**WAVE LIFE SCIENCES LTD.**

Adrift on Open Water – Limited Catalysts Until 2H20 – d/g to Market Perform

- **Bottom Line:** Over the past two weeks, initial readouts from WVE’s Duchenne muscular dystrophy (DMD) and Huntington’s disease (HD) programs have disappointed, leading to the discontinuation of the suvodirsen program (note HERE) and addition of higher doses to ongoing studies of WVE-120101/WVE-120102 (note HERE), delaying the time to next data from these clinical studies to 2H20. In light of these results, the timeline for WVE to demonstrate that controlling stereochemistry can lead to antisense oligonucleotides (ASOs) that are meaningfully differentiated from agents in development by ASO and RNA interference (RNAi) competitors is increasingly abstracted, leaving WVE shares in a catalyst vacuum until meaningful evidence of robust benefit in HD can be demonstrated. With this lack of clinically meaningful near-term catalysts until 2H20, investor focus will turn to the company’s balance sheet, and investor sentiment towards WVE shares will likely remain cautious unless WVE-120101 and WVE-120102 can convincingly produce mutant huntingtin protein (mHTT) knockdown at least in line with that shown thus far by RG6042 (IONS [MP/Roche]). Downgrade to Market Perform, $10 PT on WVE shares.

- **Lower than expected mHTT knockdown falls short of RG6042, as management hopes for better efficacy at higher doses.** WVE-120102 demonstrated 12.4% knockdown of mHTT across four dose cohorts in PRECISION-HD2, inferior to published results for RG6042 that exhibited mHTT reductions of 20% (10 mg), 25% (30 mg), 28% (60mg), 42% (90 mg), and 38% (120mg) at approximately 140 days after administration of therapy. While WVE-120102 may have advantages in specifically targeting the mutant HTT allele, and there appears to be room to evaluate higher doses in the clinic given a clean safety profile, a 12.4% mHTT knockdown is uncompetitive with RG6042, and substantial improvement vs yesterday’s results will be necessary at higher doses. Given these mixed results, we are not writing this program off – RG6042 dose had to be increased from 10 mg to 90 mg to double knockdown of mHTT, so the impact of dose escalation of WVE-120102 to 32mg from 16mg on knockdown may be similarly non-linear. RG6042 is roughly one and a half to two years ahead in clinical development and has demonstrated a greater degree of knockdown which could compound clinical enrollment challenges for WVE – due to this competitive positioning, we are reducing our probability of success for WVE-120101 and WVE-120102 programs to 30% from 50%.

- **Advantages of controlling stereochemistry in preclinical studies have not translated to the clinic thus far.** Preclinical data for

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Source: Company Information and SVB Leerink LLC Research.
Revenues in $ millions.
EPS - Diluted ($)

Key Stats: (NASDAQ: WVE)

- **Sector:** Biopharma / Genetic Medicine
- **S&P 600 Health Care Index:** 3,082.18
- **Price:** $7.99
- **Price Target:** $10.00 from $33.00
- **Methodology:** DCF 12% Discount Rate with 0% Terminal Growth Rate
- **52 Week High:** $48.64
- **52 Week Low:** $7.78
- **Shares Outstanding (mil):** 34.3
- **Market Capitalization (mil):** 274.1
- **Book Value/Share:** $4.73
- **Cash Per Share:** $6.09
- **Dividend (ann):** $0.00
- **Dividend Yield:** 0.0%

Completion: December 31, 2019, 6:00AM EDT.
Distribution: December 31, 2019, 6:00AM EDT.
WVE-120102 informed the design of a dose escalation study with a maximum dose of 16mg – while the company has not commented on specifics of this analysis, we assume the 16mg dose was expected to achieve substantial reductions in mHTT. The 10 mg dose of RG6042 appears to achieve more potent mHTT knockdown than the combined 2-16mg dose escalation dataset of WVE-120102, which leaves the impact of stereopurity on mHTT knockdown unclear. Alongside the recent clinical failure of suvodirsen, which did not show any changes in dystrophin production at the highest tolerated dose, the advantages of controlled stereochemistry observed in vitro and in animals are not translating to clinical benefit thus far.

