13/01/2022

Abliva

Gearing Up For KL1333's Pivotal Study

Sponsored Research

Price: SEK 0.54
Target Price: SEK 2.25

Analysts
Naresh Chouhan
naresh@intronhealthresearch.com
+44 207 375 9143
Dominic Rose
+44 207 375 9141

With Abliva on the brink of advancing KL1333 to the final stage of clinical development, we provide an update to the investment thesis. Since May, the company has reported positive first-in-human data for KL1333, used that data to design a registrational P2/3 study, received validation from the FDA on their dual endpoint and submitted and received approval for an IND. The next step is to secure financing for the ~2 years to run the trial, which we estimate will require $30-40m, giving financial runway to the end of 2023. Click [HERE] to download our initiation.

KL1333 Ready For Pivotal P2/3 Study

In May, Abliva reported strong early-stage data for KL1333 in 8 patients (6 treated with KL1333, 2 with placebo), showing dose-dependent improvements in two patient-reported fatigue endpoints and a functional endpoint, the 30-second Sit-to-Stand test. This provided the data needed to design the pivotal study, for which preparations are underway.

FDA Validates Dual Primary Endpoints For KL1333 Pivotal Trial

KL1333's pivotal trial will have dual primary endpoints, meaning they can file on a positive outcome on either and this approach has been validated by the FDA. The statistical power of the dataset is reduced by just ~15%.

IND Has Now Been Received For KL1333

With previous KL1333 clinical trials done in the UK & Korea, Abliva has now secured an IND, allowing them to initiate the US study when ready.

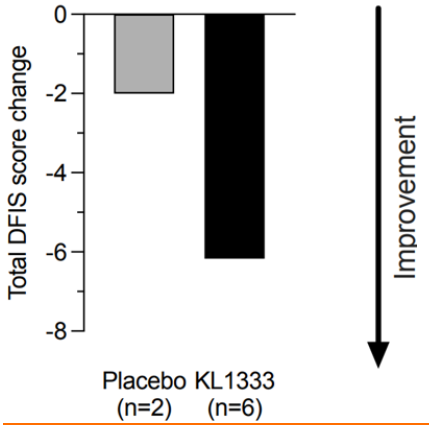
Further Capital to be Raised Imminently

We estimate that Abliva will likely need $30-40m in additional financing for the 2-year pivotal clinical trial (the final readout is most likely due around mid-2024 in our view).

NV354 to Progress to Clinical Development Next Year

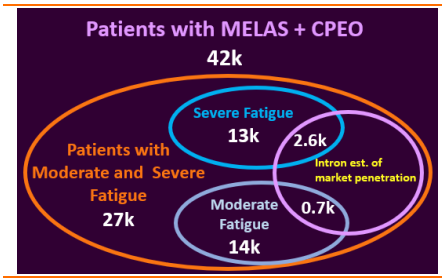
Abliva's second asset, NV354, also targeting a subset of mitochondrial diseases, received favourable feedback from the UK's MHRA and will now move into the clinic, with a P1 trial planned for H122.

Daily Fatigue Impact Score Change from Day 1 to Day 10



Source: Company reports

Target Population for KL1333 (Intron)



Source: Intron Health estimates

Summary Financials

	20A	21E	22E	23E
Sales (SEKm)	0.2	0.2	0.2	0.2
EPS (SEK)	-0.24	-0.32	-0.22	-0.25
Net cash (SEKm)	61.6	18.3	22.3	-167.4
Market cap ($m)	24			

Source: Intron Health estimates

Contents

KL1333 to Initiate Pivotal Phase 2/3 Trial

The pivotal Phase 2/3 study for Abliva's lead asset KL1333 is expected to soon initiate following feedback from the FDA that the two selected alternate primary endpoints of "mitochondrial disease-specific fatigue" and "30-second Sit to Stand assessment" are suitable. These endpoints have been clinically validated and given the lack of treatment options, Abliva could potentially file if they hit either of them, effectively providing them with a double-shot at approval. The regulator has also approved their IND application. Assuming a start in the near-term, the trial is expected to read out in mid-2024, leading to a potential launch in mid-2025.

