Evaluate Vantage

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First-quarter catalysts for the smaller players

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Important data releases are on the cards for Rhythm, Wave and Supernus, among others.

After delving into the key clinical events due for big pharma and biotech companies, *Evaluate Vantage* now looks at smaller players − those with a market cap of under $2bn.

Among them, Rhythm and Supernus are gunning to expand their patient groups, while Wave Life Sciences will hope that the New Year does not start in the same way as 2020.

Wave's shares have struggled to recover after plummeting 78% in December 2019. The company first abandoned its Duchenne muscular dystrophy project suvodirsen and then reported disappointing data with its Huntington's disease contender WVE-120102, an antisense oligonucleotide.

Now data are due on a higher dose of **WVE-120102** and a second antisense therapy for Huntington's, **WVE-120101**. The readout will include results from the 32mg dose cohort that was added to both the Precision-HD1 and Precision-HD2 studies after the lacklustre results with lower doses of WVE-120102.

Topline results from Precision-HD2 showed a 12% reduction in mutant huntingtin (mHTT) protein across four doses of WVE-120102 (2mg, 4mg, 8mg and 16mg), and although theoretically a hit the result was underwhelming compared with the competition.

Tominersen, an antisense project from Roche and Ionis, has shown 40% or greater mHTT knockdown at its highest doses in early studies and is now in phase III. Phase III open-label extension data with tominersen are due by the end of the first quarter of next year and could lead to an accelerated approval filing.

Increasing numbers

Imcivree gained approval last month in two rare genetic obesity indications, but now **Rhythm** needs to ramp up the number of patients it can treat with the therapy.

Investors are keenly awaiting phase III data in Bardet-Biedl syndrome and Alstrom syndrome, two rare genetic disorders in which sufferers experience an insatiable hunger and severe obesity beginning early in life.

Stifel analysts note that Bardet-Biedl is the main value driver for Imcivree, with around 5,000 patients globally. As a syndromic obesity associated with intellectual impairment it is easier to diagnose than Imcivree's first two approved indications.

The primary endpoint of the 30-patient pivotal trial is the proportion of patients who achieve a 10% or greater reduction from baseline in bodyweight after 52 weeks' treatment. The study comprises a 14-week double-blind placebo-controlled period, followed by a 38-week open-label stage; Imcivree is given by daily subcutaneous injection.

Stifel analysts believe that Imcivree only needs to demonstrate a ~20% response versus 10% for placebo for the trial to show statistical significance.

Supernus, meanwhile, is looking to expand **SPN-812**, a serotonin and norepinephrine modulating agent, into adults with ADHD.

The upcoming phase III is testing a flexible 200-600mg dose of SPN-812. The primary endpoint is the change from baseline in ADHD investigator symptom rating scale at six weeks.

Something to watch out for with the latest data is a potential dose-plateauing effect. In younger patients, only three out of four pivotal trials read out positively as the 600mg dose did not reach statistical significance *(Supernus struggles to gain attention, March 28, 2019).*

Supernus suffered a setback last month when the US FDA issued a complete response letter to the company's application for use in children and adolescents. This was not due to clinical data but instead concerned manufacturing. No new Pdufa date was provided.

Check out the table below for a full list of upcoming catalysts with consensus forecasts from *EvaluatePharma*. *Evaluate Vantage* has separately assessed expected catalysts for big pharma and biotech.

Q1 clinical catalysts (excludes Covid-19 data)					
Project	**Company**	**Therapy area**	**Q1 clinical catalyst**	**2026e indication sales ($m)**	**Note/ *Vantage* coverage**
Imcivree (setmelanotide)	Rhythm	Alstrom syndrome & Bardet-Biedl syndrome	Pivotal Ph3 (Q4/early Q1 2021)	881*	See text
WVE-120101 and WVE-120102	Wave/Takeda	Huntington's disease	Ph1/2 Precision-HD1 and Precision-HD2 trials, including the 32 mg dose cohorts	418	See text
MAT9001	Matinas	HTG	Ph2 Enhance-IT (crossover study MAT9001 vs Vascepa)	404	Primary endpoint % change from baseline to end of treatment in plasma triglycerides
CB-839 (telaglenastat)	Calithera	2L/3L metastatic renal cell carcinoma	Ph2 Cantata (CB-839 + Cabometyx vs Cabometyx) (late Q4/early 2021)	350	Study powered to detect 31% improvement over the 8mth PFS in the control
Ensifentrine (RPL554)	Verona	Moderate to severe COPD	Multiple dose part of ph2 (part B) due H1	335	Positive efficacy and safety data from part A (single dose) in 40 patients, pressurized metered-dose inhaler formulation
					At interim look biopsy data did

Q1 clinical catalysts (excludes Covid-19 data)					
losmapimod	Fulcrum	Facioscapulohumeral muscular dystrophy	ReDUX4 data in 80 patients, MRI data	295	not show a separation from placebo, full-body MRI data next (*Fulcrum's biopsy conundrum*)
RGX-314	Regenexbio	Wet AMD	Safety data ph2 AAViate (vs Lucentis)	287	Gene therapy delivered via suprachoroidal injection, more convenient than subretinal (surgical)
SPN-812	Supernus	ADHD	Ph3 in adults	265	See text
Domvanalimab + zimberelimab +/- etrumadenant	Arcus (Gilead stake)	1L metastatic NSCLC	Ph2 data from Arc-7 due H1	209	Should Arc-7 prove competitive Gilead could exercise opt-in rights for domvanalimab, an anti-Tigit MAb
Otividex	Otonomy	Meniere's disease	Ph3	206	Averts-1 ph3 failed, revised statistical analysis plan (negative binomial model) for the ongoing study
Margenza (margetuximab)	Macrogenics	1L gastric cancer	First data from Ph2/3 cohort A (Her2+PD-1) Mahogany H1	137	Anti-Her2 MAb now approved in late-line metastatic breast cancer, readout due in gastric cancer and decision on whether to expand enrolment for registrational purposes (*Macrogenics gets to market, but what comes next?*)
Plinabulin	Beyondspring	NSCLC	Final data Dublin-3, H1	100	Plan to file US NDA for chemotherpay-induced neutropenia early 2021
BCX9930	Biocryst	Paroxysmal nocturnal haemoglobinuria	Ph1/2	78	Treatment naive and inadequate C5 responders dosed up to 500 mg bid
					$183m IPO In

Q1 clinical catalysts (excludes Covid-19 data)					
ARQ-151 (Topical roflumilast cream)	Arcutis	Plaque psoriasis	Ph3 Dermis-1 and Dermis-2	-	Feb 2020, positive ph2, the ph3 studies are using the higher 0.3% dose
Ganaxolone	Marinus	Tuberous sclerosis complex	Ph2	-	*Marinus finds a path forward in rare epilepsies*
Pegunigalsidase alfa (PRX –102)	Protalix	Fabry disease	P3 Bright	-	2 mg/kg administered every four weeks, Pdufa in April for 1mg/kg infusion every other week
ANVS401	Annovis Bio	Alzheimer's disease and Parkinson's dissease	Ph2a, initial data due early 2021, dose response data due late summer	-	Amyloid precursor protein, a-synuclein & tau inhibitor
AMX0035	Amylyx	Alzheimer's disease	Ph2 Pegasus	-	Sodium phenylbutyrate, a HDAC inhibitor, plus taurursodiol, a bax inhibitor; aim is to prevent death of neurons

**Obesity indications not split out. HTG=hypertriglyceridemia. Sources: EvaluatePharma, company releases, analyst notes & clinicaltrials.gov.*