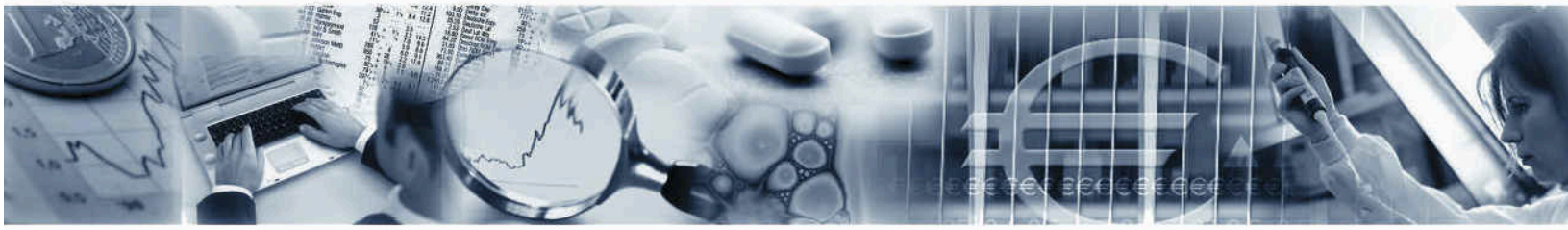


Update Report

Onconova Therapeutics Inc. (ONTX)

Leadership in high risk MDS

Chief Research Analyst

Marcel Wijma MSc

+1 (917) 460 6185 (US)

+31 (6) 1848 4204 (NL)

m.wijma@leeuwenhoeck.com

http://www.leeuwenhoeck.com

Date: 10 May 2018

Name:	**Onconova Therapeutics**
Country:	**USA**
Price:	**USD 0.37**
ISIN Code:	**US68232V3069**
Reuters Code:	**ONTX**
Market Cap (USD m):	**29.1**
EV (USD m):	**-4.4**
Cash & cash eq. (USD m):	**33.5*)**
Shares outstanding (m):	**78.6**
Volume:	**632,845**
Free float:	**79%**
52-week Range:	**0.35-2.83**

***) including the underwritten public offering in April of USD 28.75m**

	2015A	2016A	2017A
Total Revenues	11.456	5.546	0.787
Net (Loss)/Profit	(23.979)	(19.667)	(24.092)
Net loss per share (pence)	(10.54)	(4.44)	(2.68)
R&D costs	25.895	20.071	19.119
Cash increase/(decrease)	(23.783)	1.601	(17.426)
Cash and marketable sec.	19.799	21.450	4.024

Executive Summary

- Onconova Therapeutics (ONTX) is a late stage biopharmaceutical company with a focus on the development of innovative small molecule drugs to treat cancer. Its lead product is a small molecule called rigosertib that is currently in Phase III development as a second line treatment for higher risk myelodysplastic syndromes (HR-MDS). An oral version of rigosertib in combination with Celgene's Vidaza successfully concluded a Phase II trial and a pivotal Phase III trial for first-line MDS is expected to commence in 2018.

- Rigosertib acts as a so-called RAS mimetic by directly binding to the RAS binding domain (RBS) found in a number of RAS proteins. Ras proteins function as binary molecular switches that control intracellular signalling networks. Mutations or overexpression of RAS genes can lead to the production of permanently activated RAS proteins which can contribute to cancer. The three genes in humans (HRAS, KRAS and NRAS) are the most frequently mutated in 20-25% of all human tumors and up to 90% in certain types of cancer. That makes Onconova's platform applicable for multiple indications.

- Myelodysplastic Syndromes (MDS) are a group of diverse bone marrow disorders in which the bone marrow does not produce enough healthy blood cells. MDS is often referred to as a "bone marrow failure disorder". In addition, for roughly 30% of the patients diagnosed with MDS, this type of bone marrow failure syndrome will progress to acute myeloid leukemia (AML). To date, more than 1,300 patients have been enrolled in clinical trials with rigosertib. Orphan designation has been granted for rigosertib in MDS in the U.S., Europe and Japan.

- During February and April, the company successfully raised in total USD 35.0 million from public offerings. The Company's current cash position after the cash burn in the first quarter of 2018 and the proceeds of the public offerings, is USD 33.5 million. With a current market cap of USD 29.1 million, that adds up to a negative EV of USD 4.4 million. With a current quarterly cash burn of USD 5.5 million, we believe that this should be sufficient to carry out the further development of its pipeline in the coming 18 months. Furthermore, we expect the company will be able to sign a lucrative partnering deal as a result of encouraging interim data from the Phase III INSPIRE trial with rigosertib.

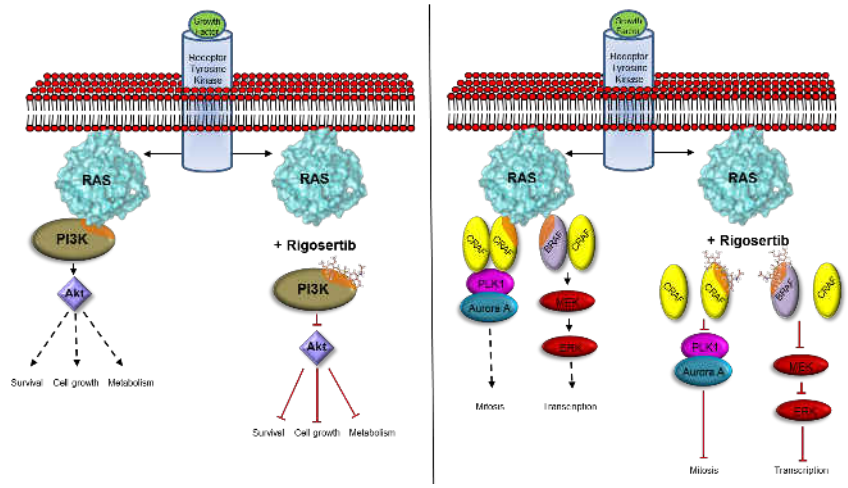
- There are a number of key milestones to focus on in the next 6-12 months which includes the commencement of the pivotal trial of the oral version of rigosertib in combination with Vidaza (Celgene) for first line HR-MDS, the interim analysis of the Phase III INSPIRE trial and the completion of the enrolment of the INSPIRE trial.

- **Based on NPV based valuation, we believe that Onconova Therapeutics is substantially undervalued at the current share price of USD 0.37. We feel that the company's current total value should be USD 267 million, or USD 3.40 per share taking into account a higher LOA and potential partnerships with rigosertib. This represents a substantial upside from the current share price.**

Company Profile

Onconova Therapeutics is an international biopharmaceutical company that is developing novel medicines for indications for which there are no existing or only inadequate therapies. With its proprietary chemistry platform, the company has built a late stage pipeline of targeted anti-cancer drugs based on specific cellular pathways while simultaneously causing minimal damage to normal cells.

The company's late stage clinical programs are focused on the high risk myelodysplastic syndrome (MDS). Its lead drug candidate, rigosertib (IV), is in Phase III trial for higher-risk MDS and an oral form of the drug has concluded Phase II for lower-risk MDS. Rigosertib is a small molecule that inhibits cellular signaling in cancer cells by acting as a Ras mimetic. Ras proteins function as binary molecular switches that control intracellular signalling networks (see graph below). Mutations or overexpression of RAS genes can lead to the production of permanently activated RAS proteins which can lead to cancer. The three genes in humans (HRAS, KRAS and NRAS) are the most commonly mutated in 20-25% of all human tumors and up to 90% in certain types of cancer. That makes Onconova' s platform applicable in multiple indications.