PMD-Specific Endpoints Validated

Following the completion of the validation study and FDA feedback, the dual endpoints of "mitochondrial disease-specific fatigue" and "30-second Sit to Stand assessment" have been selected as the primary endpoints.

- **Fatigue** is a hallmark of mitochondrial disease and will be assessed using a patient-reported fatigue outcome measure (based on NeuroQol and PROMIS fatigue ePROs) that the company validated for use in PMD patients. This measure considers factors including cognition, behaviour, communication, sleep and life participation.
- The functional **30-second Sit to Stand** endpoint consists of the scoring of subjects according to how many repetitions of sitting to standing they can achieve, with a higher score implying better muscle strength and endurance.

Pivotal Trial Readout Possible By Mid-2024

The pivotal trial will assess adult PMD patients, with subjects receiving 1 year of treatment. Abliva expect to conduct a futility analysis 1 year after trial initiation (mid-2023), but it will be too soon for any efficacy figures to be disclosed. We believe that we could see a full efficacy readout in mid-2024, which if positive, is likely to be fileable.

Study Design Gives Two Shots on Goal

Abliva have discussed their design for having two primary endpoints with the FDA and met with an encouraging response. They believe that if either endpoint is statistically positive, the trial is likely to be deemed a success. We understand that having dual endpoints is only expected to reduce the statistical power of the dataset by 15%, which seems like a sensible trade off to us. Additionally, due to the limited in-clinic participation required to conduct this trial (participants will attend in-clinic settings a maximum of 4 times), this trial has a low risk of being adversely impacted by COVID and is therefore likely to remain on track.

Table 1: KL1333 Registrational Study Design

Trial	
Design	Randomised, double-blind, parallel- group, placebo-controlled (2 placebo: 3 active)
Patients	N=120-180 (Determined at interim futility analysis) Adult primary mitochondrial disease patients with: - Multisystemic mitochondrial DNA-related disease. - Chronic fatigue - Mitochondrial myopathy/ exercise intolerance
Regimen	Oral 2x daily dosing for 12 months
Endpoints	
Primary	Fatigue 30 Second Sit to Stand
Secondary	Clinician and Patient Global Impression of Disease Severity, NMDAS, patient specific activity assessments
Interim futility analysis	Mid-2023
Study Readout	Mid-2024

Source: Company reports

Issuance Needed Before Trial Start

Before committing to a 2-year study (12-14 month enrolment phase and 12 month treatment phase), Abliva will need to secure their financial runway in our view. The company is not new to raising capital - in March 2021, they announced that they had raised SEK 80m by issuing 106.7m new shares at SEK 0.75 / share, a discount of just 1.3% to the closing share price on 30th March. This built on the SEK54.1m in new equity raised in May 2020 by issuing 83.7m new shares. Following the IND approval of KL1333, Abliva will need to raise a further $30-40m in our view to conduct the registrational P2/3 clinical study. This amount would extend the financial runway to the end of 2023 / start of 2024. For simplicity, in the table below, we assume a 300m share issuance on 1st January 2022 (~$18m at the current share price), which gives the company visibility to the end of 2022. Our valuation fully accounts for the cost of bringing KL1333 to market and launching over 2021-27.

Table 2: History of rights issues expected to continue

Shares (m)	**2019A**	**2020A**	**2021**	**2022**
Average share count for prior year	**78,500**	**171,575**	**250,321**	**378,588**
Issuance	93,075	78,746	80,025	300,000
Buybacks		0	0	0
Other		0	48,242*	26,675*
Average share count for year	**171,575**	**250,321**	**378,588**	**705,263**
Actual number of shares on 31st Dec	185,953	296,340	403,007	
Share issuance raise		**72,564**	**80,000**	**159,000**
Cash and cash equivalents	**58,319**	**61,643**	**18,256**	**22,347**

*Source: Company reports, Intron Health estimates * Adjustments for phasing of share issuances*

KL1333 is a First in Class Treatment for PMD

KL1333 is an orally administered small organic molecule derived from β-lapachone, a quinone-containing compound obtained from the Lapacho tree. It is in development for the treatment of adults with primary mitochondrial disease, the majority of which will be within the spectrum of MELAS-MEDD and CPEO-KSS (together which account for approx.

