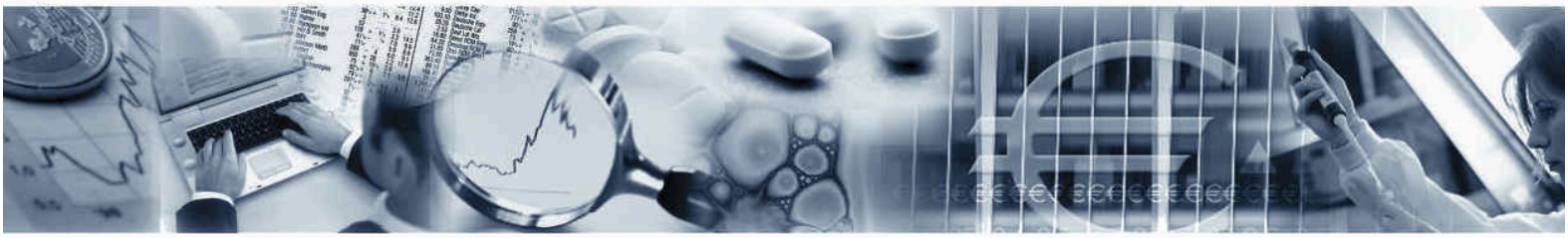

Update Report

Onconova Therapeutics Inc. (ONTX)

Ongoing Positive Progress Rigosertib

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Name:	**Onconova Therapeutics**
Country:	**USA**
Price:	**USD 1.63**
ISIN Code:	**US68232V3069**
Reuters Code:	**ONTX**
Market Cap (USD m):	**16.0**
EV (USD m):	**1.0**
Cash & cash eq. (USD m):	**15.0**
Shares outstanding (m):	**9.9**
Volume:	**118,413**
Free float:	**79%**
52-week Range:	**1.53-3.88**

USD m	2015A	2016A	2017E
Total Revenues	11.456	5.546	1.500
Net (Loss)/Profit	(23.979)	(19.667)	(22.000)
Net loss per share (pence)	(10.54)	(4.44)	(2.22)
R&D costs	25.895	20.071	20.000
Cash increase/(decrease)	(23.783)	1.601	(16.000)
Cash and marketable sec.	19.799	21.400	5.000

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. With its proprietary chemistry platform, the company has built a pipeline of targeted anti-cancer drugs based on specific cellular pathways while simultaneously causing minimal damage to normal cells. 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 in 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.

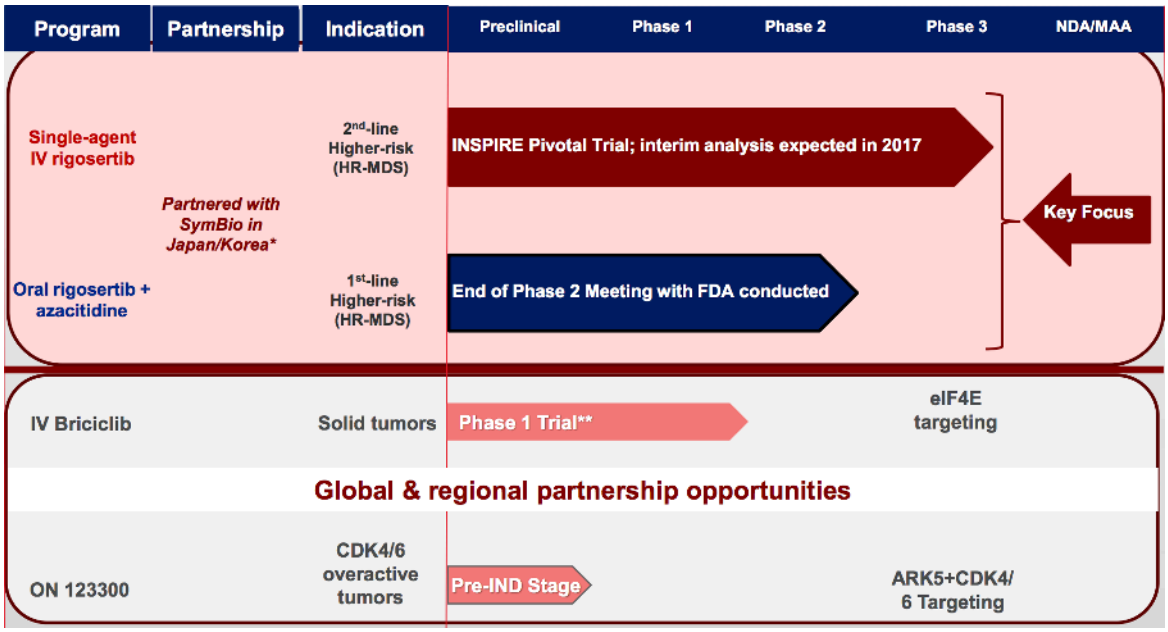
- During April and May, the company successfully raised USD 6.0 million from a public offering. The Company's cash position after the second quarter of 2017 is USD 15.0 million. With a current market cap of USD 16.0 million, that adds up to a EV of USD 1.0 million. With a current monthly cash burn of USD 1.5-1.7 million, we believe that this should be sufficient to carry out the further development of its pipeline in the coming 12 months. Furthermore, we expect the company is able to sign a lucrative partnering deal following interim data of 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 1.63. We feel that the company's current total value should be USD 139 million, or USD 14 per share taking into account a higher LOA and potential partnerships with rigosertib. This represents a substantial upside from the current share price**.

