EDISON

Nuevolution

FY18 results

Small molecules, big ambitions

Pharma & biotech

Positive progress in Nuevolution's RORγt partnership with Almirall has triggered a €1m milestone payment (SEK10.5m) and we continue to forecast that it will enter the clinic in 2019. FY18 was defined by the progress in the Amgen partnership as it opted in for two oncology programmes, further validating Nuevolution's Chemetics technology. In Nuevolution's BET-BD1 programme, a development candidate (NUE20798) has been nominated; data in animal cancer models highlight that it may have synergistic effects in combination with immunotherapies. The FY18 net loss was down year-on-year to SEK99.7m (from SEK117.5m) as a result of lower R&D costs. Net cash of SEK108m (FY17: SEK110.6m) should fund operations into 2020. We value Nuevolution at SEK20.7/share.

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/17**	12.2	(123.8)	(2.7)	0.0	N/A	N/A
12/18**	11.0	(107.3)	(2.2)	0.0	N/A	N/A
12/19e	202.4	87.2	1.1	0.0	12.5	N/A
12/20e	336.6	220.9	2.9	0.0	4.8	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments. **Restated following change of year.

Almirall milestone achieved with positive CD data

Almirall and Nuevolution have completed significant characterisation of its candidate drug (CD) leading them to believe the program could have potential best-in-class attributes; Almirall will now press forward with its plans to start a clinical trial programme in moderate to severe psoriasis patients. The partnership includes €172m in development milestones and €270m in regulatory milestones, in addition to tiered royalties on future net sales. The timing and design of any clinical trial is ultimately Almirall's decision and we await further information on these elements.

Amgen opt-ins proving the worth of NUEV technology

Nuevolution continues to demonstrate that it has the in-house ability to execute and deliver on its partnerships. In 2018, Amgen opted-in on two programmes and is now covering development costs. If Amgen exercises its option to license a candidate, Nuevolution will receive an initial licensing fee of at least $10m and potential milestone payments of up to $400m per candidate. With the collaboration spanning multiple undisclosed targets, significant financial potential exists.

Internal pipeline continues to add value

Nuevolution continues to build and strengthen its pipeline of preclinical assets and aims to monetise some of those in the near term via out-licensing. We have no visibility on the timelines for potential new deals for Nuevolution, but believe the BET-BD1 programme, which is the most advanced internal candidate, is well positioned and most likely to be out-licensed or partnered.

Valuation: SEK20.7/share (SEK1,026m)

We value Nuevolution at SEK20.7/share (SEK1,026m), vs SEK19.7/share (SEK974m) previously. The increase in value is driven by the rolling forward of our model, and we have updated net cash and FX rates.

19 March 2019

Price	**SEK13.8**
Market cap	**SEK683m**

SEK9.33/US$; US$1.13/€; SEK10.56/€

Net cash (SEKm) at 31 December 2018	108.0
Shares in issue	49.5m
Free float	55%
Code	NUEV
Primary exchange	Nasdaq Stockholm
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	3.5	(11.8)	(20.0)
Rel (local)	1.8	(20.9)	(23.3)

52-week high/low	SEK20.1	SEK10.7

Business description

Nuevolution is a Copenhagen-based biopharmaceutical company. Its patent-protected Chemetics drug discovery platform enables the selection of drugs to an array of tough-to-drug disease targets. To date it has entered into 17 agreements with major pharmaceutical companies.

Next events

Sign new out-licence/risk-sharing collaboration	2019/20
Start of Almirall's RORγt Phase I trial	2019

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Edison profile page

Investment summary

Company description: DNA-encoded drug discovery

Nuevolution is a Copenhagen-based leader in small molecule drug discovery, co-founded in 2001 by CEO Alex Haahr Gouliaev. The company's internally innovated DNA-encoded drug discovery platform, Chemetics, has been designed to rapidly select drugs for an array of tough-to-drug disease targets; the technology has been validated by multiple collaborative deals, notably the deals in 2016 with Amgen and Almirall. In addition to out-licensing deals, Nuevolution is developing a portfolio of preclinical drugs (10+ programmes); it intends to move some into the clinic itself or partner. The near-term goal remains the creation of a stable revenue stream through partnerships that can support the long-term development of Nuevolution's wholly owned assets. To date, the company has generated approximately SEK530m in revenues through collaborations. It raised net proceeds of SEK230.1m from its IPO on Nasdaq First North Premier in Stockholm, Sweden, and in 2018 it raised net proceeds of SEK104.0m from a directed issue.

Valuation: Amgen, Almirall and Janssen form basis of our rNPV

We value Nuevolution at SEK20.7/share (SEK1,026m), compared with SEK19.7/share (SEK974m) previously. This increase is predominately due to rolling forward the model; additionally, we have updated net cash and FX rates. Our valuation of SEK1,026m including net cash of SEK108.0m is based exclusively on a risk-adjusted model of the future milestones we expect from the Almirall (SEK9.7 per share), Amgen (SEK8.4 per share) and Janssen (SEK0.5 per share) deals, using a 12.5% discount rate. We note near-term milestones are a core driver of our valuation; any change in the timing or size of these from our assumptions would have a material effect on our valuation. We have not ascribed value at this point to the unique platform and multiple early stage candidates.

Sensitivities: Clinical validation is the long-term focus

Nuevolution is subject to drug development risks, including clinical development delays or failures; however, the company's 15+ compounds in parallel development helps to reduce the risk typically associated with pure-play biotechs. Additional sensitivities exist around IP protection, regulatory risks, competitor successes, partnering setbacks and financing and commercial risks. While Nuevolution's strategy minimises the business risk associated with drug development by partnering early on in development, general risk remains in the partner's willingness to progress these partnerships. One of the key sensitivities for Nuevolution is the successful transition of molecules discovered by its Chemetics programme into clinical-stage development, which would enable further validation of its technological capabilities. Financing needs depend on milestone revenues from existing partners and potential new partnering activities; delay or failure to receive future milestones would generate a funding gap during FY20.