40% of PMD). These diseases cause a wide range of severe symptoms, most particularly fatigue and there are around 40,000 patients in the US and Europe. The drug holds Orphan Drug Designation in both regions. Abliva in-licensed KL1333 from Yungjin Pharm and have exclusive global rights for the drug, excluding Korea and Japan.

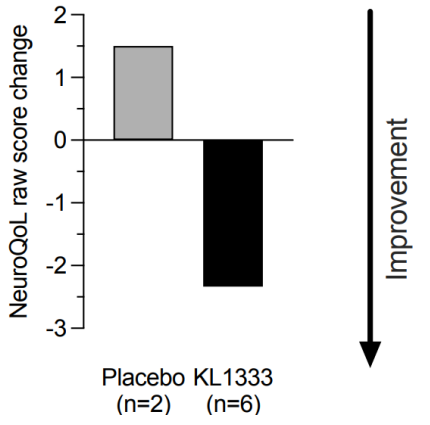
KL1333 treats mitochondrial disease by increasing the concentration of NAD+ to normal levels. This increased NAD+/NADH ratio has a two-pronged effect which helps to treat the underlying condition by increasing ATP production and increasing mitochondrial biogenesis. Based on our assumptions, we believe the drug could generate up to $150m/year ($750m/year when fully de-risked) and we value it at SEK2.41/share based on a 2024 launch.

Recent Data Has Been Highly Positive

In May, Abliva reported positive human efficacy signals in their phase 1a/b trial for KL1333 in primary mitochondrial disease (PMD). This is the first human efficacy data that Abliva have reported for their lead asset and as such is an encouraging and important development.

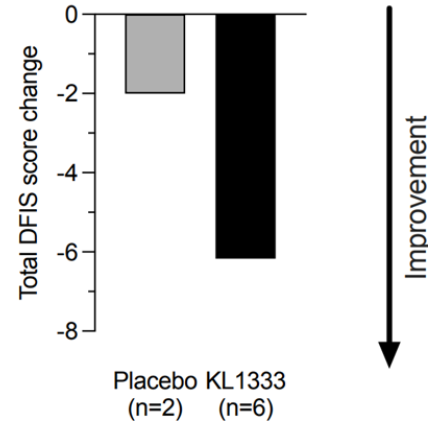
The positive data was generated by a cohort of eight PMD patients within the study, six of whom were dosed with KL1333 and two with placebo. This cohort was not powered to show superiority, but the patients that received KL1333 had numerically superior improvements in two patient-reported fatigue endpoints and the 30-second Sit-to-Stand endpoint. For the latter measure, there was almost a 2 repetition difference from baseline - an improvement of ≥2 repetitions has been defined as the minimum clinically significant difference.