Investigations to understand the critical biochemical and biological mechanisms of Ras function are at the forefront of cancer research. Studies have shown that Ras interacts with a large number of effector proteins by a highly conserved mechanism that involves the switch region of Ras and the Ras-binding domains (RBDs) of its effector proteins. Because these interactions play an essential role in oncogenic Ras function, inhibiting them constitutes an attractive and important therapeutic approach for myeloid neoplasias and other cancers.

Based on new mechanism of action data published last year, Onconova is initiating a collaborative development program focusing on a group of rare diseases with a well-defined molecular basis in expression or defects involving the Ras Effector Pathways. Since "RASopathies" are rare diseases affecting young children, the company is setting up a multifaceted collaborative program involving patient advocacy, government and academic organizations. The RASopathies are a group of rare diseases which share a well-defined molecular basis in expression or defects involving Ras Effector Pathways. They are usually caused by germline mutations in genes that alter the RAS subfamily and mitogen-activated protein kinases that control signal transduction and are among the most common genetic syndromes. Together, this group of diseases can impact more than 1 in 1000 individuals, according to RASopathiesNet.

In January 2018, the company entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI), part of the National Institutes of Health (NIH). Under the terms of the CRADA, the NCI will conduct research, including preclinical laboratory studies and a clinical trial, on rigosertib in pediatric cancer associated RASopathies.

As part of the CRADA, Onconova provides rigosertib supplies and initial funding towards non-clinical studies. The NCI is funding the majority of the research, including the cost of the clinical trial, which is expected to start later this year. A clinical trial protocol has been developed and will

be reviewed by the Institutional Review Board. While the NCI will conduct a trial for RASopathy

related cancers in pediatric patients, Onconova will focus on Juvenile Myelomonocytic Leukemia (JMML), a well-described RASopathy affecting children, which is incurable without an allogenic hematopoietic stem cell transplant.

Recent Partnerships

In December 2017, Onconova entered into a license and collaboration agreement with HanX Biopharmaceuticals, Inc. ("HanX"), a company focused on development of novel oncology products, for the further development, registration and commercialization in China of ON 123300. This compound has the potential to overcome the limitations of current generation CDK 4/6 inhibitors. Under the terms of the agreement, the company received an upfront payment, regulatory and commercial milestone payments, as well as royalties on Chinese sales. The key feature of the collaboration is that HanX will provide all funding required for Chinese IND enabling studies performed for Chinese Food and Drug Administration IND approval. Onconova and HanX also intend for these studies to comply with the FDA standards. Accordingly, such studies may be used by us for an IND filing with the FDA. Together with HanX Onconova will oversee the IND enabling studies. Outside of China, Onconova maintains global rights.

In March 2018, Onconova also announced that it has entered into an exclusive license agreement with Swiss biotech company Pint Pharma GmbH to commercialize rigosertib in Latin America. In exchange for these rights, Pint will make investment totaling up to USD 2.5 million by purchasing shares at a premium to market. In addition, Pint Pharma will make additional regulatory, development and sales-based milestone payments to Onconova of up to USD 42.75 million and pay double digit tiered royalties on net sales in Latin America. Onconova will supply the finished product for sale in the licensed territories. Pint Pharma will also support Onconova's clinical trial initiatives in the territory

Update Pipeline: Focus on Rigosertib

Below is an overview of Onconova's clinical pipeline. Onconova's lead product is a small molecule called rigosertib that is currently in Phase III development as a second line treatment for higher risk myelodysplastic syndromes (HR-MDS). In January of this year, the company decided to move forward with the Phase III INSPIRE trial following a very promising interim analysis. A first line oral version of rigosertib in combination with azacitidine in HR-MDS also showed positive Phase II data as well and is expected to be in a pivotal phase III trial in 2018H2. Preparations have already begun.

Disease	Formulation	Indication	Stage	Expected Timelines	Potential Market Opportunity (US)/Benefit	
MDS*	Intravenous	HR-2nd line. No approved product following HMA failure	Phase 3	Interim analysis completed Phase 3 completion 2019	~5,000 patients	No directly competing FDA approved product in the market
	Oral	HR-1st line In combination with AZA	Phase 2	Phase 3 protocol, SPA process, in 2018	~18,000	No oral NCE approved since 2005
	Oral	Lower Risk	Phase 2	Select patient population in 2018	>10,000	Longer potential duration of treatment
RASopathies^	Intravenous and oral	JMML/other Ras Pathway diseases	Phase 1	• NIH CRADA signed • Proof of concept in 2019	Rare disease	Pediatric clinical trial

Source: Onconova Therapeutics

Rigosertib in development as second line treatment for HR-MDS

Onconova's most advanced therapy in development is IV rigosertib as second line treatment for patients with HR-MDS after failing hypomethylating agent therapy (HMA). End of 2015 a Phase III pivotal trial was initiated. The **IN**ternational **S**tudy of **P**hase III IV **R**igos**E**rtib, or INSPIRE, is based on guidance received from the FDA and European Medicines Agency and derives from the findings of the previous ONTIME Phase III trial. INSPIRE is a multi-center, randomized controlled study to assess the efficacy and safety of IV rigosertib in HR-MDS patients under 82 years of age who had progressed on, or failed to respond to, or relapse after previous treatment with HMAs

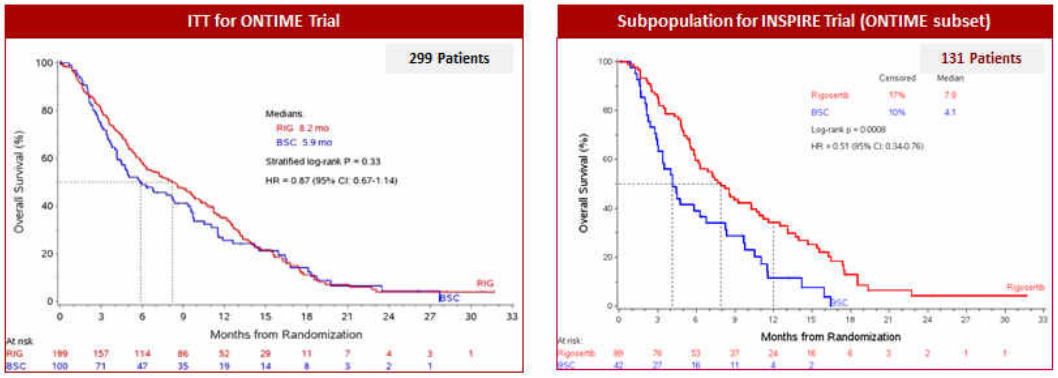
within the first nine cycles of initiation of HMA treatment. The trial initially enrolls approximately 225 patients randomized at a 2:1 ratio into two treatment arms: IV rigosertib plus Best Supportive Care versus Physician's Choice plus Best Supportive Care.

