EDISON

Atossa Genetics

Clinical update

Endoxifen to start Phase II studies shortly

Pharma & biotech

Atossa Genetics is preparing to start Phase II studies of both its oral and topical endoxifen formulations in Q218. Endoxifen, an estrogen receptor (ER) antagonist, is being advanced in topical form to treat high mammographic breast density (MBD), and also as an oral drug to prevent cancer recurrence in women refractory to tamoxifen. The company plans to raise $20m in equity through a rights offering in May 2018, which we believe should fund the Phase II endoxifen trials through completion.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/16	0.0	(7.2)	(29.52)	0.0	N/A	N/A
12/17	0.0	(7.2)	(10.01)	0.0	N/A	N/A
12/18e	0.0	(11.2)	(4.23)	0.0	N/A	N/A
12/19e	0.0	(7.2)	(2.70)	0.0	N/A	N/A

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

More rapid steady-state levels with oral endoxifen

In February 2018, Atossa reported new data from its prior Phase I study, suggesting that the median time for patients to reach the steady-state serum levels of endoxifen while taking daily oral doses was seven days vs 50-200 days for patients taking oral tamoxifen daily. Oral endoxifen may thus provide therapeutic plasma endoxifen levels weeks or even months earlier than oral tamoxifen, which may potentially provide a more rapid onset of therapeutic effect.

Topical endoxifen study started in men

Atossa is advancing its topical endoxifen for gynecomastia (male breast enlargement), and that it started a 24-patient Phase I study of topical endoxifen in men. There are no FDA-approved therapeutics for gynecomastia, although selective estrogen receptor modulation (SERM) drugs such as tamoxifen have been used off-label. Topical endoxifen could potentially provide improved tolerability vs tamoxifen in this group, and may provide better assurances of therapeutic effect given that 6-10% of men do not metabolize tamoxifen effectively.

Valuation: Equity valuation of $30.0m

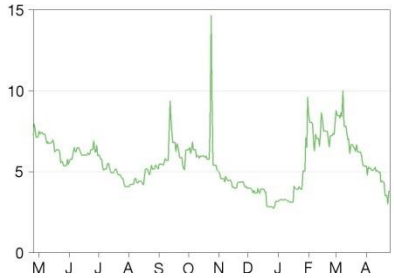
Atossa's 2017 operating cash burn rate was $6.6m, and we expect it to increase in 2018 to $11.5m, as the firm proceeds with larger Phase II studies on endoxifen. Atossa had $7.3m net cash at year-end 2017, and we expect its funds on hand to last into late Q318. After rolling forward our estimates, we now obtain an rNPV valuation of $24.7m, up from $18.4m previously. After including Q118 estimated net cash of $5.2m, we obtain an equity valuation of $30.0m (vs $24.6m previously), or $11.30 per fully diluted (FD) share (before considering any potential dilution from funding requirements). Atossa recently announced a rights offering to raise up to $20m in Series B Convertible Preferred Stock (SBCPS) and warrants in May 2018. If the rights are fully exercised and if SBCPS converted to common shares (CS), the number of CS outstanding will increase by 214%. As it is unknown how many rights will be exercised, we have not included this offering in our forecasts, but plan to update our model once the offering has concluded.

26 April 2018

Price	**US$3.72**
Market cap	**US$10m**

Estimated net cash ($m) at Q118	5.2
Shares in issue	2.65m
Free float	99%
Code	ATOS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(40.2)	(4.6)	(48.3)
Rel (local)	(41.3)	2.6	(53.2)

52-week high/low	US$14.6	US$2.7

Business description

Based in Seattle, WA, Atossa Genetics is a clinical-stage pharmaceutical firm developing therapeutics and delivery methods to treat breast cancer and other breast conditions. Intraductal microcatheter-delivered fulvestrant and endoxifen are both in clinical stages of development.

Next events

Start Phase II study of oral endoxifen	Q218
Start Phase II study of topical endoxifen	Q218

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Edison profile page

Endoxifen set to start Phase II trials

Atossa's lead product candidate, endoxifen, a tamoxifen metabolite intended to provide selective estrogen receptor (ER) antagonism for breast cancer prevention, is being prepared to start Phase II studies in Q218, for both topical and oral use. The topical formulation, applied like a lotion, is being advanced for the treatment of high mammographic breast density (MBD), a condition associated with increased risk for the development of breast cancer. There are no approved pharmaceuticals for the reduction of MBD. The oral formulation is being developed to prevent cancer recurrence in patients who do not benefit from taking (or who are refractory to) oral tamoxifen, often due to a genetic predisposition that impairs tamoxifen metabolism. Atossa reported positive top-line data from Phase I studies in both the oral and topical formulations in H217, which demonstrated favorable safety and early signs of pharmacokinetics.

Exhibit 1: Upcoming catalysts

Event	Timing
Start Phase II topical endoxifen study	Q218
Start Phase II oral endoxifen study	Q218
Guidance for completion of oral and topical endoxifen Phase II studies	H218

Source: Atossa Genetics

Tamoxifen is well established for the treatment and prevention of breast cancer, given its association with ER antagonistic effects (blocking estrogen from binding to its receptors). However, such therapeutic effects are only realized by a few of tamoxifen's active metabolites, and not by the parent molecule itself. When dosed orally, tamoxifen is metabolized in the liver by enzymes (including cytochrome P450 isoforms) into multiple metabolites, the most significant of which (in terms of ER antagonism contribution and plasma concentration in patients with normal tamoxifen metabolism) is endoxifen (4-hydroxy-N-desmethyltamoxifen) and, to a lesser extent, afimoxifene (4-hydroxytamoxifen).[1,2] Atossa believes that administering endoxifen can provide several advantages compared to tamoxifen.