Financials: Funded into 2020

For the full year 2018, revenues were SEK11.0m, a slight reduction on the previous period (FY17: SEK12.2m). R&D costs decreased slightly on the previous year to SEK91.0m (FY17: SEK107.3m), while SG&A remained essentially flat at SEK28.5m (FY17: SEK28.3m). Net cash as of 31 December 2018 of SEK108.0m (gross cash: SEK111.1m) should be sufficient for Nuevolution to operate in FY19 without the need for additional revenue or funds. We forecast significant near-term revenues from the Amgen and Almirall deals, with our model forecasting that Amgen will exercise its option on one of the programmes and Almirall will start a Phase I trial (triggering a milestones to Nuevolution), both before the end of FY19. These payments make up the majority of our revenue forecast in this financial year (FY19) and either failure to achieve this or changes to the timing/size of the payment would have a material effect on our forecasts and valuation. We will continue to monitor both Almirall and Amgen and may look to readdress these assumptions in H219 if no

external announcements have been forthcoming. We note we have updated our historical financials to reflect the new December year end (from June previously) and the restated accounts.

Partnerships: On solid ground

Nuevolution continues to successfully advance its partnered programmes with Almirall, Amgen and Janssen (Exhibit 1) to value inflection points. In both July 2018 and November 2018, Amgen exercised its right to opt in on two separate undisclosed programmes (multi-target collaboration across oncology and neuroscience), and has assumed responsibility for all further costs incurred by both parties. Amgen is eligible to exercise its option to license one of these programmes; if it does, Nuevolution would receive an initial licensing fee of at least $10m per programme.

In February 2019, Nuevolution announced Almirall had paid the first milestone (€1m, SEK10.5m) in its (RORγt) collaboration following successful completion of significant preclinical research studies. As per the out-licensing agreement signed in December 2016, progression of Nuevolution's asset into Phase I trials is subject to Almirall's discretion. With recent failures in the space (Allergan's AGN-242428 and AstraZeneca's AZD0284) the delays in reaching this milestone are due to Almirall and Nuevolution ensuring that they have identified any liabilities and that the attrition of competitor compounds is not endemic to the mechanism of action (ie RORγt inhibitor).

The confidential nature of the collaborations mean little material information has been forthcoming, although we expect this to change as assets enter the clinic. We predict that in 2019 Almirall moves the RORγt inhibitor into the clinic (in dermatology and psoriatic arthritis indications), and Amgen takes up the licence option on the first product candidate to emerge from the Nuevolution collaboration. We forecast that both could generate significant revenues in the form of milestone payments; however, in the near term, two key sensitivities remain in the timing and size of expected milestones from both the initiation of Almirall's Phase I trial and Amgen's research project option.

Exhibit 1: Nuevolution's partnered pipeline

Target/ Indication	Stage	Partner	Deal terms	Notes
RORγt (inverse agonist) Chronic inflammatory diseases	Preclinical	Out licensed to Almirall in dermatology and psoriatic arthritis	Nuevolution received €11.2m (SEK109m) gross as an upfront licence payment for the RORγt inverse agonist programme (in dermatology and psoriatic arthritis indications). The deal could provide Nuevolution with up to €172m in development and regulatory milestones, as well as €270m in commercial sales milestones and tiered royalties on future net sales.	RORγt plays an important part in the generation of pro-inflammatory cytokines, notably IL-17A, which is implicated in multiple inflammatory and autoimmune conditions. Inverse agonists of RORγt inhibit this pathway and Nuevolution's product candidates (under Almirall's stewardship) could provide oral-based treatments for psoriasis (PsO) and psoriatic arthritis (PsA). Feb 2019: Nuevolution received €1m (SEK10.5m) milestone payment for successful completion of significant preclinical research studies. All remaining development is now being undertaken by Almirall.
Undisclosed target(s) Cancer & CNS diseases	Preclinical	Drug discovery collaboration with Amgen	Multi-target research programme with $410m in research, development and commercial milestones plus royalties for each programme. Nuevolution is responsible for the early research, while the preclinical development, clinical development and commercialisation of the product are Amgen's responsibility. If Amgen exercises its option to license a candidate, Nuevolution will receive an initial licensing fee of at least $10m.	Amgen has exercised its right to opt in on the two undisclosed "fast-tracked" cancer targets (multi-target collaboration) and has assumed responsibility for all further costs incurred by both parties. In the first fast-track cancer programme, Amgen and Nuevolution are jointly optimising programme compounds for target selectivity and subsequent further in vivo efficacy studies. The second programme is completing its small molecule compound optimisation with extensive activity profiling, mechanism-of-action validation and x-ray crystallisation studies. A third programme is in earlier stages of hit optimisation.
Undisclosed targets Various	Discovery: various	Drug discovery collaboration with Janssen	Technology access agreement. Agreement was signed in October 2015 (undisclosed upfront) and to date Nuevolution has thrice publicly announced an expansion of the agreement, receiving payments of $0.6m in June 2016, March 2017 and January 2018.	Payment (January 2018) of $0.75m was a result of J&J exercising its option to license one of its research programmes. The disease target is in the area of anti-infectives. Nuevolution is entitled to further research, development and commercialisation milestones, in addition to royalties on net sales.
GRP78 Cancer	Discovery: hit-to-lead	50% ownership*	N/A	GRP78 is a member of the chaperone family of proteins; it is over-expressed in many tumour types including breast cancer and brain tumours. Selected compounds are now in the control of CRT/ICR and further progression is reliant on them

Source: Nuevolution, Edison Investment Research. Note: *Collaboration with CRT and ICR.