Beginning of this year, Onconova decided to move forward with the Phase III INSPIRE pivotal trial following a very promising interim analysis. The DMC recommended continuation of the trial with a one-time expansion in enrollment, using a pre-planned sample size re-estimation, consistent with the Statistical Analysis Plan (SAP). The INSPIRE pivotal trial is studying intravenously-administered (IV) rigosertib in patients with higher-risk myelodysplastic syndromes (MDS) who have progressed on, failed to respond to, or relapsed after prior hypomethylating agent (HMA) therapy. The Company remains blinded to the interim analysis results. The expanded INSPIRE study will continue to enroll eligible patients based on the current trial design of the overall ITT population and will increase enrollment by adding 135 patients to the original target to reach a total enrollment of 360 patients, with the aim of increasing the power of the trial. Currently, the INSPIRE study is active at approximately 175 trial sites in 22 countries across four continents, and has enrolled more than 170 patients. In Japan, patients have been enrolled to this study by SymBio Pharmaceuticals, its collaboration partner for Japan and Korea. Onconova believes that this trial is the most advanced study for a new therapeutic agent in this indication, and there are no FDA approved therapies specifically for MDS patients after failure of front-line HMAs. Top line results are to be performed after 288 events which can be achieved in 2019H1, concurrent with enrollment completion. The company expects that more than 70% of the patients in the trial are part of the very high risk subgroup.

Parameter	ONTIME Trial	INSPIRE Trial
Total patients	299(270*)	225
Sites	79+	167
Geography	U.S. and EU (6 countries)	U.S., EU, Japan, Israel, Australia (>20 countries)
Indication	Post-HMA HR-MDS	Post-HMA HR-MDS
Key Eligibility Criteria		
Age	No upper limit	< 82 years**
Duration of HMA therapy	No restriction	≤ 9 months and/or ≤ 9 cycles over 12 months**
Time after HMA therapy	≤ 24 months	≤ 6 months
Efficacy Analysis		
Primary endpoint	Overall Survival	Overall survival
Basis for approval	ITT analysis	ITT *or* IPSS-R VHR subgroup
Interim look	No	Yes

*Original trial was for 270 patients; over-enrollment driven by site interest and patient need
+Most productive site (MD Anderson) provided ~15% of total enrollment; enrolled first patient for INSPIRE
** as per amendment 2 (age) or pending amendment 3 (9 cycles over 12 months rather than 9 months, but including 9 months)

Data from ONTIME paper* published in *Lancet Oncology*



In June 2017, Onconova presented a poster at ASCO focusing on "Further Rationale for Rigosertib in a Second-line HR-MDS Setting." Bone marrow response was evaluated as a surrogate for survival in this trial of 64 patients who had failed hypomethylating agents. 22% of these patients achieved marrow complete response (mCR) and 47% of patients achieved disease stabilization.

Oral Rigosertib in combination with Azacitidine as first line therapy in HR-MDS

Onconova is also developing an oral version of rigosertib as a first line treatment in HR-MDS patients in combination with azacitidine. In 2015, Azacitidine was approved in Europe as a single agent therapy for elderly AML patients, as many members of this population cannot endure commonly used intensive chemotherapy. This approval provides a clear regulatory path for combination studies in elderly AML. While the continuous infusion (CI) schedule is acceptable in the higher-risk MDS population, especially for second-line patients, such a schedule would not be favoured in less advanced disease settings such as lower-risk MDS and most solid tumours. For this reason, Onconova has also developed an oral formulation of rigosertib.

Oral rigosertib has been developed as a single agent and in combination with azacitidine. Previous studies have demonstrated that Low-Risk (LR) MDS patients with intermittent oral rigosertib treatment at a dose of 560 mg BID show a transfusion independence rate (TI), as defined by the IWG 2006 criteria, of 44%[1]. Oral rigosertib in combination with AZA is being studied in patients with Higher-risk (HR) MDS. Initial results of the Phase II study with oral rigosertib (840 mg /day 3 out of 4 weeks) in combination with azacitidine in patients with MDS demonstrated an overall response rate of 76%; 62% in patients following hypomethylating agent (HMA) failure; and 85% in HMA naïve patients[2]. In both single agent and combination studies, oral rigosertib has been associated with hematuria in a subset of patients which has been shown to be dose and administration scheme dependent[3].The results reported here are from a dose exploration study in HR MDS patients with an increased oral rigosertib dose (1120 mg/day 3 out of 4 weeks) and focus on the impact of risk-mitigation strategies in minimizing the incidence of urinary adverse events (UAEs); including hematuria. The mitigation strategies included prescribing the second dose of rigosertib earlier in the day and encouraging bladder emptying at bedtime.

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1 Raza,et al, Blood 2017 130:1689

2 Navada et al, EHA, 2017

3 Garcia-Manero G,Blood 2016 128:2011

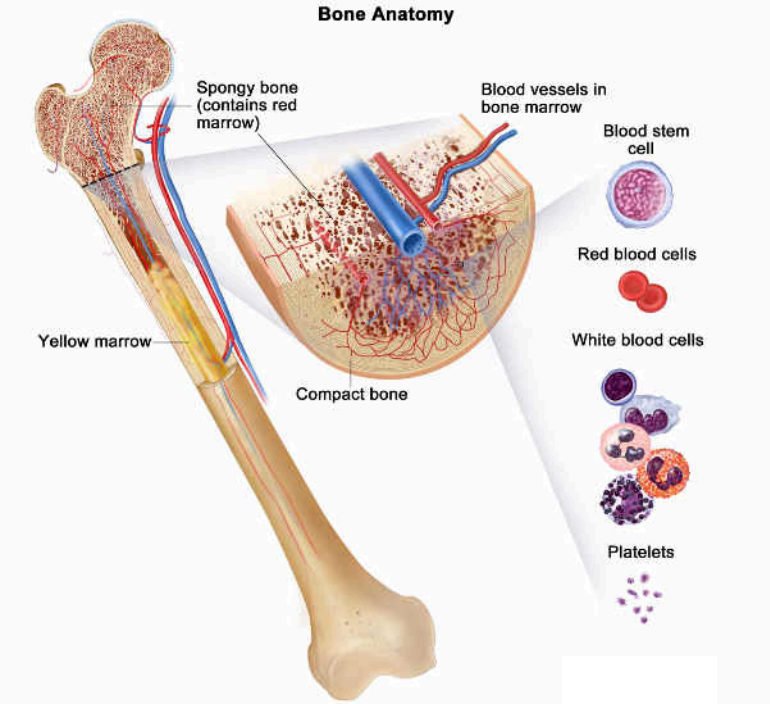
The reported incidence of hematuria of any grade with single agent azacitidine is 6.3%, including 2.3% grade 3 and 4 events (per product insert). In the combination trial of oral rigosertib (total dose of 840 mg/day 3 out of 4 weeks) and azacitidine, the incidence of hematuria was 48%, with grade 3 or grade 4 AEs of 12%. In the new study, in 37 patients studied with oral rigosertib (total dose of 1120 mg/day 3 out of 4 weeks) and azacitidine employing prophylactic risk-mitigating strategies to minimize hematuria, a significantly lower incidence of grade 1 & 2 hematuria (11%), and no grade 3 or 4 hematuria have been seen to date.

At the EHA in Madrid, Spain in June 2017, the company presented data demonstrating responses of oral rigosertib with azacitidine in AML and MDS, as well as oral rigosertib as a single agent. Eight AML patients were evaluable for response, with an overall response rate (ORR) of 37.5%, and responses in both secondary and refractory AML. Two additional patients had stable disease (25%). Responses were durable, with the longest response in AML approaching one year. Among 33 evaluable MDS patients, ORR was 76%. Complete remission (CR) in eight (24%), concurrent marrow CR (mCR) and hematologic improvement (HI) in 10 (30%), mCR alone in six (18%), and HI alone in 1 (3%). ORR was 85% in hypomethylating agent (HMA) naïve patients and 62% in HMA resistant patients.