Update Pipeline: Focus on Rigosertib

Below is an overview of Onconova's 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), with interim data expected in 2017Q4. A first line oral version of rigosertib in combination with azacitidine in HR-MDS recently showed positive Phase II data as well and is expected to be in a pivotal phase III trial in 2018. Preparations have already begun.



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 Rigos**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

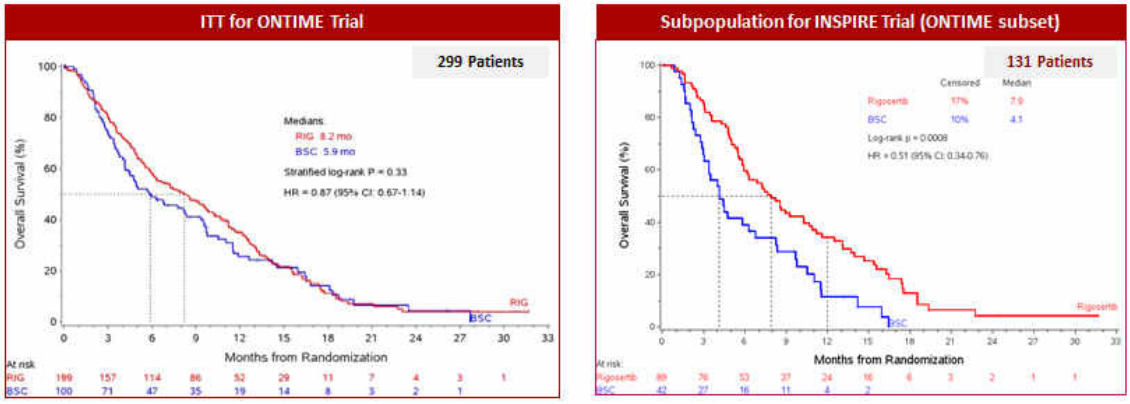
study to assess the efficacy and safety of IV rigosertib in HR-MDS patients under 82 years of age who had progressed on, or failed to respond to, or relapse after previous treatment with HMAs within the first nine cycles of initiation of HMA treatment. The trial currently enrolls approximately 225 patients randomized at a 2:1 ratio into two treatment arms: IV rigosertib plus Best Supportive Care versus Physician's Choice plus Best Supportive Care. The primary endpoint of INSPIRE is overall survival and an interim analysis is anticipated. As of July 31st, in 72 sites in 16 countries enrollment is taking place. The company expects full enrollment in 2018Q1 with topline data in 2018H1. An interim analysis is planned in before year end. This analysis will be triggered after reaching 88 events (deaths). Although it is difficult to accurately forecast the timing of this milestone, based on when Onconova expect to finalize our statistical analysis plan, enrolment statistics, and the company's expectations for survival of the trial population, the interim is expected in 2017Q4. The Statistical Analysis Plan (SAP) for interim and top-line analysis is under review by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