Pipeline progresses; two programmes nearing the clinic

The wholly owned pipeline continues to progress well, with clinical readiness of its two lead programmes (RORγt and BET-BD1 inhibitors) the focus. In the BET-BD1 programme, NUE20798 has been selected as the lead programme candidate following positive data on its bioavailability and its mechanism of action (animal model data demonstrated it has an anti-fibrotic effect and it may be synergistic with immunotherapies).

Fuelled by Nuevolution's Chemetics technology, the company has a number of late-stage preclinical assets, alongside more than 10 earlier-stage programmes (varying from hit identification to hit optimisation). Exhibit 2 highlights Nuevolution's pipeline, which is set to deliver multiple inflection points over the coming 12–18 months.

Exhibit 2: Nuevolution's non-partnered pipeline

Target	Indication	Stage	Ownership	Notes
RORγt (inverse agonist)	Chronic inflammatory diseases	Preclinical	Other indications outside of dermatology and psoriatic arthritis. 100% ownership Nuevolution	RORγt plays an important part in the generation of pro-inflammatory cytokines, notably IL-17A, which is implicated in multiple inflammatory and autoimmune conditions. Nuevolution retains the rights to pursue other indications, primarily focusing on ankylosing spondylitis (AS), with inflammatory bowel disease (IBD) as a secondary indication.
BET-BD1	Cancer, fibrosis (IPF, NASH) and inflammatory diseases	Preclinical	100% ownership Nuevolution	BET-BD1 is a novel target class offering a new mode of action for treating cancer and inflammatory diseases. With numerous BET inhibitors in clinical development for oncology, Nuevolution has chosen to pursue atopic dermatitis (AD) and/or psoriasis as the primary indication, with secondary indications in fibrosis (scleroderma) and lupus.
IL-17A	Inflammatory diseases	Discovery: lead optimisation	100% ownership Nuevolution	IL-17A inhibitors work downstream of RORγt in the pro-inflammatory cascade. Small molecule inhibitors of this target are much sought after in drug discovery, as they are likely to offer more favourable dosing and cost than the antibody-based therapies currently on the market for PsO, PsA and AS.
TYK2		Discovery: lead optimisation	100% ownership Nuevolution	Tyrosine kinase 2 (TYK2) is a member of the Janus kinase (JAK) family, which sits downstream of cytokine receptors and mediates inflammatory signalling. To date, there are no marketed TYK2 inhibitors.
RIPK1		Discovery: lead optimisation	100% ownership Nuevolution	Receptor-interacting serine/threonine-protein kinase 1 (RIPK1) is a signalling kinase in the tumour necrosis factor receptor (TNF) pathway, and acts to regulate inflammation and cell death in tissues throughout the body. It plays a role in a range of inflammatory diseases and is of particular interest in the neuroinflammatory processes thought to drive some neurodegenerative disorders.
RORγt (agonist)	Cancer	Discovery: hit optimisation	100% ownership Nuevolution	In conjunction with the RORγt inverse agonist (inhibitor) programmes, Nuevolution's Chemetics platform has also enabled the identification of agonists (activators) that have potential applications in immunoncology. Currently hits are being optimised and tested in vivo (mouse breast tumour model).
Undisclosed targets	Various	Discovery: various	100% ownership Nuevolution	10+ discovery programmes in a range of undisclosed indications including oncology, inflammatory diseases and immunoncology.

Source: Nuevolution, Edison Investment Research

BET-BD1: The potential of epigenetics

One of Nuevolution's most advanced programmes is focused on developing inhibitors of the first binding domain (BD1) of the bromodomain and extra-terminal domain (BET) family of proteins. Bromodomains act as epigenetic regulators of multiple genes in the immune system and are novel targets for both immunology and oncology; no drugs of this class have been approved to date. FY18 results highlight Nuevolution's BET-BD1 project transition through a key milestone, nominating NUE20798 as primary candidate (and NUE23530 as a backup compound). With NUE20798 now progressing through to the final stages of preclinical development (regulatory safety studies), serendipitously, scale up of NUE20798 has yielded a new formulation that demonstrates a significantly improved oral-drug profile, with 80% of the compound taken up into systemic circulation after oral dosing (vs 20% previously). We expect the project could be ready for investigatory new drug (IND) filing in FY19 and although transitioning a compound into the clinic would most likely be through a new partner, this could also facilitated by Nuevolution.

Through various preclinical models, Nuevolution had shown its BET-BD1 inhibitors have scope in the treatment of auto immune disorders, such as atopic dermatitis (eczema) and systemic lupus erythematosus (SLE); it has also identified its inhibitors can regulate the transcription of genes (and biomarkers) responsible for a range of fibrotic diseases, such as scleroderma, idiopathic pulmonary fibrosis (IPF) and non-alcoholic steatohepatitis (NASH). Recently Nuevolution has demonstrated (in vivo, mice) that its candidate molecule NUE20798 could have a synergistic effect in combination with PD-1 immune checkpoint inhibitors, broadening the scope for how it could be utilised in the treatment of cancers (particularly fibrotic tumours).

We note that numerous BET inhibitors are in development mainly targeting oncology indications. However, these clinical candidates are generally non-selective in nature and target the majority of BET proteins. Some of the most advanced BET inhibitors are highlighted in Exhibit 3. We note that none of these candidates are in development for inflammatory conditions, likely as a result of their range of toxicities, which are not as accepted outside of oncology indications.