Following the receipt of the final minutes from the End-of-Phase II discussion with the FDA in 2016Q3, a Scientific Advice process was initiated with the EMA and was completed in July 2017. Based on this feedback, the company is designing a Phase III protocol for a 1:1 randomized controlled trial of oral rigosertib + azacitidine compared with azacitidine + placebo in first-line patients with HR-MDS. Onconova initiated the FDA Special Protocol Assessment (SPA) process following completion of the ongoing Expansion Phase I/II trial. This expansion phase was designed to enrol up to approximately 40 patients. The key objectives are to optimize dosing and schedule of administration of oral rigosertib in combination with azacitidine.

High Risk Myelodysplastic Syndromes (MDS)

Myelodysplastic syndromes (MDS) are a group of cancers in which immature blood cells in the bone marrow do not mature or become healthy blood cells. In a healthy person, the bone marrow makes blood stem cells (immature cells) that become mature blood cells over time.

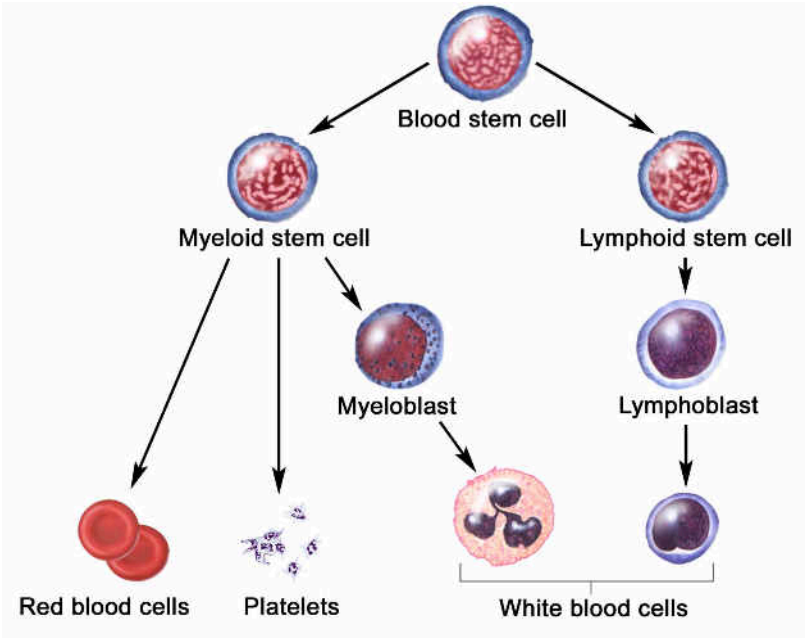


A blood stem cell may become a lymphoid stem cell or a myeloid stem cell. A myeloid stem cell becomes one of three types of mature blood cells:

- Red blood cells that carry oxygen and other substances to all tissues of the body.
- Platelets that form blood clots to stop bleeding.
- White blood cells that fight infection and disease.

In a patient with a myelodysplastic syndrome, the blood stem cells (immature cells) are ineffective in becoming more mature red blood cells, white blood cells, or platelets in the bone marrow and

eventually released into the blood. These immature blood cells, called blasts, do not mature in the way they should. These blasts are assumed to interfere with the bone marrow's ability to produce healthy white blood cells, red blood cells, and platelets to form in the bone marrow. When there are fewer healthy blood cells, infection, anemia, or easier bleeding may occur. Thus, many patients with MDS require frequent blood transfusions. In most cases, the disease worsens and the patient develops progressive bone marrow failure. In advanced stages of the disease, immature blood cells, or blasts, leave the bone marrow and enter the blood stream, leading to acute myelogenous leukemia ("AML"), which occurs in approximately one-third of patients with MDS.



With a few exceptions, the exact causes of MDS are unknown. Some evidence suggests that certain people are born with a tendency to develop MDS. This tendency can be thought of as a switch that is triggered by an external factor. If the external factor cannot be identified, then the disease

is referred to as "primary MDS". Radiation and chemotherapy for cancer are among the known triggers for the development of MDS. Patients who take chemotherapy drugs or who receive radiation therapy for potentially curable cancers, such as breast or testicular cancers, Hodgkin's disease and non-Hodgkin's lymphoma, are at risk of developing MDS for up to 10 years following treatment. MDS that develops after use of cancer chemotherapy or radiation is called "secondary MDS" and is usually associated with multiple chromosome abnormalities in cells in the bone marrow. This type of MDS often develops rapidly into AML. The most common symptom is anaemia, which if severe would require blood transfusion. Other symptoms are also haematopoiesis related, including neutropenia (low neutrophil count), thrombocytopenia (low platelet count) and the consequential symptoms of infection or bleeding.

Myelodysplastic syndrome (MDS) is difficult to treat. Although the only curative treatment option is allogeneic bone marrow transplant, most patients with MDS are older and not appropriate candidates for this approach. Therefore, novel strategies are needed. The prognosis and treatment for MDS vary depending on the patient's International Prognostic Scoring System (IPSS) score. Patients with a low/intermediate-1 risk score (IPSS 0-1), who may live with their disease for a number of years, have been the focus of many of the new biological, targeted therapies. Patients with higher scores (intermediate-2 and high risk; IPSS ≥ 1.5) are at higher risk of transformation to acute myelogenous leukemia (AML) and have been the focus of more intensive therapies and novel chemotherapeutic agents. Most patients with high-risk disease die from their disease within 1 year of diagnosis.

Hypomethylating agents (HMAs) have been a major focus of clinical research over the last few years and have been evaluated in patients with advanced HR-MDS. Most higher-risk and some lower-risk MDS patients in the United States are treated with azacitidine or decitabine, the two approved HMAs for treatment of MDS. A provider of information services and technology for the healthcare industry estimates that in the year ended June 2012, approximately 12,500 MDS patients in the United States received treatment with HMAs.

A significant number of higher-risk MDS patients fail or cannot tolerate treatment with azacitidine or decitabine, which represent the current standard of care for higher-risk MDS patients, and almost all patients who initially respond to therapy eventually progress. Median survival time of higher-risk MDS patients who have failed HMAs is less than one year. Accordingly, we believe that a new therapy that would extend survival in these patients would represent a major contribution in the treatment of MDS.

HMAs are believed to inhibit the methylation of DNA. Methylation is a biochemical process involving the addition of a methyl group to DNA and plays an important role in gene expression during cell division and differentiation. Hypomethylation may also restore normal function to genes that are critical for differentiation and proliferation. By contrast, rigosertib is designed to block multiple oncogenic pathways through a RAS mimetic mechanism and/or interfering with RAS function. Because we believe rigosertib has a mechanism of action that is different from HMAs, it may be active in patients who have failed treatment with those drugs. Furthermore, rigosertib's distinct potential mechanism of action has been shown to combine well with approved HMAs and preclinical studies testing the combination of rigosertib with azacitidine have demonstrated synergy between the two agents. Based on these studies and our current understanding of the potential mechanism of action of rigosertib, we believe that rigosertib also has the potential to be developed in combination with azacitidine for first line or second line MDS patients and for patients with AML who are not candidates for standard induction chemotherapy; or second line AML who have failed induction chemotherapy.