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)

When analyzing the patients in ONTIME that met the HMA treatment duration and age restriction, there was a 7.9-month median OS in the rigosertib arm compared to a 4.1 median OS in the best supportive care arm (p=0.0008). See also the graphs below. If Onconova is able to repeat this result in the INSPIRE trial, it would demonstrate the drug's efficacy and provide a novel therapy for HR MDS patients.

Data from ONTIME paper* published in *Lancet Oncology*



In June, 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.

The current standard of care for higher-risk MDS patients is one of two approved hypomethylating agents (Azacitidine and Decitabine, approved by the FDA in 2004 and 2006). Although these drugs are currently the mainstays in HR-MDS therapy, their overall response rate and duration of benefit is limited to a subset of eligible patients and all responding patients. Therefore, there is an urgent need for developing therapeutic options for newly diagnosed MDS patients.

The 09-08 trial tested oral rigosertib in combination with injectable azacitidine in a dose ranging study (Phase I), followed by an expansion cohort (Phase II) to evaluate the efficacy and safety of the combination. Both 1st-line and 2nd-line HR-MDS patients were included in the study. At the EHA in Madrid, Spain last June, 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.

Earlier, Phase I and Phase II data in first and second-line higher risk (HR)-MDS patients were presented at the 2016 ASH Meeting and updated at the 2017 EHA and MDS Foundation meetings.

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. 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 plans to initiate the FDA Special Protocol Assessment (SPA) process following completion of the ongoing Expansion Phase I/II trial. This expansion phase is designed to enroll up to approximately 40 patients. The key objectives are to optimize dosing and schedule of administration of oral rigosertib in combination with azacitidine. After appropriate amendments were filed with the regulatory agencies, Onconova started the expansion phase of this trial. Four sites are now open in the U.S. and the company plans to activate additional sites in US, Europe and Australia. The first patient was enrolled in April.

A Phase III trial, which is planned to be conducted globally, requires additional financing.

Financials

For the first six months of 2017, total revenues amounted to USD 0.5 million compared to USD 3.7 million in the same period in the previous year. Expenses for the period totaled to USD 13.4 million (2016H1: USD 16.6 million) including R&D expenses of USD 9.5 million. Net loss for this period decreased by USD 1.7 million to USD 10.9 million

At June 30, 2017, the company had cash and cash equivalents of USD 15.0 million, a decrease of USD 6.4 million compared to the end of 2016. In April/May 2017, the company issued a small raise with proceeds of approximately USD 6.0 million. In the last few quarters, the average burn rate is USD 5.6 million per quarter.

Profit & Loss Statement

USD mln	2015A	2016A	2017E
Revenues	11.456	5.546	1.500
R&D Costs	25.895	20.071	20.000
SG&A	9.533	9.178	8.000
Operating Profit/(Loss)	(23.972)	(23.703)	(22.000)
Income Taxes	0	0	0
Net Profit/(Loss)	(24.023)	(19.667)	(22.000)

Consolidated statement of cash flows

USD mln	Dec 31st 2015A (12 months)	Dec 31st 2016A (12 months)	Dec 31st 2017E (12 months)
Cash flow from operating activities	(31.238)	(15.813)	(20.000)
Cash flow from investing activities	-	-	-
Cash flow from financing activities	7.464	17.423	10.000
Cash and cash equivalents at beginning of the period	43.582	19.900	21.400
Net change in cash and cash equivalents	(23.783)	1.601	(18.000)