Chart 1: Neuro-QoL SF Fatigue Change from baseline to Day 10



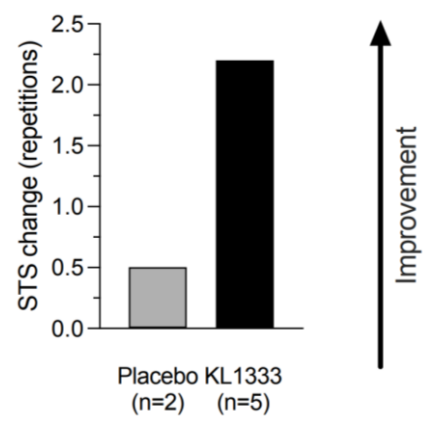
Source: Company reports

Chart 2: Daily Fatigue Impact Score Change from Day 1 to Day 10



Source: Company reports

Chart 3: 30s Sit to Stand Change from baseline to Day 10



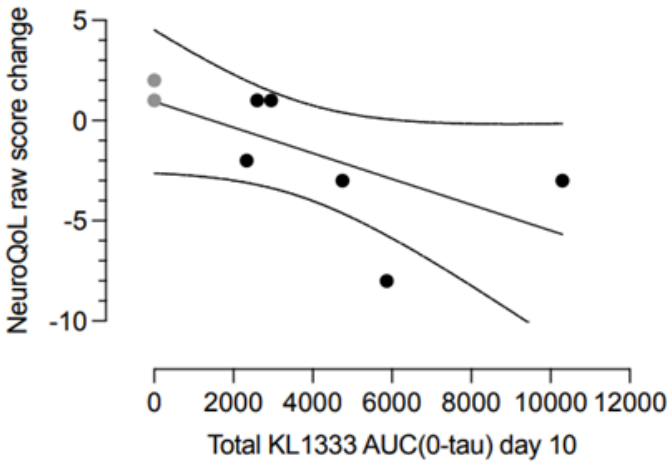
Source: Company reports

Improvements were Dose-Dependant

Importantly, a dose-dependent effect was found, implying that KL1333 was the likely driver of those differences. Only 10 days of dosing was carried out, so this data provides evidence that KL1333 also acts rapidly.

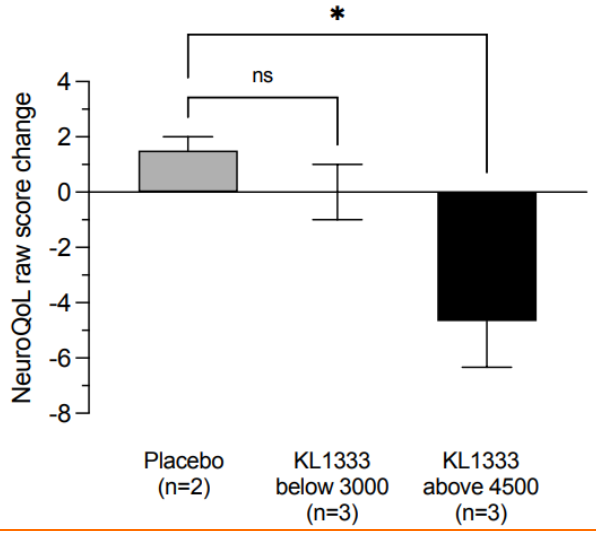
Moreover, patients were only dosed up to 50mg/day of KL1333, which was deliberately low and in the next study this dose will increase to 100mg/day, so even stronger data is a possibility. No serious adverse safety signals were found in the trial (in both healthy volunteers or the eight person PMD cohort) and further supportive pharmacokinetic data was generated.

Chart 4: Neuro-QoL SF Fatigue



Source: Company reports

Chart 5: Neuro-QoL SF Fatigue



Source: Company reports

Good Safety Profile

KL1333 has a strong safety profile with over 100 healthy volunteers and patients dosed throughout development with no serious adverse events or safety signals. The asset is generally well tolerated with the main dose-limiting factor being gastrointestinal side effects, which was improved by administering smaller amounts of KL1333 two-three times a day rather than once.

In a completed pharmacology study assessing the interaction of KL1333 with seven CYP enzymes responsible for metabolising drugs, the asset was found to only mildly inhibit CYP1A2, one of the less common enzymes. As CYP enzymes are often essential for the metabolism of some medicines, this lack of significant inhibition is an important feature of KL1333 that should enable safe co-administration of other drugs.

KL1333's US IND Has Received FDA Approval

Abliva received FDA approval of their Investigational New Drug (IND) application for KL1333 in November 2021, allowing the start of their registrational study in 2022.

An IND approval signifies a successful preclinical program, as the drug candidate is now deemed by regulators to be safe for human trials. This is evidenced by preclinical data in animal pharmacology and toxicology studies, stability and manufacturing information, as well as detailed

protocols for proposed clinical trials to assess whether initial trails will expose subjects to unnecessary risk. Previous clinical trials have been carried out in the UK and Korea, so a US IND has not been required.