Exhibit 3: Bromodomain and extraterminal domain (BET) inhibitors in clinical development

Drug	Company/partner	Delivery	Status	Indication(s)	Notes
Apabetalone (RVX-208)	Resverlogix	Oral	Phase III	Coronary artery disease	BETonMACE is a global Phase III study in patients with type 2 diabetes and coronary artery disease, investigating the ability of Apabetalone to reduce the risk of major adverse cardiovascular events. Top-line results can be expected in H219. We note that Apabetalone binds preferentially (c 20-fold) to the second binding domain (BD2), as opposed to NUE20798, which binds preferentially to BD1 (>100-fold selective).
BMS-986158	Bristol-Myers Squibb	Oral	Phase I/II	Cancer	Currently in a Phase I/II development investigating it as both a monotherapy and in combination with BMS's PD-1 inhibitor Opdivo (nivolumab) for the treatment of cancer. Interim data was presented at ESMO2018 that showed it was generally well tolerated as a monotherapy with thrombocytopenia being the only dose-limiting toxicity.
INCB057643	Incyte	Oral	Phase I/II	Cancer	Completed Phase I/II study (December 2018) in patients with a range of advanced solid tumours and hematologic malignancies. Preliminary results from the trial were presented at ASH2017 and showed the maximum tolerated dose was established in the Phase I study at 12mg qd. Expanded Phase II cohorts are investigating treatment as a monotherapy and in combination with standard of care treatments; complete data are yet to be published.
GSK525762	GlaxoSmithKline	Oral	Phase II	Cancer	Under investigation in multiple Phase II studies for various indications.
RG6146 (TEN-010)	Roche/Tensha	Oral	Phase Ib	Cancer	Currently in two Phase Ib clinical trials in patients with various hematologic malignancies, investigating its use as a monotherapy and in combination with other standard of care treatments.

Source: Edison Investment Research

Although we expect Nuevolution will partner its BET-BD1 programme prior to clinical development, should it decide to progress a candidate molecule into clinic, it could significantly grow the value of a licensing deal; we highlight that Tensha Therapeutics was acquired by Roche in 2016, primarily for its Phase I asset, BET inhibitor TEN-010 (renamed RG6146), for an upfront cash payment of $115m and up to $420m of milestone-based payments.

RORγt inverse agonist: Only the best will do

Nuevolution continues the progression of its RORγt programme (outside Almirall indications) in ankylosing spondylitis (prioritised) and inflammatory bowel disease. RORγt is an important master control switch of immune system activation and a potential novel target for the treatment of autoimmune diseases (by immune suppression) and cancer immunotherapy (by immune activation). RORγt plays a critical role in the generation of mature T-cells, particularly Type 17 effectors that produce an array of cytokines, notably IL-17A (IL-17A enables the recruitment of key immune components to sites of inflammation).

In Q418, Nuevolution tested several back-up compounds (including in a vivo efficacy IL23-induced ear dermatitis model) and noted that some of them had superior characteristics to that of the current lead candidate. Based on this data and contractual obligations with Almirall, Nuevolution will now proceed to nominate a backup compound for development with the option to pursue a best-in-class RORγt inhibitor for clinical testing in ankylosing spondylitis. Ankylosing spondylitis (AS) is a chronic inflammatory arthritis predominately affecting the spine and sacroiliac joints. Over the course of time chronic inflammation of the spine (spondylitis) can lead to a complete fusion of the vertebrae (ankyloses) and loss of mobility of the spine.

Novartis's Cosentyx (secukinumab) is the first and thus far only IL-17 inhibitor approved for AS (RORγt works upstream). It received FDA approval in January 2016. It is an IL-17 inhibitor

(antibody IV treatment) that is also approved for psoriasis and psoriatic arthritis. Novartis reported combined sales of $2.8bn across all three indications in FY18, its third full year of launch. If a RORγt inhibitor is to succeed both clinically and commercially it will likely need to demonstrate comparable efficacy and safety to that of Cosentyx. In our view, the market would be very receptive to a competitively priced oral RORγt inhibitor that has comparable efficacy and safety to IL-17 antibodies. The ability to capture a small percentage of this market could be transformational for a company of Nuevolution's size. However, we note any such sales are at least several years off, assuming any compound is clinically successful.

One of the most advanced RORγt inverse agonists was AGN-242428, in Phase II development by Allergan (through the acquisition of Vitae Pharmaceuticals for $639m in cash). However, it has failed in a Phase II trial due to undisclosed safety reasons and was written off in Q118. We note the RORγt inverse agonists field remains a difficult one as additionally highlighted by the Phase I suspension of AstraZeneca's asset AZD0284 (due to preclinical findings) and GSK's termination of the development of GSK-2981278. However, there remains substantial opportunity for a company that can safely target RORγt and large pharma remains interested, as evidenced by AbbVie having initiated a RORγt inhibitor programme. Its lead compound ABBV-157 is partnered with Inventiva and has entered a Phase I trial in moderate to severe psoriasis.

IL-17A: A major opportunity for oral therapy

Nuevolution is developing an IL-17A small molecule inhibitor for the treatment of a range of inflammatory diseases. The programme is currently in lead optimisation and Nuevolution is preparing for the selection of a topical development candidate. Targeting IL-17A directly is a proven strategy for treating moderate to severe PsO, PsA and AS, with anti-IL-17A monoclonal antibody therapies approved across all these indications including Novartis's Cosentyx and Eli Lily's Taltz. Several other antibody therapies acting against other pro-inflammatory cytokines (IL-23 and TNFα) are also approved as treatments. Although costly, injectable biologic agents have revolutionised the treatment of these chronic inflammatory conditions and generate significant revenue streams (eg FY18: Cosentyx $2.8bn).