- **Shares are likely to be range-bound due to lack of meaningful clinical catalysts in 2020.** The PRECISION-HD1 and -HD2 timelines have been aligned, with data updates for both now pushed to 2H20. The C9ORF72 amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) programs – the only other programs we ascribe value to in our model – are expected to enter the clinic in 2H20, and earliest data readouts are unlikely until 2021/2022. We struggle to see a clear catalyst to change investor sentiment towards WVE shares until the 2H20 PRECISION-HD1 and -HD2 readouts, making our former Outperform rating untenable.

- **Model Changes:** We reduce our probability of success for the HD program to 30% from 50%. We push out timelines for HD by one year to match the PRECISION-HD1 and -HD2 delay announced yesterday. We also push back assumed timelines for FTD and ALS programs by two years – given the very small size of these populations compared to HD, the more advanced stage of competing tofersen (IONS), we believe these programs will be met with substantial recruitment challenges, as WVE has seen in its HD program previously (note HERE).
INVESTMENT THESIS

We rate WVE shares Market Perform. Wave Life Sciences is a biotechnology company that is focused on developing oligonucleotide-based therapeutics for devastating rare diseases. WVE has generated preclinical data suggesting that stereopure (only a single enantiomer) antisense oligonucleotides (ASOs) can have improved potency, less immunogenicity, and longer stability than racemic mixtures. Initial clinical data from Huntington's disease (HD) and Duchenne muscular dystrophy (DMD) programs, however, have yet to show clinical differentiation from non-stereopure oligonucleotide therapies. WVE is collaborating with Takeda on several CNS indications, providing research expense support and extending the company's cash cushion ahead of Takeda’s decision to opt-in to their lead CNS program in Huntington’s disease (HD), structured as a 50/50 profit share. Updated results from the HD program are expected 2H20, though this timing is subject to hitting enrollment timelines in the face of competition from ongoing studies by Roche/IONS. We are inclined to stay on the sidelines given this abstracted catalyst path and clinical trial execution risk.

VALUATION

We derive a $10 price target for WVE shares using a discounted cash flow analysis by forecasting cash flows through 2030 and assigning a 0% terminal growth rate and 12% discount rate. We account for Wave's share of its 50:50 global profit share collaboration with Takeda on Huntington's disease, ALS, and frontotemporal dementia (FTD) programs using a 30% probability of success in HD and 20% POS in familial ALS and FTD, with neither program entering the market prior to 2024. In our DCF valuation we are using the fully diluted share count, including outstanding Series A preferred shares and stock options.

RISKS TO VALUATION

The risks to our view, outlook, and valuation for WVE include any major change in the price or reimbursement coverage in the United States or Europe for rare disease drugs. Our revenue forecasts for WVE are subject to the risk of better-than-expected market share for competing products in Huntington’s disease (including but not limited to modeled oligo competitor IONS), or unmodeled competitive entrants using disruptive technologies such as gene editing or gene therapy. Other risks include clinical and regulatory disappointments for WVE’s drug candidates in excess of that factored into our probability adjustments. Additionally, if drug candidate sales and profitability fail to match our estimates, further dilutive financing may be required in order to support future commercial operations and clinical development of pipeline agents.
### WVE P&L (in $M, except per share data)

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### Model Drivers

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### Total R&D (including cost-sharing) 170.1

### Total SG&A (including cost-sharing) 45.0

### R&D (% of revenues) 857%

### SG&A (% of revenues) 227%

Source: SEC Filings and SVB Leerink Estimates

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WAVE LIFE SCIENCES LTD.

December 31, 2019
## WVE DCF Analysis


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### Free Cash Flow

| 2019E 2020E 2021E 2022E 2023E 2024E 2025E 2026E 2027E 2028E 2029E 2030E | 168.5 | 137.3 | 76.2 | 41.4 | 76.0 | 123.9 | 65.0 | 3.7 | 56.8 | 107.3 | 155.4 | 193.2 |