Valuation

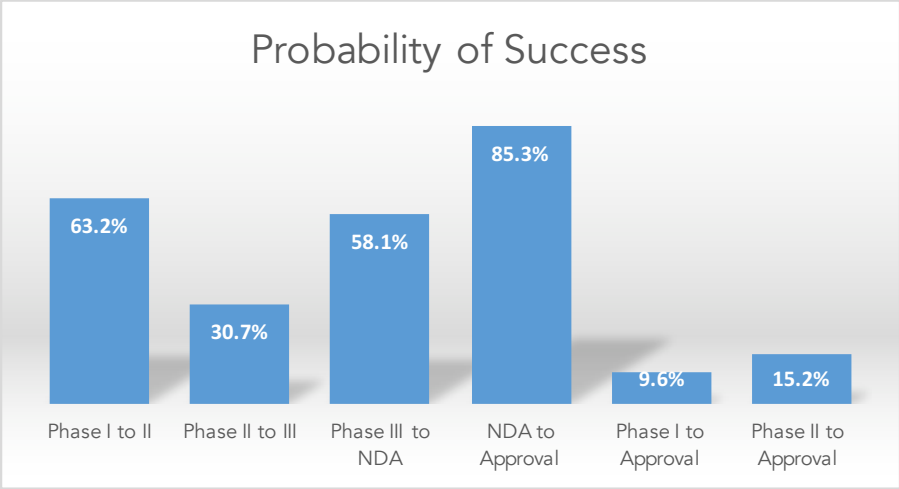
We have increased our valuation on Onconova to USD 139 million from USD 102 million due to the fact that we have increased the LOA for Onconova's lead product rigosertib and lowered the discount rate from 15% to 14%. At this moment we do not address value to other programs in Onconova's pipeline. This is a potential upside for the company. Due to the increased number of outstanding shares, the value per share will be USD 14 instead of USD 15.

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.

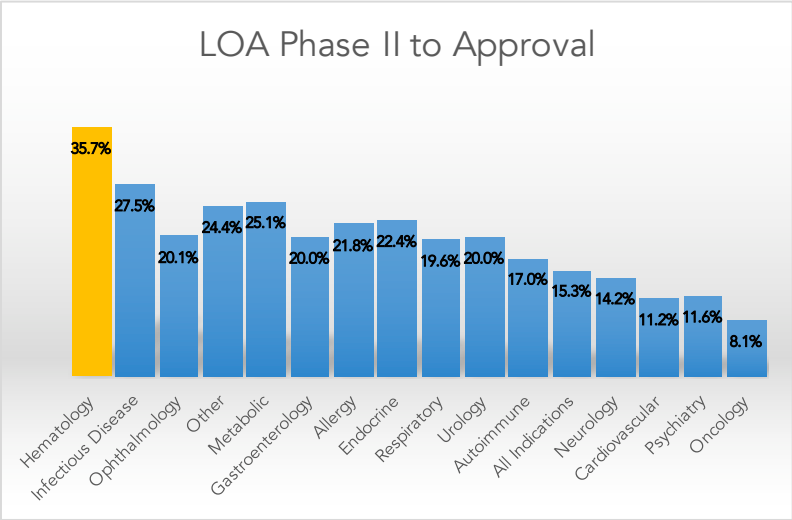
The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted for safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in 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)