Few Competitors For a Multi-$Bn Market

There are no FDA-approved therapies for the treatment of mitochondrial disease with the current standard of care focused on symptom alleviation. Several assets are in development for various mitochondrial diseases. Competitors also choosing to examine Fatigue in their studies include Mitobridge, Khondrion and RENEO.

Table 3: Assets in development for mitochondrial diseases

Asset	Company	Phase	Indication	Trial	Regimen	Primary Endpoints	Secondary Endpoints	Readout
Vatiquinone (PTC743)	PTC Therapeutics	Pivotal Ph2/3	Mitochondrial epilepsy	MIT-E NCT04378075	Vatiquinone 15mg/kg, 3x per day vs placebo	Change in observable motor seizures per 28 days	Disease-related hospital days, Status epilepticus occurrence, Seizure frequency, CarerQoL-7D	Q322
MA-0211 (ASP0367)	Mitobridge (Astellas)	Pivotal Ph2/3	PMM	MOUNTAINSIDE NCT04641962	Low/High dose ASP0367 1x daily vs placebo	6-minute walk test, Safety, Pharmacokinetics,	5 Times Sit to Stand test, Neuro-QoL SF Fatigue, Modified Fatigue Impact Scale, Patient Global Impression of Change	2023
Sonlicromanol	Khondrion	Ph2b	MELAS adult	KHENERGYZE	50/100mg Sol vs placebo	Cognitive functioning	Executive, Psychomotor, Working memory assessed by Cogstate computerised testing	2022
		Ph2	MELAS	KHENERGYC	Paediatric equiv dose Sol vs placebo	Gross Motor Function Measure - 88	9 Hole Peg Test – motor skill Dystonia, Ataxia PEDI-CAT NeuroQL-SF	2022
REN001	RENEO	Ph2	PMM	STRIDE NCT04535609	100mg REN001 orally 1xdaily vs placebo	Distance walked during Walk test	Modified Fatigue Impact Scale Patient Global Impression of Change Score	2023
KL13333	Abliva	Pivotal Ph 2/3	PMD	FALCON	Oral 2x daily dosing	Fatigue 30s Sit to Stand	Clinician and Patient Global Impression of Disease Severity NMDAS Patient specific activity assessments	2023

Source: Company reports, clinicaltrials.gov

NV354 to Progress to Clinic in 2022

Abliva's second asset NV354 will move into the clinic having received favourable feedback from the UK regulatory authority, the MHRA. The company has identified a suitable formulation and will continue to assemble the preclinical documentation for a Clinical Trial Application to facilitate the start of the Phase I trial in 2022. This favourable verdict is significant as it provides further external validation for this molecule and the company's technology.

We see ~4x Upside to Current Price

We value Abliva using a Sum-of-the-Parts methodology. We only value the cash flows over 2021-37 and do not include a terminal value in our calculations. We also use very high-risk adjustments and ignore some potential sources of value including off-label sales, regional sales outside of US/EU/UK and all of the R&D programmes outside of KL1333 and NV354. Our SOTP implies a target price of SEK2.25/share and assumptions include:

- WACC of 11%
- Tax of 21.4% (Swedish corporate tax rate after tax losses used up)
- R&D and G&A expenses to 2027 are NPV'd and deducted; this is sufficient to bring the two major drugs to approval

Table 4: Intron Health valuation of Abliva

	Value (SEKm)	Value / share (SEK)
KL1333 (risk-adjusted)	1,828	2.59
NV354 (risk-adjusted)	416	0.59
Other revenues to 2025	1	0.00
Corporate & R&D costs to 2027	-678	-0.96
Net (debt) cash in 2022	22	0.03
Total (risk-adjusted) value	**1,588**	**2.25**
Target price		**2.25**
Share price	0.54	
Upside multiple	**4.2x**	