Financials

Recently, Onconova published its 2017FY figures which were in line with our expectations. Net loss came in at USD 24.1 million compared to USD 19.7 million in 2016. Expenses for R&D amounted to USD 19.1 million (2016: USD 20.1 million). By the end of 2017, cash and cash equivalents totaled USD 4.0 million. In February, the company announced the closing of a USD 10 million underwritten public offering of 9,947,500 shares of common stock or common stock equivalents and warrants to purchase an aggregate of 994,750 shares of Onconova's Series A convertible preferred stock, including the exercise in full of the underwriter's option to purchase additional securities, at the public offering price of USD 1.01 per share and accompanying Preferred Stock Warrant. Onconova also issued to the underwriter a preferred stock warrant to purchase 49,737.5 shares of Series A convertible preferred stock. In April the company announced the pricing of an underwritten public offering of 67,647,058 shares of its common stock and warrants to purchase up to an aggregate of 1,691,176.450 shares of Onconova's Series B convertible preferred stock at a public offering price of USD 0.425 per share and accompanying Preferred Stock Warrant. The gross proceeds of the Offering amounted to approximately USD 28.75 million. Based on the Company's cash burn for 2017 and its current projections, Onconova expects that cash and cash equivalents will be sufficient to fund ongoing trials and operations into 2019Q4.

Profit & Loss Statement

USD mln	2015A	2016A	2017A
Revenues	11.456	5.546	0.787
R&D Costs	25.895	20.071	19.119
SG&A	9.533	9.178	7.405
Operating Profit/(Loss)	(23.972)	(23.703)	(25.737)
Income Taxes	0	0	0
Net Profit/(Loss)	(24.023)	(19.667)	(24.092)

Consolidated statement of cash flows

USD mln	Dec 31st 2015A (12 months)	Dec 31st 2016A (12 months)	Dec 31st 2017A (12 months)
Cash flow from operating activities	(31.238)	(15.813)	(23.820)
Cash flow from investing activities	-	-	-
Cash flow from financing activities	7.464	17.423	6.360
Cash and cash equivalents at beginning of the period	43.582	19.849	21.450
Net change in cash and cash equivalents	(23.783)	1.601	(18.000)

Valuation

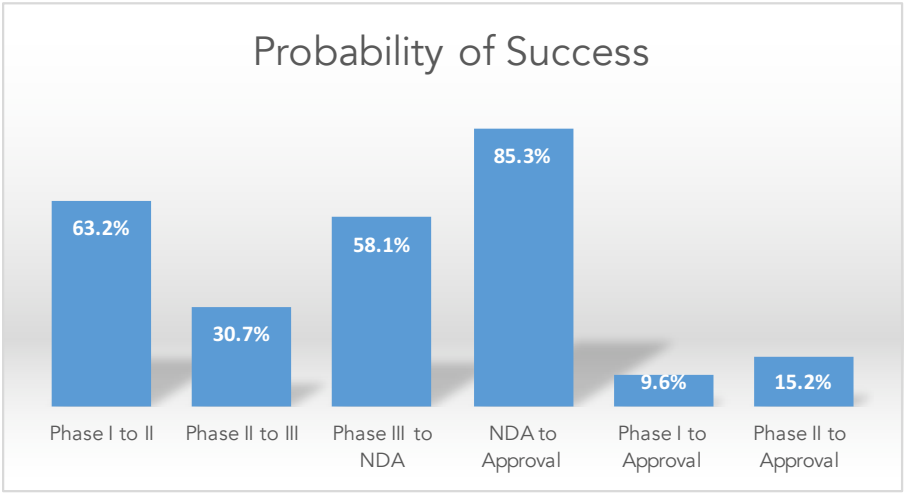
We have increased our valuation on Onconova to USD 267 million from USD 178 million due to the fact that we have increased the LOA for Onconova's lead product rigosertib and lowered the discount rate from 12% to 11%. At this moment we do not address value to other programs in Onconova's pipeline. This is a potential upside for the company. Due to the increased number of outstanding shares, the value per share will be lowered to USD 3.40.

Phase Success and Likelihood of Approval (LOA)

In estimating a value for the clinical programs with rigosertib, we made use of several studies that were done on the clinical development success rates for investigational drugs to measure success rates for investigational drugs. We analyzed individual drug program phase transitions from January 1, 2006 to December 31, 2015. For the ten years studied, 9,985 transitions in the Biomedtracker database were analyzed. A phase transition is the movement out of a clinical phase – for example, advancing from Phase I to Phase II development, or being suspended after completion of Phase I development. These transitions occurred in 7,455 clinical drug development programs, across 1,103 companies (both large and small), making this the largest study of its kind. With this broad set of data, we aimed to capture the diversity in drug development across levels of novelty, molecular modalities, and disease indications. Only company-sponsored, FDA registration-enabling development programs were considered; investigator-sponsored studies were excluded from this analysis.

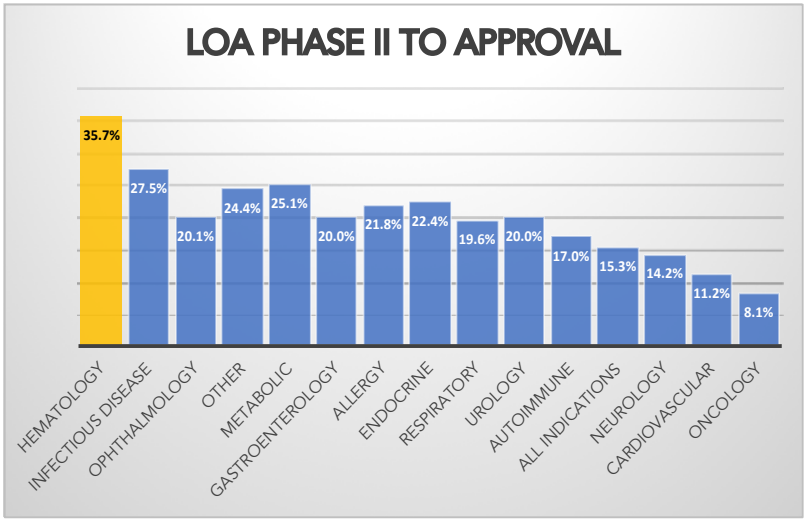
The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted for safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in this report. Phase I success rates may also benefit from delayed reporting bias, as some larger companies may not deem failed Phase I programs as material and thereby not report them in the public domain. The Phase II transition success rate (30.7%, n=3,862) was substantially lower

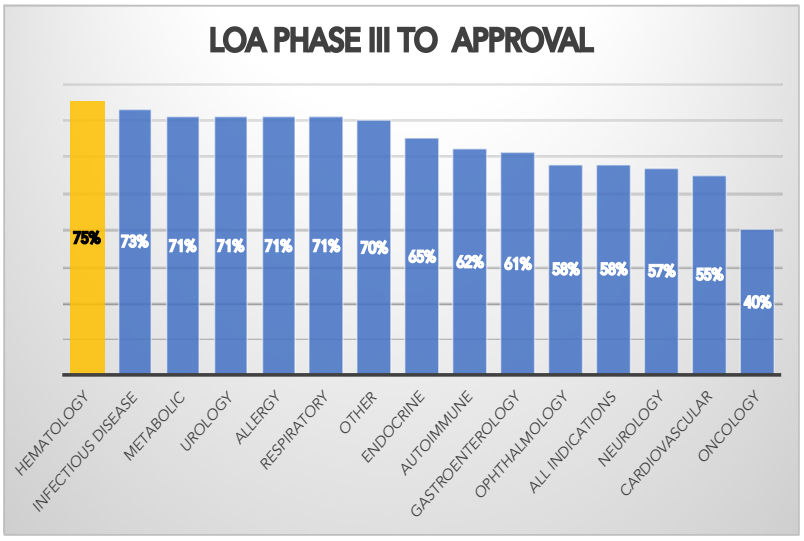
than Phase I, and the lowest of the four phases studied. As this is generally the first stage where proof-of-concept is deliberately tested in human subjects, Phase II consistently had the lowest success rate of all phases. This is also the point in development where industry must decide whether to pursue the large, expensive Phase III studies and may decide to terminate development for multiple reasons including commercial viability. The second-lowest phase transition success rate was found in Phase III (58.1%, n=1,491). This is significant as most company-sponsored Phase III trials are the longest and most expensive trials to conduct. The probability of FDA approval after submitting a New Drug Application (NDA) or Biologic License Application (BLA), taking into account re-submissions, was 85.3% (n=1,050). Multiplying these individual phase components to obtain the compound probability of progressing from Phase I to U.S. FDA approval (LOA) reveals that only 9.6% (n=9,985) of drug development programs successfully make it to market (see graph below)