### NPV FCF

| Total NPV | 230 | 126 | 64 | 30 | 51 | 72 | 34 | 24 | 40 | 51 | 57 | 476 |

### Net cash ($MM) 3Q19A

| 209 |

### Implied market cap ($MM)

| 439 |

### Fully diluted shares (MM) 3Q19A

| 44 |

### DCF Value per share ($)

| $10.01 |

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**Discount Rate**

12.0%

**Terminal Growth Rate**

0.0%

Source: SEC filings and SVB Leerink Estimates

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### Total NPV

230

### Net cash ($MM) 3Q19A

209

### Implied market cap ($MM)

439

### Fully diluted shares (MM) 3Q19A

44

### DCF Value per share ($)

$10.01

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<tr>
<th>Stock (Ticker Symbol)</th>
<th>Lateral Impact (Other companies/ stocks)</th>
<th>Drug (Brand or chemical name)</th>
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<th>Event or Trial Details</th>
<th>Expected Timing</th>
<th>Specific Event Date if known or specified</th>
<th>Impact: High &gt; 9%</th>
<th>Medium 3 - 9%</th>
<th>Low &lt; 2%</th>
<th>Estimated Stock Up/Down % on Best/Worst Outcomes</th>
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Source: SVB Leerink LLC Equity Research and Company Filings
Disclosures Appendix

Analyst Certification

I, Mani Foroohar, M.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

Rating and Price Target History for: Wave Life Sciences Ltd. (WVE) as of 12-27-2019

Valuation

We derive a $10 price target for WVE shares using a discounted cash flow analysis by forecasting cash flows through 2030 and assigning a 0% terminal growth rate and 12% discount rate. We account for Wave's share of its 50:50 global profit share collaboration with Takeda on Huntington's disease, ALS, and frontotemporal dementia (FTD) programs using a 30% probability of success in HD and 20% POS in familial ALS and FTD, with neither program entering the market prior to 2024. In our DCF valuation we are using the fully diluted share count, including outstanding Series A preferred shares and stock options.

Risks to Valuation

The risks to our view, outlook, and valuation for WVE include any major change in the price or reimbursement coverage in the United States or Europe for rare disease drugs. Our revenue forecasts for WVE are subject to the risk of better-than-expected market share for competing products in Huntington's disease (including but not limited to modeled oligo competitor IONS), or unmodeled competitive entrants using disruptive technologies such as gene editing or gene therapy. Other risks include clinical and regulatory disappointments for WVE’s drug candidates in excess of that factored into our probability adjustments. Additionally, if drug candidate sales and profitability fail to match our estimates, further dilutive financing may be required in order to support future commercial operations and clinical development of pipeline agents.
Valuation

Our 12 month price target for IONS is $58 per share based on discounted cash flow methodology. We forecast sales of Tegsedi, royalties from Spinraza, ongoing R&D revenue, and risk-adjusted sales or royalties from key pipeline agents and partnered programs. We explicitly model expenses and resulting cash flows through 2030, and assume a 10.0% discount rate (consistent with all companies in our coverage universe with revenue generated from approved products that are wholly-owned and independently commercialized in at least one end-market), and a 0% terminal growth rate. Additionally, we factor in IONS’s 4Q19E net cash balance in our valuation.

Risks to Valuation

The risks to our view, outlook, and valuation for IONS include any major change in the price or reimbursement coverage in the United States or Europe for rare disease drugs such as Tegsedi, Spinraza, and the company’s key pipeline drugs. Our forecast for Tegsedi is also subject to the risk of better-than-expected market share for patisiran, tafamidis, and AG10, or unmodeled competitive entrants using disruptive technologies such as gene editing. Other risks for IONS include clinical and regulatory disappointments for the pipeline in excess of that factored into our probability adjustments. Additionally, if sales and profitability fail to match our estimates, or Ionis is unable to continue to secure cash flow generating research and development partnerships in line with our forecasts, dilutive financing may be required in order to support future commercial operations and clinical development of pipeline agents.
### Distribution of Ratings/Investment Banking Services (IB) as of 09/30/19

<table>
<thead>
<tr>
<th>Rating</th>
<th>Count</th>
<th>Percent</th>
<th>IB Serv./Past 12 Mos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUY [OP]</td>
<td>148</td>
<td>74.4</td>
<td>54</td>
</tr>
<tr>
<td>HOLD [MP]</td>
<td>48</td>
<td>24.1</td>
<td>3</td>
</tr>
<tr>
<td>SELL [UP]</td>
<td>3</td>
<td>1.5</td>
<td>0</td>
</tr>
</tbody>
</table>

### Explanation of Ratings

**Outperform (Buy):** We expect this stock to outperform its benchmark over the next 12 months.

**Market Perform (Hold/Neutral):** We expect this stock to perform in line with its benchmark over the next 12 months.

**Underperform (Sell):** We expect this stock to underperform its benchmark over the next 12 months.

The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.
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