Source: Intron Health estimates

Financial Statements

Group P&L

Table 5: Abliva AB P&L

SEK (000s)	2020A	2021	2022	2023	2024	2025	2026	CAGR 21-26
Revenues	**216**	**214**	**214**	**214**	**214**	**89,234**	**300,376**	**326.2%**
growth	*61%*	-1%	0%	0%	0%	41696%	237%	
Cost of goods	0	0	0	0	-21	-8,923	-30,038	
growth						N/A	236.6%	
as % of sales	0.0%	0.0%	0.0%	0.0%	-10.0%	-10.0%	-10.0%	
Royalties paid out	0	0	0	0	0	-872	-3,259	
Gross profit	**216**	**214**	**214**	**214**	**192**	**79,439**	**267,079**	**316.3%**
Gross margin	***100.0%***	**100.0%**	**100.0%**	**100.0%**	**90.0%**	**89.0%**	**88.9%**	
External expenses	-46,072	-101,358	-131,766	-151,531	-169,715	-186,686	-205,355	15.2%
growth	*-27.0%*	120.0%	30.0%	15.0%	12.0%	10.0%	10.0%	
as % of sales	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
Personnel cost	-13,305	-17,962	-20,656	-23,754	-28,505	-41,333	-59,932	27.3%
growth	*-10.5%*	35.0%	15.0%	15.0%	20.0%	45.0%	45.0%	
as % of sales	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
D&A	-2,558	-2,632	-2,510	-2,520	-2,794	-3,117	-3,446	
as % of sales	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
OOI/OOE	1,648	-600	0	0	0	0	0	-100.0%
as % of sales	*763%*	-281%	0.0%	0.0%	0.0%	0.0%	0.0%	
EBIT	**-60,071**	**-122,339**	**-154,718**	**-177,591**	**-200,821**	**-151,696**	**-1,654**	**-57.7%**
EBIT margin	*N/A*	N/A	N/A	N/A	N/A	-170.0%	-0.6%	
growth	*-22.1%*	103.7%	26.5%	14.8%	13.1%	-24.5%	-98.9%	
Interest expense	-30	-12	-12	-12	-12	-12	-12	
Interest received	107	0	0	0	0	0	0	
Associates/JVs	0	0	0	0	0	0	0	
Pre-tax profit	**-59,994**	**-122,351**	**-154,730**	**-177,603**	**-200,833**	**-151,708**	**-1,666**	
Tax	0	0	0	0	0	0	0	
Effective tax rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	
Net profit	**-59,994**	**-122,351**	**-154,730**	**-177,603**	**-200,833**	**-151,708**	**-1,666**	
Minorities	5	0	0	0	0	0	0	
Net income	**-59,989**	**-122,351**	**-154,730**	**-177,603**	**-200,833**	**-151,708**	**-1,666**	**-57.7%**
Number of shares (basic, 000s)	250,321	378,588	705,263	705,263	705,263	705,263	705,263	
EPS	**-0.24**	**-0.32**	**-0.22**	**-0.25**	**-0.28**	**-0.22**	**0.00**	**-62.6%**
growth	***-46.6%***	**34.8%**	**-32.1%**	**14.8%**	**13.1%**	**-24.5%**	**-98.9%**	