Source: BIO Industry Analysis

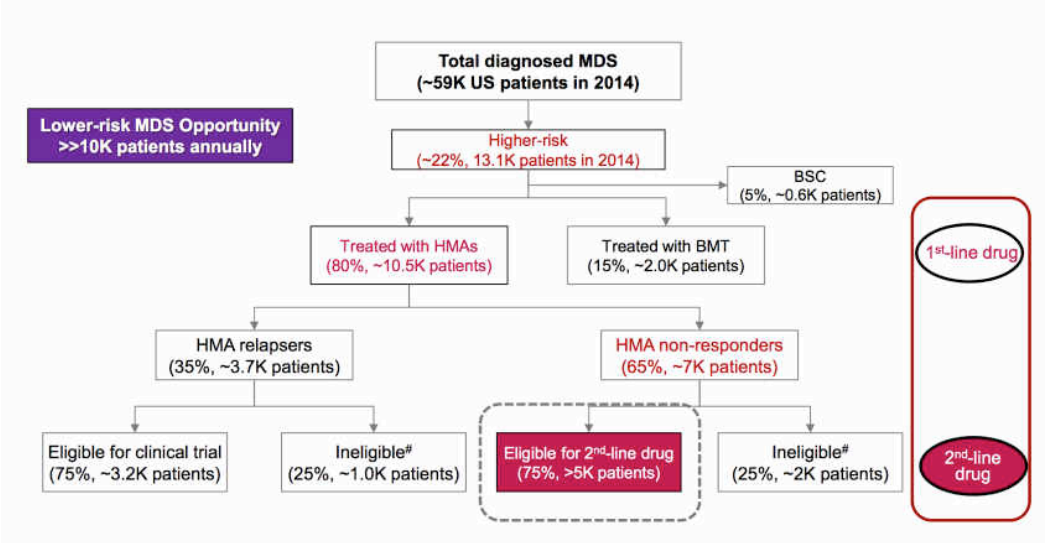
Major disease areas were segmented according to the convention used by Biomedtracker, and categorized 21 major diseases and 558 indications for the 2006-2015 timeframe. As can be seen in the graphs below, there is a wide range of Likelihood of Approval (LOA) from Phase I, II and III.





Valuation rigosertib in HR-MDS (IV) and LR-MDS (oral)

In estimating a value for rigosertib in MDS, we took into account potential markets in the US, Europe and Japan with a total number of patients of 60,000 in the US, 105,000 in Europe and 10,000 in Japan, with a market launch in the US in 2019, 2020 in Europe and 2021 in Japan. For the second line therapy (HR-MDS IV) we calculate the number of eligible patients to be 9%. (23% x 80% x 65% x 75%, see graph below), whereas for first line oral therapy in HR-MDS we calculate the number of eligible patients to be 18%. We calculate a Risk adjusted Discount Rate of 11%. Annual pricing per treatment is set at USD 60,000 which is comparable with pricing of competitive drugs like Vidaza. In Europe we calculate lower price of USD 40,000 due to lower reimbursement. For the first line oral therapy we have worked annual pricing of USD 40,000 and USD 28,000 as this is part of a combination therapy. Although we believe that Onconova will potentially partner its program in MDS with a large pharmaceutical, in our model we have calculated its value by marketing the drug independently. In Japan we go with a royalty of 20% based on its partnership with SymBio. We estimate that a peak market share of 15-20% is possible. In line with the report of BioMedTracker (see hematological disorders, we used a LOA of 35% and 75% for Phase II and Phase III respectively. This leads to a total valuation of USD 267 million or USD 3.30 per share.



Source: Onconova

Valuation rigosertib HR-MDS IV US Market

Year	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	
No of patients US (yoy growth 3.5% as of 2015)	76,337	79,009	81,774	84,636	87,598	90,664	93,837	97,122	100,521	104,039	
No of patients eligible (9%)	6,183	6,400	6,624	6,856	7,095	7,344	7,601	7,867	8,142	8,427	
Penetration	1.8%	3.6%	5.4%	8.1%	10.8%	12.6%	14.4%	16.2%	17.1%	18.0%	
Total Revenues (USD m)	6.9	14.5	22.8	35.7	49.8	60.7	72.5	85.3	94.1	103.6	
Margin 50%	3.5	7.3	11.4	17.9	24.9	30.4	36.3	42.7	47.1	51.8	
WACC 11%	0.73	0.66	0.59	0.53	0.48	0.43	0.39	0.35	0.32	0.29	
NPV (million)	2.5	4.8	6.8	9.5	12.0	13.2	14.2	15.0	14.9	14.8	
Total NPV (million)											**107.7**
LOA 75%											**80.8**

Valuation rigosertib HR-MDS IV EU Market

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	
No of patients EU (yoy growth 3.5% as of 2015)	138,265	143,104	148,113	153,297	158,662	164,215	169,963	175,912	182,069	188,441	
No of patients eligible (9%)	11,199	11,591	11,997	12,417	12,852	13,301	13,767	14,249	14,748	15,264	
Penetration	1.8%	3.6%	5.4%	8.1%	10.8%	12.6%	14.4%	16.2%	17.1%	18.0%	
Total Revenues (USD m)	6.4	13.3	20.8	32.7	45.5	55.5	66.4	78.0	86.1	94.7	
Margin 50%	3.2	6.6	10.4	16.3	22.8	27.8	33.2	39.0	43.1	47.4	
WACC 11%	0.66	0.59	0.53	0.48	0.43	0.39	0.35	0.32	0.29	0.26	
NPV (million)	2.1	3.9	5.6	7.9	9.9	10.9	11.7	12.4	12.3	12.2	
Total NPV (million)											**88.8**
LOA 75%											**66.6**

Valuation rigosertib HR-MDS IV Japanese Market

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	
No of patients Japan (yoy growth 3.5% as of 2015)	13,140	13,600	14,076	14,568	15,078	15,606	16,152	16,717	17,303	17,908	
No of patients eligible (9%)	1,064	1,102	1,140	1,180	1,221	1,264	1,308	1,354	1,402	1,451	
Penetration	1.8%	3.6%	5.4%	8.1%	10.8%	12.6%	14.4%	16.2%	17.1%	18.0%	
Total Revenues (USD m)	1.3	2.7	4.2	6.6	9.2	11.3	13.4	15.8	17.5	19.2	
Royalty Symbio 20%	0.0	0.3	0.9	1.3	1.8	2.2	2.7	3.2	3.5	3.8	
Milestone payment SymBio	8.0	5.0									
WACC 11%	0.57	0.51	0.45	0.40	0.36	0.32	0.29	0.26	0.23	0.20	
NPV (million)	5.3	3.1	0.3	0.4	0.6	0.7	0.8	0.9	0.9	0.9	
Total NPV (million)											**14.7**