Small molecules generally have four key advantages over biologics: the ability to target intracellular components (potential to reach novel targets), cheaper cost of production (lower pricing), oral or topical dosing (improved compliance vs injectable) and shorter half-life (important if side effects need to be controlled). While offering important practical advantages, novel small molecule drug candidates have high efficacy hurdles to meet, while ensuring low toxicity profiles. Directly targeting the IL-17A protein/protein interaction (PPI) with a small molecule is no easy feat because of the large flat protein structures involved. Enabled by Nuevolution's Chemetics platform, hit identification utilised one of Nuevolution's 40 trillion compound collections to identify three series amenable to lead optimisation. Structural elucidation of these inhibitors bound to IL-17A protein has highlighted distinct mechanisms of binding across the series, which increases Nuevolution's chances of developing small molecule candidates. Furthermore, in vivo proof-of-concept work has demonstrated efficacy comparable to an anti-IL-17A antibody for one of the lead assets (NUE), when dosed subcutaneously in a collagen-induced arthritis mouse model.

A look at the small molecule IL-17A inhibitor competitor space shows few potential competitor products in development (HitGen, C4X Discovery) and Nuevolution's programme is well positioned to deliver first-in-class clinical candidates.

Early pipeline generating excitement

Outside of the lead assets, the RORγt agonist and GRP78 programmes in addition to newly disclosed TYK2 and RIPK1 programmes (plus 10 additional programmes) continue to add value as they progress through the various stages of discovery. TYK2 and RIPK1 complement Nuevolution's

other programmes, with their scope likely to focus on inflammation and oncology, aligning well with its growing preclinical experience in these areas. Both compounds are currently in lead optimisation. We note recent news from a post marketing study in February 2019 that demonstrated Pfizer's JAK1–3 inhibitor Xeljanz (tofacitinib) (Tyrosine kinase 2 [TYK2] is a member of the Janus kinase [JAK] family) increased risk of pulmonary embolism and death. There remains a significant opportunity if a selective inhibitor of TYK2 can overcome the safety issues of JAK inhibitors. For an overview of the TYK2 and RIPK1 programmes, please see our previously published report (Clinical development in 2019).

In addition to RORγt inverse agonist (inhibitor) programmes, Nuevolution is developing RORγt agonists (activators) that have potential applications in immunoncology. One of the most advanced RORγt agonists is in development by Lycera, which is currently running a Phase I/IIa trial investigating RORγt agonist LYC-55716 in patients with solid tumours and a Phase Ib trial investigating a combination with Keytruda (pembrolizumab) in patients with non-small cell lung cancer (NSCLC). Latest data was presented at ESSO 2018 on both trials. In the Keytruda combination data is in its infancy with only three patients reported on to date; however, there were no reported serious adverse events. In the monotherapy Phase IIa study, 10 of 63 patients (16%) had stable disease for four or more months.

The GRP78 programme is being conducted in collaboration with Cancer Research Technology (CRT) UK and the Institute of Cancer Research (ICR) UK. The programme aims to identify compounds that target GRP78, an intracellular protein that is believed to support cancer cell survival. Compounds that have been selected by Nuevolution are now in the control of CRT/ICR where they are being tested in various cancer cell lines. Further progression of this programme will depend on CRT/ICR.

We note that multiple other undisclosed programmes are in development by Nuevolution and we expect these will come to the forefront as the lead assets are either out licensed or clinically developed internally.

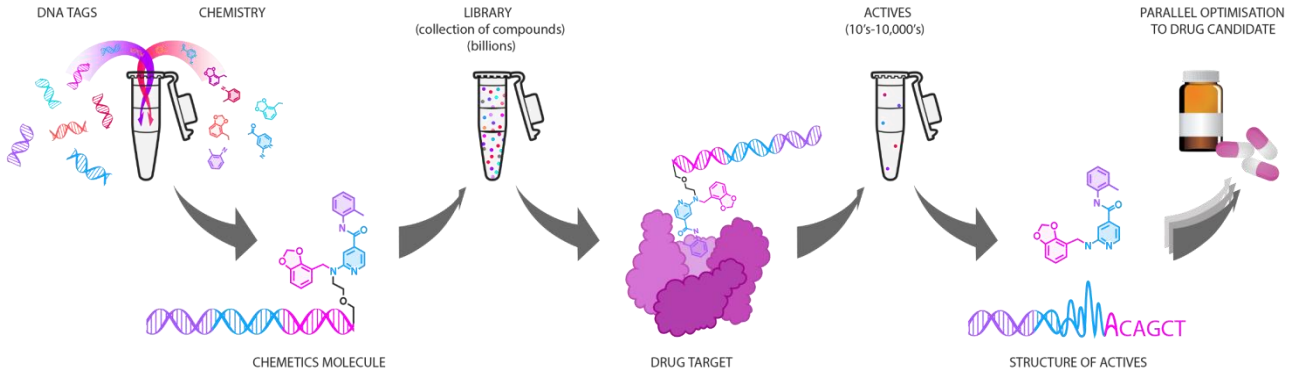
Chemetics: Accelerating the discovery process

Nuevolution's pipeline is underpinned by its platform technology Chemetics, which enables both a rapid and cost-effective way of identifying chemical starting points (hit identification) for small molecule drug discovery. High-throughput screening (HTS) has been a cornerstone of drug discovery; with the boom of combinatorial chemistry during the 1990s, substantial libraries of compounds could be generated (10^4–10^7), facilitating the ability of HTS to identify hit matter. However, the time taken to build and screen collections of this magnitude through conventional techniques, and ultimately their ability in identifying compounds for "tough-to-drug" targets, has presented a ceiling limit for their utility and combinatorial chemistry has fallen out of favour. With the advent of high-throughput sequencing, platforms have now emerged that utilise DNA-encoded libraries (such as Chemetics), revolutionising the hit discovery process.