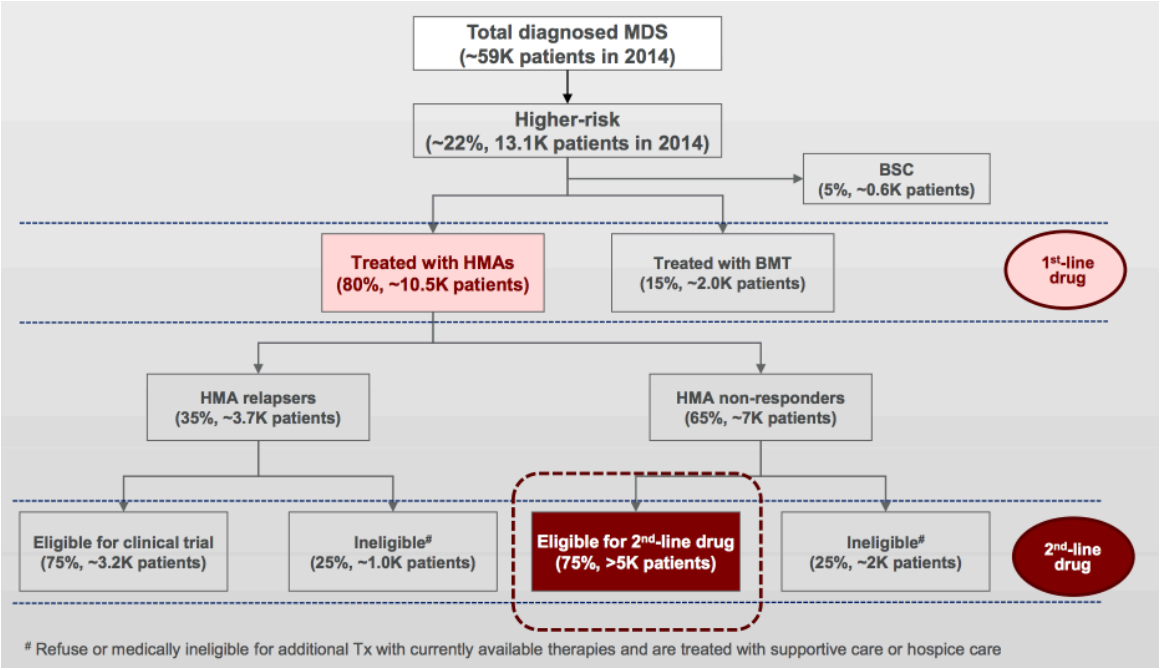
Source: BIO Industry Analysis

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 14%. 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 30,000 due to lower reimbursement. For the first line oral therapy we have worked annual pricing of USD 40,000 and USD 20,000 as this is part of a combination therapy. Although we believe that Onconova will potentially partner its program in in MDS with a large pharmaceutical, in our model we have calculated its value by marketing the drug independently. In Japan with 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 36%. This leads to a total valuation of USD 139 million or USD 14 per share.



Source: Onconova

Valuation rigosertib HR-MDS IV US Market

Year	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	
No of patients US (yoy growth 3.5% as of 2015)	73,755	76,337	79,009	81,774	84,636	87,598	90,664	93,837	97,122	100,521	
No of patients eligible (9%)	5,974	6,183	6,400	6,624	6,856	7,095	7,344	7,601	7,867	8,142	
Penetration	1.5%	3.0%	5.3%	6.8%	8.3%	10.1%	11.7%	12.9%	14.3%	15.0%	
Total Revenues (USD m)	**5.5**	**11.6**	**21.2**	**28.5**	**36.4**	**46.3**	**56.4**	**65.0**	**75.0**	**82.6**	
Margin 50%	2.8	5.8	10.6	14.2	18.2	23.2	28.2	32.5	37.5	41.3	
WACC 14%	0.66	0.57	0.50	0.43	0.38	0.33	0.28	0.25	0.21	0.19	
NPV (million)	2.2	4.1	6.6	7.8	9.5	10.2	10.7	11.0	10.7	10.3	
Total NPV (million)											**92.5**
LOA 36%											**33.8**

Valuation rigosertib HR-MDS IV EU Market

Year	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	
No of patients EU (yoy growth 3.5% as of 2015)	133,589	138,265	143,104	148,113	153,297	158,662	164,215	169,963	175,912	182,069	
No of patients eligible (9%)	10,821	11,199	11,591	11,997	12,417	12,852	13,301	13,767	14,249	14,748	
Penetration	1.5%	3.0%	5.3%	6.8%	8.3%	10.1%	11.7%	12.9%	14.3%	15.0%	
Total Revenues (USD m)	**6.1**	**12.7**	**23.3**	**31.3**	**39.9**	**50.9**	**61.9**	**71.3**	**82.4**	**90.6**	
Margin 50%	3.0	6.4	11.6	15.6	20.0	25.4	30.9	35.7	41.2	45.3	
WACC 14%	0.57	0.50	0.43	0.38	0.33	0.28	0.25	0.21	0.19	0.16	
NPV (million)	1.8	3.3	5.3	6.2	7.6	8.2	8.6	8.8	8.5	8.3	
Total NPV (million)											**66.6**
LOA 36%											**24.3**