Valuation rigosertib HR-MDS first line oral US Market

Year	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	
No of patients US (yoy growth 3.5% as of 2015)	13,140	13,600	14,076	14,568	15,078	15,606	16,152	16,717	17,303	17,908	
No of patients eligible (18%)	14,222	14,719	15,234	15,768	16,320	16,891	17,482	18,094	18,727	19,382	
Penetration	1.8%	3.6%	5.4%	8.1%	10.8%	12.6%	14.4%	16.2%	17.1%	18.0%	
Total Revenues (USD m)	11.2	23.5	36.9	57.8	80.6	98.3	117.4	138.1	152.4	167.7	
Margin 50%	5.6	11.8	18.4	28.9	40.3	49.2	58.7	69.1	76.2	83.8	
WACC 11%	0.59	0.53	0.48	0.43	0.39	0.35	0.32	0.29	0.26	0.23	
NPV (million)	3.3	6.3	8.9	12.5	15.8	17.3	18.6	19.7	19.6	19.5	
Total NPV (million)											**122.1**
LOA 40%											**48.8**

Valuation rigosertib HR-MDS first line oral EU Market

Year	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	
No of patients EU (yoy growth 3.5% as of 2015)	143,104	148,113	153,297	158,662	164,215	169,963	175,912	182,069	188,441	195,036	
No of patients eligible (18%)	25,759	26,660	27,593	28,559	29,559	30,593	31,664	32,772	33,919	35,107	
Penetration	1.80%	3.60%	5.40%	8.10%	10.80%	12.60%	14.40%	16.20%	17.10%	18.00%	
Total Revenues (USD m)	14.4	30.1	47.2	74.1	103.2	125.9	150.4	176.9	195.1	214.7	
Margin 50%	7.2	15.1	23.6	37.0	51.6	62.9	75.2	88.4	97.6	107.4	
WACC 11%	0.53	0.48	0.43	0.39	0.35	0.32	0.29	0.26	0.23	0.21	
NPV (million)	3.9	7.3	10.2	14.5	18.2	20.0	21.5	22.8	22.6	22.4	
Total NPV (million)											**140.9**
LOA 40%											**56.3**

Recent Achievements and Near Term Milestones

In the past 12 months, Onconova has already reached a number of important mile stones that brought the company back on track towards commercialization of its lead candidate:

- Apr/May 2017: Successful secondary raise with proceeds of USD 6 million
- May/June 2017:Presentations at the ASCO, MDS Foundation and EHA conferences
- Jan 2018: Positive interim analysis Phase III INSPIRE Trial
- Jan 2018: Launch of "RASopathies" rare-disease collaboration with the National Cancer Institute (NCI), academic investigators and patient advocacy groups
- March 2018: Partnership for Latin America

In the coming 12-18 months we expect a number of important mile stones that can drive the stock price upwards. These are:

- Phase III protocol and Special Protocol Assessment for Rigosertib Combination trial
- Completion enrollment Phase III INSPIRE trial
- Initiation of Phase III oral rigosertib + azacitidine in first line HR-MDS

Competitive Landscape

During examination of comparable companies, we looked at companies that have a focus on hematological diseases particular MDS. The table below provides an overview of the companies and their specific target. Compared to the competitive landscape, Onconova is clearly at the forefront in MDS.

Overview Drugs in Clinical Development and Approved in MDS

Company	Product	Activity/Target	Stage
Celgene	Vidaza	DNA Methyltransferase (DNMT)	Approved
Otsuka	Dacogen	DNA Methyltransferase (DNMT)	Approved
Celgene	Revlimid	Immune system; Angiogenesis; E3 ubiquitin ligase	Approved
Acceleron Pharma	Luspatercept	Transforming Growth Factor-beta (TGF-beta) Receptor	Phase III
CTI BioPharma	Tosedostat	Aminopeptidase	Phase II/III
Geron	Imetelstat	Telomerase	Phase II/III
Eli Lilly	Galunisertib	Transforming Growth Factor-beta (TGF-beta) Receptor	Phase II/III
Syros Pharma	Tamibarotene	Retinoic acid receptor (RARs)	Phase II
Cyclacel	Sapacitabine	DNA Synthesis	Phase II
Helsinn Healthcare/ MEI Pharma	Parcinostat	Histone Deacetylase (HDAC)	Phase II
Incyte	INCB54828	Fibroblast Growth Factor Receptor (FGFR)	Phase II

Celgene

Celgene Corporation is a biopharmaceutical company focused on the discovery, development, and commercialization of therapies for the treatment of cancer and immune-inflammatory related diseases. The company has two approved products against MDS, Vidaza (Azacitidine) and Revlimid (lenalidomide). Vidaza, is used mainly in the treatment of MDS for which it received approval by the FDA in May, 2004. In two randomized controlled trials comparing azacitidine to supportive treatment, 16% of subjects with MDS who were randomized to receive azacitidine had a complete or partial normalization of blood cell counts and bone marrow morphology, compared to none who received supportive care, and about two-thirds of patients who required blood transfusions

no longer needed them after receiving azacitidine. Revlimid was approved in 2004 for multiple myeloma. Revlimid has also shown efficacy in MDS. It was approved by the FDA on December 27, 2005 for patients with low or intermediate-1 risk MDS with 5q- with or without additional cytogenetic abnormalities. A completed Phase II, multi-centre, single-arm, open-label study evaluated the efficacy and safety of Revlimid monotherapy treatment for achieving haematopoietic improvement in red blood cell (RBC) transfusion dependent subjects with low- or intermediate-1-risk MDS associated with a deletion 5q cytogenetic abnormality. 63.8% of subjects had achieved RBC-transfusion independence accompanied by a median increase of 5.8 g/dL in blood Hgb concentration from baseline to the maximum value during the response period. Major cytogenetic responses were observed in 44.2% and minor cytogenetic responses were observed in 24.2% of the evaluable subjects. Improvements in bone marrow morphology were also observed. The results of this study demonstrate the efficacy of Revlimid for the treatment of subjects with Low- or Intermediate-1-risk MDS and an associated del 5 cytogenetic abnormality. Lenalidomide was approved on June 17, 2013 by the EMA for use in low- or intermediate-1-risk MDS patients who have the deletion 5q cytogenetic abnormality and no other cytogenetic abnormalities, are dependent on red blood cell transfusions, and for whom other treatment options have been found to be insufficient or inadequate.

Otsuka

Otsuka Pharmaceutical Co is a Japanese company and engaged in the manufacturing, distributing, exporting, and importing of pharmaceuticals, clinical testing equipment, medical equipment, food products, cosmetics and other related products. In 2014, Otsuka acquired the rights to Dacogen (Decitabine from Eisai. Dacogen was developed by SuperGen (now Astex Pharmaceuticals, Inc.) as a therapeutic agent for MDS and acute myeloid leukemia (AML) possessing cell differentiation-inducing activity through the inhibition of DNA methylation. U.S.-based MGI Pharma., (acquired by Eisai Inc. in 2008) acquired worldwide rights to develop and market Dacogen from SuperGen, Inc. and sublicensed worldwide rights (except for the U.S., Canada and Mexico) to Janssen

Pharmaceutical. Dacogen was approved for sale in the U.S. and is currently indicated for treatment for MDS including previously treated and untreated de novo and secondary MDS of all hematological subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and for intermediate-1, imtermediate-2, and high-risk MDS. Janssen is responsible for R&D and commercialization of Dacogen in the EU (where it is approved for acute myeloid leukemia (AML)) and in other specified countries (where it is approved for AML and/or MDS).