DNA-encoded libraries (DELs) consist of compounds that have been tagged with a unique sequence of DNA that encodes for its structure. Mixtures of these tagged compounds can be screened simultaneously against a drug target of interest and those that bind can be identified based on their unique DNA sequence (Exhibit 4). The process by which Nuevolution generates its DELs (split-and-mix technique) means libraries can be produced that are several orders of magnitude larger (10^7–10^{13} compounds) than those traditionally produced. By comparative example, producing a library of this magnitude through conventional means would require the handling and storage of several tonnes of material, whereas Chemetics enables these libraries to be generated in one vial, assayed together and readily sequenced to identify hits. For a deeper

overview of the Chemetics platform, please refer back our initiation note Chemetics proof is in the deal making.

Exhibit 4: Chemetics overview



Source: Nuevolution

Although Chemetics helps overcome this first hurdle of identifying hit matter, validating these hits and their subsequent development towards candidate nomination presents a multitude of additional hurdles. The efficiency of Chemetics means that Nuevolution can pursue multiple biological targets in parallel (c 15 projects per year) at a significantly lower cost to other HTS platforms, increasing Nuevolution's chances of progressing a compound through the discovery process. With compounds now reaching candidate nomination, Nuevolution has passed significant milestones, demonstrating it can facilitate end-to-end preclinical drug development through leveraging Chemetics. We have highlighted in the past and still maintain that transitioning a candidate into the clinic, either by itself or through a partner, would further validate its approach.

Competitors: The next wave of small molecule development

An explosion of deal making in the sector has pushed many companies into the limelight and the competitive landscape for Nuevolution is outlined in Exhibit 5. While this highlights the pure-play drug discovery companies, major strides are being taken by large pharmaceutical companies. GSK, one of the first pharmaceutical companies to see the potential of the technology, acquired Praecis Pharmaceuticals (a developer of DNA-encoded drug libraries) in 2007 for $55m before entering into a licensing agreement with Nuevolution. This granted GSK further (Intellectual Property) freedom to operate in 2009 and GSK now has two clinical candidates derived from its DEL platform:

- GSK2982772 – an RIPK1 inhibitor currently in Phase II development for ulcerative colitis; and
- GSK2256294 – an epoxide hydrolase inhibitor that has completed Phase I trials.

The partners listed in Exhibit 5 highlight the interest that the industry has in these platform technologies.

Exhibit 5: DEL platform companies

Company	Sector	Technology	Partners	Notes
HitGen (private)	Service/ pipeline	DNA barcoding	Bayer, Merck Sharp Dohme, Genentech (Roche), Boehringer Ingelheim, Biogen, Cyclofluidic, Janssen (J&J), Takeda	HitGen has entered into several new collaborations in 2018 (undisclosed deal terms) in conjunction with receiving an IND for its oncology candidate (HDAC I/IIb inhibitor) from the Chinese NMPA.
X-Chem (private)	Service	DNA barcoding	Vertex, Bristol-Myers Squibb, ONO, Gilead, AstraZeneca, Taiho Pharma, AbbVie, Bayer, Janssen (J&J), Sanofi, Roche, Pfizer	Multiple deals have been signed including with Taiho Pharma (worth up to $352m in total, plus royalties), Bayer (worth up to $528m plus royalties) and Vertex, which was expanded in January 2019 to cover 14 targets in total.
Philochem (subsidiary of Philogen)	Service	DNA barcoding	Pfizer, AbbVie, Jansen(J&J), Bayer, Boehringer Ingelheim, Merck Serono, Celgene, Novartis	Several new collaborations have been announced in January 2019 including with Novartis, Janssen and Celgene. No details are available regarding terms or stage of any deals.
Vipergen (private)	Service	DNA templating	Gilead, Merck, Amgen, Takeda, Bayer	Vipergen has entered into multiple multi-target drug discovery agreements (no target or financial details disclosed).
DiCE Molecules (private)	Service	DNA templating (directed evolution)	Sanofi, Genentech (Roche)	Development programme with Sanofi to identify therapeutics for up to 12 targets. $50m upfront with further $184m in milestones per target signed in March 2016.

Source: Edison Investment Research, DiCE Molecules, HitGen, X-Chem

Financials

For the full year 2018 revenues were SEK11.0m, a slight reduction on the previous period (SEK12.2m in FY17). Revenue resulted from both the Janssen and Amgen collaborations and was a mix of upfront payments (SEK3.1m), milestone payments (SEK6.3m) and contract work (SEK1.6m). We forecast a significant increase in FY19 revenue to SEK202.4m. This is driven by our forecast that Almirall will enter the clinic in 2019 with its licensed RORγt inverse agonist and that this will trigger a substantial milestone (c SEK75m) for Nuevolution. Additionally, we forecast that Amgen will in-license an asset in 2019 to the approximate value of SEK100m and that the Janssen partnership will contribute c SEK10m to Nuevolution's revenue stream. We note that there is significant sensitivity around our forecast revenue streams as we have limited visibility on the progress of the Amgen, Almirall and Janssen partnerships. Amgen and Almirall payments make up the majority of our revenue expectations in this financial year (FY19) and either failure to achieve this or changes to the timing/size of the payments would have a material effect on our forecasts. We will continue to monitor both Almirall and Amgen and may look to readdress these assumptions in H219 if no external announcements have been forthcoming.

R&D costs decreased slightly on the previous year to SEK91.0m (FY17: SEK107.3m) due to a reduction in expenses related to external CROs (toxicology tests) and lower patent expenses; however, costs continue to be mainly driven by the two most advanced programmes (BET-BD1 and RORγt). SG&A remained essentially flat at SEK28.5m (FY17: SEK28.3). We forecast FY19 R&D and SG&A of SEK91.9m and SEK24.2m, respectively. The reduction in SG&A forecasts for FY19 over FY18 is a result of the one-off associated costs that arose from the Nasdaq up-listing in FY18.