Source: Intron Health estimates

Group Balance Sheet

Table 6: Abliva AB balance sheet

SEK (000s)	2020A	2021	2022	2023	2024	2025	2026
ASSETS							
Intangible assets	74,021	75,403	75,961	88,528	103,321	118,381	133,712
PP&E	384	365	347	329	313	297	282
Associates	13,101	13,101	13,101	13,101	13,101	13,101	13,101
Other non-current assets	0	0	0	0	0	0	0
Non-current assets	**87,506**	**88,869**	**89,408**	**101,958**	**116,735**	**131,779**	**147,095**
Inventories	0	0	0	0	64	17,847	60,075
Trade/other receivables	928	1,021	1,123	1,235	1,359	1,495	1,644
Other current assets	586	586	586	586	586	586	586
Cash & cash equivalents	61,643	18,256	22,347	-167,410*	-382,649*	-566,705*	-625,389*
Non-current assets	**63,157**	**19,863**	**24,056**	**-165,589***	**-380,641***	**-546,778***	**-563,083***
Total assets	**150,663**	**108,732**	**113,464**	**-63,631***	**-263,905***	**-414,999***	**-415,988***
LIABILITIES							
Borrowings	0	0	0	0	0	0	0
Other non-current liabilities	92	92	92	92	92	92	92
Non-current liabilities	**92**	**92**	**92**	**92**	**92**	**92**	**92**
Borrowings	0	0	0	0	0	0	0
Trade payables	4,201	4,621	5,083	5,592	6,151	6,766	7,442
Provisions	0	0	0	0	0	0	0
Other current liabilities	6,008	6,008	6,008	6,008	6,008	6,008	6,008
Current liabilities	**10,209**	**10,629**	**11,091**	**11,600**	**12,159**	**12,774**	**13,450**
Total liabilities	**10,301**	**10,721**	**11,183**	**11,692**	**12,251**	**12,866**	**13,542**
EQUITY							
Share capital	14,817	14,817	14,817	14,817	14,817	14,817	14,817
Additional paid in capital	660,025	740,025	899,025	899,025	899,025	899,025	899,025
Translational reserves	616	616	616	616	616	616	616
Retained earnings (losses)	-535,096	-657,447	-812,177	-989,781	-1,190,614	-1,342,322	-1,343,988
Minority interests	0	0	0	0	0	0	0
Total equity	**140,362**	**98,011**	**102,281**	**-75,323***	**-276,156***	**-427,864***	**-429,530***
Total liabilities and equity	**150,663**	**108,732**	**113,464**	**-63,631**	**-263,905**	**-414,999**	**-415,988**

Source: Intron Health estimates

** Abliva will need to conduct a raise, but we do not currently forecast this due to the uncertainty of timing and amounts (but our valuation factors in these costs)*

Group Cash Flow

Table 7: Abliva AB Cash Flow

SEK (000s)	2020A	2021	2022	2023	2024	2025	2026
Operating income	-60,071	-122,339	-154,718	-177,591	-200,821	-151,696	-1,654
D&A	2,558	2,632	2,510	2,520	2,794	3,117	3,446
Other non-cash adjustments	107	0	0	0	0	0	0
Change in inventories	0	0	0	0	-64	-17,783	-42,228
Change in trade receivables	0	-93	-102	-112	-124	-136	-149
Change in trade payables	0	420	462	508	559	615	677
Other working capital movements	-10,122	0	0	0	0	0	0
Interest received	0	0	0	0	0	0	0
Interest paid	-30	-12	-12	-12	-12	-12	-12
Tax paid	0	0	0	0	0	0	0
Cash flow from operations	**-67,558**	**-119,391**	**-151,860**	**-174,688**	**-197,668**	**-165,895**	**-39,921**
Purchase of PP&E	0	-35	-33	-31	-30	-28	-27
Disposals of PP&E	0	0	0	0	0	0	0
Purchase of intangibles	-1,407	-2,961	-3,016	-3,038	-3,541	-4,133	-4,735
Milestones paid out	0	-1,000	0	-12,000	-14,000	-14,000	-14,000
Cash flow from investment	**-1,407**	**-3,995**	**-3,049**	**-15,070**	**-17,571**	**-18,161**	**-18,762**
Proceeds from share issuance	72,564	80,000	159,000	0	0	0	0
Other	-269	0	0	0	0	0	0
Cash flow from financing	**72,295**	**80,000**	**159,000**	**0**	**0**	**0**	**0**
Beginning cash & cash equivalents	**58,319**	**61,643**	**18,256**	**22,347**	**-167,410**	**-382,649**	**-566,705**
Change in cash	3,330	-43,387	4,091	-189,757	-215,239	-184,056	-58,683
FX impact	-6	0	0	0	0	0	0
Ending cash & cash equivalents	**61,643**	**18,256**	**22,347**	**-167,410***	**-382,649***	**-566,705***	**-625,389***

Source: Intron Health estimates

** Abliva will need to conduct a raise, but we do not currently forecast this due to the uncertainty of timing and amounts (but our valuation factors in these costs)*

General Disclosures and Disclaimer

Full 12-month historical recommendation changes are available on request

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