Acceleron Pharma

Acceleron is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative therapeutics to treat serious and rare diseases. lead therapeutic candidate, luspatercept, is being evaluated in Phase III studies for the treatment of the hematologic diseases, MDS) and beta-thalassemia under a global partnership with Celgene. Luspatercept is a modified activin receptor type IIB fusion protein that acts as a ligand trap for members in the Transforming Growth Factor-Beta (TGF-beta) superfamily involved in the late stages of erythropoiesis (red blood cell production). Luspatercept regulates late-stage erythrocyte (red blood cell) precursor cell differentiation and maturation. This mechanism of action is distinct from that of erythropoietin (EPO), which stimulates the proliferation of early-stage erythrocyte precursor cells. Acceleron and Celgene are jointly developing luspatercept as part of a global collaboration. Acceleron and Celgene are enrolling Phase III clinical trials that are designed to evaluate the safety and efficacy of luspatercept in patients with MDS (the "MEDALIST" study) and in patients with beta-thalassemia (the "BELIEVE" study).

Geron

Geron is a clinical stage biopharmaceutical company focused on the collaborative development of a first-in-class telomerase inhibitor, imetelstat, in hematologic myeloid malignancies. Imetelstat is

a specific inhibitor of telomerase that is administered by intravenous infusion. This first-in-class compound, discovered by Geron, is a specially designed and modified short oligonucleotide, which targets and binds directly with high affinity to the active site of telomerase. On November 13, 2014, Geron entered into an exclusive worldwide license and collaboration agreement with Janssen Biotech, to develop and commercialize imetelstat for oncology, including hematologic myeloid malignancies, and all other human therapeutics uses. Under the terms of the agreement, Geron received an upfront payment of USD 35 million and is eligible to receive additional payments up to a potential total of USD 900 million for the achievement of development, regulatory and commercial milestones, as well as royalties on worldwide net sales. Imetelstat is currently in a clinical development program called IMerge. IMerge is a Phase II/III clinical trial evaluating imetelstat in transfusion dependent patients with Low or Intermediate-1 risk MDS who have relapsed after or are refractory to prior treatment with an erythropoiesis stimulating agent (ESA). The clinical trial is in two parts: Part 1 is a Phase II, open-label, single-arm design in approximately 30 patients and Part 2 is a Phase III, randomized, double-blind, placebo-controlled design in approximately 170 patients. The primary efficacy endpoint is the rate of red blood cell transfusion-independence lasting at least 8 weeks. Part 1 of the trial is fully enrolled.

Cyclacel

Cyclacel is a biopharmaceutical company developing oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious diseases. Sapacitabine, Cyclacel's most advanced product candidate, is the subject of SEAMLESS, a Phase III trial, which has completed enrollment and is being conducted under an SPA with the U.S. FDA as front-line treatment for acute myeloid leukemia (AML) in the elderly, and other indications, including MDS. Sapacitabine is currently being evaluated in Phase II trials in elderly patients with MDS. Sapacitabine is an oral nucleoside analogue prodrug that acts through a novel mechanism. The compound interferes with DNA synthesis by introducing single-strand DNA breaks leading to arrest of the cell division cycle at G2 phase and development of double-strand DNA breaks.

Syros Pharmaceuticals

Syros is focused on discovering and developing treatments for cancer and immune-mediated diseases. It is building a pipeline of gene control medicines, including two lead programs SY-1425, a potent and selective RARa agonist that is initially developing for genomically defined subsets of patients with relapsed or refractory acute myeloid leukemia (AML) and relapsed high-risk MDS, and SY-1365, a selective CDK7 inhibitor, which are initially developing in acute leukemia. SY-1425 is currently in a Phase II trial. This ongoing Phase II clinical trial of SY-1425 is a biomarker-directed multi-center, open-label trial exploring safety and efficacy in relapsed or refractory AML and high-risk MDS patients, newly diagnosed AML patients 60 years of age or older who are not suitable candidates for standard chemotherapy and low-risk transfusion-dependent MDS patients with high levels of *RARA* gene expression. The primary endpoint is overall response rate for AML and high-risk MDS patients and red blood cell transfusion-independence rate for low-risk MDS patients. Other endpoints include assessment of pharmacodynamic markers, duration of response, safety and tolerability, and overall and progression-free survival.

Helsinn Pharma/Mei Pharma

Helsinn is a privately owned cancer supportive care pharmaceutical group with an extensive portfolio of marketed products and a broad development pipeline. MEI Pharma, Inc. (Nasdaq: MEIP) is a San Diego-based oncology company focused on the clinical development of novel therapies for cancer. The Company's lead drug candidate is Pracinostat, a potential best-in-class, oral HDAC inhibitor that that has been granted Breakthrough Therapy Designation from the FDA in combination with azacitidine for the treatment of patients with newly diagnosed AML who are ≥75 years of age or unfit for intensive chemotherapy. In May 2016 both companies entered into a partnership for pracinostat. The deal provides the complementary resources from both organizations to rapidly advance Pracinostat into Phase III clinical development and expand into additional indications, including high-risk MDS. Under the terms of the agreement, Helsinn got exclusive worldwide rights, including manufacturing and commercialization rights, and will be

responsible for funding the global development of Pracinostat. As compensation for such grant of rights, MEI Pharma received near-term payments of USD 20 million, comprised of a USD 15 million upfront payment and a USD 5 million payment upon dosing of the first patient in the upcoming Phase III study of Pracinostat in newly diagnosed AML patients unfit to receive induction therapy. In addition, MEI Pharma will be eligible to receive up to USD 444 million in potential development, regulatory and sales-based milestone payments, along with additional tiered royalty payments in selected territories. As part of the development and commercialization agreement, Helsinn and MEI Pharma will also collaborate to explore an optimal dosing regimen of Pracinostat in combination with azacitidine for the treatment of high-risk MDS. This clinical study commenced in August 2017. The randomized, double-blind, placebo-controlled study will enroll approximately 500 eligible patients worldwide. Patients will be randomized 1:1 to receive pracinostat or placebo with azacitidine as background therapy. The primary endpoint of the study is overall survival. Secondary endpoints include, among others, morphologic complete remission (CR) rate, event free survival (EFS) and duration of CR.

Rafael Pharmaceuticals

Rafael Pharmaceuticals, Inc. is a privately held, clinical-stage, oncology-focused pharmaceutical company committed to the development and commercialization of therapies that exploit the metabolic differences between normal cells and cancer cells. Cornerstone's first-in-class clinical lead compound, CPI-613 is being evaluated in multiple Phase I, I/II, and II clinical studies. The U.S. FDA has designated CPI-613 an orphan drug for the treatment of acute myeloid leukemia (AML), pancreatic cancer and myelodysplastic syndromes (MDS). The FDA has given Rafael approval to initiate pivotal clinical trials in acute myeloid leukemia (AML), and has designated CPI-613 an orphan drug for the treatment of pancreatic cancer, AML, and myelodysplastic syndromes (MDS).

Analyst: Marcel Wijma MSc
Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.

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