Nuevolution received a tax reimbursement of SEK7.6m (vs SEK6.3m) as a result of the Danish R&D tax credit programme. The net loss for year was SEK99.7m vs SEK117.6m in the previous period.

Net cash as of 31 December 2018 of SEK108.6m (gross cash SEK111.1m) should be sufficient for Nuevolution to operate in FY19 without need for additional revenue from either existing or new partnerships. We note that we have updated our historical financials to reflect the new December year end (from June previously) and the restated accounts.

Valuation: SEK20.7/share (SEK1,026m)

We value Nuevolution at SEK20.7/share (SEK1,026m), compared with SEK19.7/share (SEK974m) previously. This increase is predominately due to rolling forward the model, in addition to updating net cash and FX rates. Our underlying operational assumptions remain unchanged.

Our valuation of SEK1,026m including net cash of SEK108.0m is based exclusively on a risk-adjusted model of the future milestones we expect from the Almirall (SEK9.7 per share), Amgen (SEK8.4 per share) and Janssen (SEK0.5 per share) deals using a 12.5% discount rate. Our operational assumptions for Almirall, Amgen and Janssen remain unchanged. We note that in the near term, two key sensitivities remain in the timing and size of expected milestones from both the initiation of Almirall's Phase I trial (forecast for FY19) and Amgen taking the option on one of the research projects (forecast for FY19). Specifically for the Amgen deal, our valuation is based purely on potential development milestones, with no value included from product launches. For Almirall, the majority of the value lies in milestone payments (63%), given the long timeframe to potential launch of the product, with a smaller contribution from royalties on sales (37%).

We have not ascribed value at this point to the unique platform and multiple early stage candidates. We note that the ability to attract and secure deals for these assets will be key to the evolution into a profitable operation and that any new deals would add upside to our current valuation. We note that lead programmes RoRγt inhibitor (outside of Almirall's selected indications) and BET-BD1 at this stage seem the most likely to be partnered or out licensed. We would expect any out-licensing deals terms to be similar to those of the 2016 Almirall deal. As such, we believe any potential deal could add approximately SEK10/share to our valuation, an approximate 50% potential upside. However, due to uncertainties on exact indications, markets and clinical status, the number could vary substantially from this estimate.

Exhibit 6: Sum-of-the-parts NPV

Product	Partner	Indication	Phase	NPV of milestone payments (SEKm)	rNPV of milestone payments (SEKm)	NPV of royalties on sales (SEKm)	rNPV of royalties on sales (SEKm)	Total rNPV (SEKm)	Total rNPV/ share (SEK)
RORγt inhibitor	Almirall	Psoriasis & PsA	Preclinical	1,324.0	300.4	1782.1	178.2	478.6	9.7
Various	Amgen	Oncology & neuroscience	Drug discovery	808.8	416.0	0.0	0.0	416.0	8.4
	Janssen	Anti-infective	Drug discovery	52.5	23.3	0.0	0.0	23.3	0.5
Net cash (at 31 December 2018)								108.0	2.2
Valuation								**1,026.0**	**20.7**

Source: Edison Investment Research

Almirall assumptions

We continue to assume $1.9bn indicative peak sales (2032) in the US and Europe, launch in 2027 in both regions, an 8% royalty rate on sales and a 10% probability of achieving NDA and approval milestones. Our deal milestone estimates are c €8m on the start of Phase I in 2019; c €16m on start of Phase II in FY19/20; c $34m on start Phase III in FY23/24; c €52m on NDA filing; and €65m on approval in FY27. These anticipated milestones are key to our near-term forecasts and as such any change in the timings or size of these would have a material effect on our valuation.

Amgen assumptions

Given the unknowns in the Amgen deal, in terms of timing, number of targets and specific therapeutic indications, we have made some general assumptions outlined below to derive a contribution of SEK8.4 a share to our valuation.

We continue to forecast three Nuevolution/Amgen programmes are in-licensed by Amgen in 2019, 2020 and 2021, precipitating an estimated ~SEK101.5m ($12.3m) in milestones each year as a result of Amgen exercising its option to take forward the individual assets. We assume that Nuevolution incurs no further R&D costs for the two opted-in Amgen programmes (according to the terms of the partnership agreement). We note these assumptions on milestones remain a significant sensitivity to our valuation, and any changes in the timing and size of these, or if they are never realised, would have a material impact on our valuation. We assume that no products make it to the market, which we believe is realistic considering industry drug approval rates. However, we note that the majority of current value rests in near-term clinical achievements more than would arise from any distant potential sales milestones. We assume that one product candidate makes it to a Phase III trial (20% probability), while the other two reach Phase II (30% probability) and Phase I (40% probability) trials. Revenue is inherently difficult to predict but we assume that milestones are activated upon classical development and business achievements (eg initiation of Phase I, II, III trials, NDA submission, launch and sales).

Janssen assumptions

We continue to estimate that Nuevolution currently has three Janssen assets in development, which we assume could be worth up to $30m per asset in milestone payments if they reach the market. However, due to the inherent risks in drug development we assume none of the products in development is approved and that one asset each starts a Phase I trial, a Phase II trial and a Phase III trial. As such, the total milestones per asset are adjusted to reflect the relative progress. We currently do not forecast royalties as the indications are unknown. As such, this could provide further upside to our valuation.