Valuation rigosertib HR-MDS IV Japanese Market

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	
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 (9%)	1,064	1,102	1,140	1,180	1,221	1,264	1,308	1,354	1,402	1,451	
Penetration	1.%	3.6%	6.3%	8.1%	9.9%	12.1%	14.0%	155%	17.1%	18.0%	
Total Revenues (USD m)	**1.2**	**2.6**	**4.7**	**6.3**	**8.1**	**10.3**	**12.5**	**14.5**	**16.7**	**18.4**	
Royalty Symbio 20%	0.2	0.5	0.9	1.3	1.6	2.1	2.5	2.9	3.3	3.7	
Milestone payment SymBio	8.0	5.0									
WACC 12%	0.57	0.51	0.45	0.40	0.36	0.32	0.29	0.26	0.23	0.20	
NPV (million)	4.1	2.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5	
Total NPV (million)											**12.8**

Valuation rigosertib HR-MDS first line oral US Market

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	
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.%	3.6%	6.3%	8.1%	9.9%	12.1%	14.0%	155%	17.1%	18.0%	
Total Revenues (USD m)	**10.8**	**22.5**	**41.2**	**55.3**	**70.7**	**90.0**	**109.5**	**126.2**	**145.8**	**160.4**	
Margin 50%	5.4	11.2	20.6	27.7	35.3	45.0	54.8	63.1	72.9	80.2	
WACC 14%	0.50	0.43	0.38	0.33	0.28	0.25	0.21	0.19	0.16	0.14	
NPV (million)	2.8	5.1	8.2	9.7	11.9	12.7	13.3	13.7	13.3	12.8	
Total NPV (million)											**103.5**
LOA 36%											**37.8**

Valuation rigosertib HR-MDS first line oral EU Market

Year	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	
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.%	3.6%	6.3%	8.1%	9.9%	12.1%	14.0%	155%	17.1%	18.0%	
Total Revenues (USD m)	**9.8**	**20.6**	**37.6**	**50.6**	**64.6**	**82.3**	**100.2**	**115.5**	**133.3**	**146.7**	
Margin 50%	4.9	10.3	18.8	25.3	32.3	41.2	50.1	57.7	66.7	73.4	
WACC 14%	0.43	0.38	0.33	0.28	0.25	0.21	0.19	0.16	0.14	0.12	
NPV (million)	2.2	4.1	6.6	7.8	9.5	10.2	10.7	11.0	10.6	10.3	
Total NPV (million)											**83.0**
LOA 36%											**30.3**

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:

- July 2016: Successful rights issue close; proceeds of USD 17.4 million
- Sept 2016: Successful End of Phase II meeting for oral rigosertib + azacitidine, pivotal trial ahead
- Oct 2016: KOL meeting featuring novel ras targeted moa of rigosertib
- Dec 2016: 3 ASH presentations including Phase II data for rigosertib + Azacitidine in MDS/AML
- Apr/May 2017: Successful secondary raise with proceeds of USD 6 million
- May/June 2017:Presentations at the ASCO, MDS Foundation and EHA conferences

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

- Interim analysis Phase III INSPIRE trial
- Phase 3 protocol and Special Protocol Assessment for Rigosertib Combination trial
- Completion enrollment Phase III INSPIRE trial
- Launch of "RASopathies" rare-disease collaboration with the National Cancer Institute (NCI), academic investigators and patient advocacy groups
- 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
Cornerstone Pharma	CPI-613	Redox Homeostasis^ Tricarboxylic Acid (TCA) Cycle/Citric Acid Cycle (CAC))	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 is expected to commence in the first half of 2017. In a related transaction, Helsinn made a USD 5 million equity investment in MEI Pharma.

Cornerstone Pharmaceuticals

Cornerstone 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). No recent news flow was found on the MDS trial which is currently in Phase II (according to the company's website).

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.