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SAVE the DATE....

19th Bioshares Biotech Summit

7–8 August 2025

Hobart, Tasmania

Companies covered: AVR, CYP, MSB, SNT, Top Six Picks

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-35.8%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - May '14)	26.6%
Year 14 (May '14 - May '15)	23.0%
Year 15 (May '15 - May '16)	33.0%
Year 16 (May '16 - May '17)	16.8%
Year 17 (May '17 - May '18)	-7.1%
Year 18 (May '18 - May '19)	-2.3%
Year 19 (May '19 - May '20)	39.5%
Year 20 (May '20 - May '21)	86.8%
Year 21 (May '21 - May '22)	-15.6%
Year 22 (May '22 - Dec '22)	-2.2%
Year 23 (CY2023)	-15.4%
Year 24 (CY2024)	30.2%
Cumulative Gain	1750%
Av. Annual gain (23 yrs)	17.2%

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Extract from Bioshares –

Syntara – Early Positive Data in Phase II Myelofibrosis Study

Syntara (SNT: $0.06) has released some positive early (interim) data from its Phase II study with SNT-5505 for the treatment of myelofibrosis. More interim data will be announced in March of next year, with final data in the second half of 2025.

Based on the quality of these results, Syntara immediately conducted a placement for $15 million at $0.06 per share. After further data is available from those patients who have reached the 12-month treatment mark by the end of March, the company will meet with the FDA to discuss the path forward for a pivotal Phase IIc/III trial.

Phase II Study Results

In this Phase II study, 16 patients were enrolled. Of those, 12 are continuing treatment, with three having ceased treatment after six months, and one patient dying from congestive heart failure unrelated to SNT-5505.

Whilst this was an open label study like the previous Phase II trial, the difference in this study is that patients enrolled were receiving standard-of-care treatment ruxolitinib as well, and patients are treated for up to 12 months, compared to just six months in the previous trial.

In this study, eight of the 13 evaluable patients (62%) have achieved more than a 50% reduction in their myelofibrosis symptom score (TSS50). This appeared to improve with treatment duration, which is to be expected given the long-term change that SNT-5505 seeks to achieve a reduction in fibrosis in the bone marrow.

[In the earlier Phase II study, of the 10 evaluable patients who received six months of therapy, 40% experienced at least a 20% improvement in their myelofibrosis symptom score.]

On the measure of changes in spleen volume, of the 10 evaluable patients in this study, 20% achieved at least a 35% spleen volume reduction, which is the cutoff measure for responders. [This compares to no changes in the previous study.]

Of particular interest, in those five patients who have been on treatment for nine months so far, 80% experienced a continued reduction in spleen volume after the first 12 weeks.

In this study, the platelet counts were "generally stable across the cohort, with few major hematological toxicities reported". [In the previous study, eight of the 10 evaluable patients achieved stable or improved platelet counts.]

It should be noted that in this study, the benefit from SNT-5505 is in a patient population that has been on ruxolitinib treatment for a median period of 3.2 years.

Continued over

Discussion

As should be expected, the impact of therapy appears to be growing with duration of treatment with SNT-5505, which Syntara CEO Gary Phillips said is a somewhat novel occurrence in therapies in this disease area.

Outcomes in patients who have been on long term ruxolitinib therapy have been achieved, including one patient who had been on ruxolitinib treatment for five years and achieved a 100% reduction in the total symptom score.

With the good safety profile of SNT-5505 compared to competitors (see table), Phillips said that the efficacy profile is competitive with compounds ahead of Syntara in the clinic.

In this study so far, SNT-5505 achieved a better symptom score than other drugs in development, but equal to or slightly lower reduction in spleen volume.

Professor Clair Harrison, who works in the myelofibrosis field at Guy's and St Thomas' NHS Foundation Trust, participated in the recent Syntara investor call. Professor Harrison said that it is important to *not see* the spleen increase in volume, with SNT-5505 not expected to achieve a significant decrease in spleen volume (given its mechanism of action).

The high number of patients achieving a greater than 50% improvement in the symptom score was very encouraging, said Phillips.

With respect to endpoints in the forthcoming pivotal study, Phillips expects the primary endpoint will the percentage of patients who achieve a greater than 50% reduction in their total symptom score. The secondary endpoint is unclear. In Bioshares' view, it is unlikely to be changes in spleen volume. (JAK inhibitors, such as ruxolitinib, are assessed on reductions in spleen volume, however that's due to their specific mechanism of action, which treats the symptoms and not the underlying disease.)

Professor Harrison stressed that symptoms of patients are a big issue, as are any changes in the grading of fibrosis levels in the bone marrow. Changes in blood properties can be expected to see a 'subtle drift' according to Dr Harrison, until there is a substantial change in the bone marrow. She also sees the positive monotherapy data from the previous trial as being important, noting that the data from the two Phase II studies has been consistent.

A pivotal study is likely to require 300-350 patients, believes Phillips, with the trial length likely to be six or 12 months. Phillips said there is a huge need in this disease for new therapies to work alongside the existing and new JAK inhibitors.

This current trial was fully recruited in August. As such, 12-month data can be expected after August next year.

Bioshares recommendation: **Speculative Buy Class A**

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Myelofibrosis Drugs in Development

Compound (company)	Therapeutic effect	Adverse events (incidence)
Navitoclax (Abbvie)	Inhibits fibrosis	Thrombocytopenia (56%), anemia (32%)
Navtemadlin (Kartos)	Inhibits MDM1	Thrombocytopenia (28%), anemia (18%)
Pelabresib (Novartis)	Inhibits BET-mediated gene transcription	Thrombocytopenia (28%), anemia (18%)
SNT-5505 (Syntara)	Pan-LOX inhibitor	No treatment-related serious AEs

2025 Bioshares Top Six Stocks

Syntara – More Positive Data Expected from Phase II Myelofibrosis Study

Syntara (SNT: $0.06) has achieved encouraging data now from two Phase II studies in myelofibrosis. On the back of the recent interim results (see page 1) the company has been able to raise $15 million.

In 2025, we can expect to see more maturing data from the current Phase II study underway where 16 patients have been recruited. The effect of the company's drug candidate, which treats the underlying fibrosis in the bone marrow in this disease, can be expected to improve with longer duration of treatment, with early signs that this is already occurring.

The next step for the company is to meet with the FDA to discuss the structure of a pivotal study, which may involve between 300-350 patients at this point.

Syntara will need to either raise additional funds for this study, or strike a licensing deal. Myelofibrosis has been a very active disease area for drug licensing deals or acquisitions. Since 2022 three acquisitions have occurred for drug assets valued between US$1.7 - US$2.9 billion. These assets were at the end of Phase III, filed for approval or recently launched.

Syntara is capitalized at $95 million.

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How Bioshares Rates Stocks

For the purpose of valuation, Bioshares divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, Bioshares grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks. For both groups, the rating "Take Some Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages of commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

Corporate Subscribers: Cogstate, Syntara Dimerix, Patrys, Imugene, Chimeric Therapeutics, Neuren Pharmaceuticals, Aroa Biosurgery, Anteris Technologies, Immuron, Clinuvel Pharmaceuticals, Botanix Pharmaceuticals, Island Pharmaceuticals, LBT Innovations