Exhibit 7: Financial summary

Accounts: IFRS; year end 31 December; SEK000s	2017*	2018*	2019e	2020e
Income statement				
Total revenues	12,222	10,973	202,369	336,646
Reported gross profit	12,222	10,973	202,369	336,646
SG&A (expenses)	(28,258)	(28,489)	(24,216)	(24,458)
R&D costs	(107,331)	(90,958)	(91,868)	(92,786)
Adjusted EBIT	(123,059)	(106,108)	86,286	219,402
Reported EBIT	(123,059)	(106,108)	86,286	219,402
Finance income/ (expense)	(778)	(1,183)	958	1,513
Adjusted PBT	(123,837)	(107,291)	87,244	220,915
Reported PBT	(123,837)	(107,291)	87,244	220,915
Income tax expense	6,278	7,568	(30,535)	(77,320)
Adjusted net income	(117,559)	(99,723)	56,709	143,595
Reported net income	(117,559)	(99,723)	56,709	143,595
Earnings per share				
Basic EPS (SEK)	(2.7)	(2.2)	1.1	2.9
Diluted EPS (SEK)	(2.7)	(2.1)	1.1	2.7
Adjusted basic EPS (SEK)	(2.7)	(2.2)	1.1	2.9
Adjusted diluted EPS (SEK)	(2.7)	(2.1)	1.1	2.7
Average number of shares - basic (m)	42.9	45.9	49.5	49.5
Average number of shares - diluted (m)	43.7	46.8	52.8	52.8
Number of shares outstanding -end period (m)	42.9	49.5	49.5	49.5
Balance sheet				
Property, plant and equipment	6,340	5,178	5,419	5,648
Other non-current assets	0	0	0	0
Total non-current assets	11,674	10,759	11,000	11,229
Cash and equivalents	114,758	111,101	166,568	308,934
Trade and other receivables	0	0	0	0
Other current assets	0	0	0	0
Total current assets	125,084	123,527	178,994	321,360
Non-current loans and borrowings	2,810	1,813	1,813	1,813
Total non-current liabilities	2,810	1,813	1,813	1,813
Trade and other payables	0	0	0	0
Current loans and borrowings	1,375	1,243	1,243	1,243
Other current liabilities	3,032	0	0	0
Total current liabilities	22,857	16,696	15,696	14,696
Equity attributable to company	111,091	115,777	172,486	316,080
Cash flow statement				
Profit before tax	(123,837)	(107,291)	87,244	220,915
Depreciation of tangible assets	1,770	1,860	259	271
Share based payments	186	(118)	0	0
Other adjustments	778	1,183	(958)	(1,513)
Movements in working capital	101,967	(5,385)	0	0
Net cash from operating activities (pre-tax)	(19,136)	(109,751)	86,545	219,673
Interest paid / received	(788)	(1,240)	958	1,513
Income taxes paid	(12,984)	5,046	(30,535)	(77,320)
Cash from operations (CFO)	(32,908)	(105,945)	56,967	143,866
Capex (includes acquisitions)	(1,234)	(266)	(500)	(500)
Other investing activities	(9)	(28)	0	0
Cash used in investing activities (CFIA)	(1,243)	(294)	(500)	(500)
Net proceeds from issue of shares	0	104,201	0	0
Other financing activities	(1,412)	(1,345)	(1,000)	(1,000)
Cash from financing activities (CFF)	(1,412)	102,856	(1,000)	(1,000)
Increase/(decrease) in cash and equivalents	(35,563)	(3,383)	55,467	142,366
Cash and equivalents at beginning of period	147,682	114,758	111,101	166,568
Cash and equivalents at end of period	114,758	111,101	166,568	308,934

Source: Edison Investment Research, Nuevolution accounts. Note: *Restated following change of year end.

Contact details	Revenue by geography
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Management team

Chief Executive Officer: Alex Haahr Gouliaev	Chief Financial Officer: Johnny Stilou
Alex Haahr Gouliaev holds an MSc and a PhD in chemistry from Aarhus University, Denmark. He is a co-founder of Nuevolution and served as executive vice president, chemistry and drug discovery from 2001 until he was appointed CEO in September 2005. Prior to co-founding Nuevolution, he was director of medicinal chemistry, member of the management group, and a member of the board of directors at NeuroSearch, where he worked for six years.	Johnny Stilou holds an MSc in business economics & auditing from Copenhagen Business School. Johnny joined Nuevolution in February 2018 and has extensive experience in biotech and medtech. His most recent position was as CFO with Fritz Schur Technical Group. From 2008–16 he was CFO at Veloxis Pharmaceuticals, a Nasdaq Copenhagen-listed mid-cap company. Johnny has extensive experience in investor relations, financing and M&A. Originally, he was an auditor at KPMG.
Chief Scientific Officer: Thomas Franch	**Chief Business Officer: Ton Berkien**
Thomas Franch holds an MSc and a PhD in molecular biology from Odense University, Denmark. Thomas joined Nuevolution in 2001, and has been a key scientist for the development and patent protection of the Chemetics technology. From 2006, he served both as chief technology officer and director of biology, leading the company's biology function and technological efforts including process optimisation. Thomas was appointed chief scientific officer in 2012. Prior to joining Nuevolution, Thomas was the CEO of RNA Tech Aps.	Ton Berkien joined the company in 2014. His most recent position was at Takeda/Nycomed, where he was acting head of corporate development/M&A, responsible for several M&A transactions. Prior to Takeda, he held a similar position at Nycomed Pharmaceuticals. During 2003–07, Ton was director of competitive intelligence at Ferring Pharmaceuticals.

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SEB Venture Capital	20.4
Stiftelsen Industrifonden	18.2
SEB Utvecklingsstiftelse	6.6
SEB-Stiftelsen	5.0
Avanza Pensionförsäkrings AB	3.2

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