Topical treatment seeks targeted efficacy with fewer AE

A topical formulation of endoxifen, if it can deliver significant targeted amounts of drug to breast tissue with minimal systemic absorption, could potentially play a meaningful therapeutic role by providing the local ER antagonistic therapeutic activity associated with tamoxifen, while reducing the risks of systemic adverse events (AE) associated with the oral drug (due to lowered/minimized systemic absorption).

Atossa believes that the optimal potential market for topical therapy (to deliver ER inhibition with less AE risk than oral drug) would be for the prevention or treatment of MBD. Breast tissue consists of lobules (glands), ducts, and fatty and fibrous connective tissue; generally, dense breast tissue has higher quantities of fibrous or glandular tissue and less fat content. According to the Breast Imaging Reporting and Data System (BI-RADS) defined by the American College of Radiology (ACR), there are four degrees of breast density composition (see Exhibit 2 below).

[1] *ClinPharmacolTher*. 2011 May;89(5):708-17. doi: 10.1038/clpt.2011.27.

[2] Schroth W, Antoniadou L, Fritz P, et al. *J ClinOncol.* 2007 Nov 20;25(33):5187-93.

Exhibit 2: Breast density composition categories (BI-RADS categories)

Type	Description
A	The breasts are almost entirely fatty
B	There are scattered areas of fibroglandular density
C	The breasts are heterogeneously dense, which may obscure small masses
D	The breasts are extremely dense, which lowers the sensitivity of mammography

Source: American College of Radiology

Tamoxifen is the only known approved prescription product that has been unequivocally shown to reduce breast density[3] although it has not been approved by the FDA for this purpose (MBD reduction). Further, due in part to the risks for AE (including thromboembolic complications), tamoxifen has not generally been employed for MBD reduction. Some studies suggest that oral acetylsalicylic acid (ASA) or other anti-inflammatories may reduce MBD too, but other studies have not found such an association.[4]

Studies link high breast density with cancer risk

A topical treatment with tamoxifen-like effects for reducing MBD and possibly fewer side effects could have a meaningful chemo-preventative market, given that a US study following over 202,000 women found that MBD is a significant independent predictor for increased breast cancer risk.[5] The study found that 39.3% of premenopausal and 26.2% of postmenopausal breast cancers could potentially be averted if all women with heterogeneously or extremely dense breasts (BI-RADS C or D) shifted to scattered fibroglandular breast density (BI-RADS B).

Phase I topical endoxifen data show safety and early signs of absorption

In H217, Atossa reported positive results from both the topical (n=24) and oral (n=24) administration arms of its Phase I safety study conducted in Australia on endoxifen. There were no clinically significant adverse events or safety or tolerability signals for either form in the placebo-controlled, repeat-dose, 28-day study on healthy female volunteers (aged between 18 and 65).

The Phase I topical arm data suggested that endoxifen may cross the skin barrier when applied daily to the breast, as measureable blood endoxifen levels increased in a dose-dependent manner (dose arms tested were 1mg, 3mg, and 5mg/breast). Atossa reported that each of the patients (in the treatment and placebo arms) treated topically were subject to an equal number of blood draws for the purpose of measuring plasma levels of endoxifen. In the draws, it measured the number of samples taken where the plasma endoxifen level was measured at or above 2ng/mL. In the treatment arms, there was a dose-related increase in the taken samples reaching the threshold: two in the 1mg/breast arm, seven in the 3mg/breast arm and 11 in the highest dose (5mg/breast) arm. However, it is challenging to estimate the actual significance of this dose-response effect, since the mean plasma level per group was not disclosed, the number of blood draws taken per patient or per treatment arm was not disclosed, and the relationship between therapeutic efficacy (in terms of reducing breast density) and the plasma endoxifen levels resulting from a topical breast administration have not been established.

The Phase II study on topical endoxifen scheduled to start in Q218 will be conducted at Stockholm South General Hospital in Sweden in affiliation with the Karolinska Institutet. Atossa initially planned a recruitment target of up to 480 patients, but this may be revised prior to enrolment as study specifics have not been finalized. The primary endpoint is MBD reduction as assessed through imaging (likely at three and/or six months following initial dosing), as well as safety and tolerability. The firm has guided that it plans to complete the study in H218.

[3] Cuzick J, Warwick J, Pinney E et al. *J Natl Cancer Inst*. 2004 Apr 21;96(8):621-8.

[4] McTiernan A, Wang CY, Sorensen B, et al. *Cancer Epidemiol Biomarkers Prev*. 2009 May;18(5):1524-30.

[5] Engmann NJ, Golmakani MK, Miglioretti DL et al. *JAMA Oncol*. 2017 Sep 1;3(9):1228-1236

Oral endoxifen for reducing cancer recurrence risk

Following surgical treatment for atypical hyperplasia (AH) or non-invasive estrogen-receptor-positive (ER+) breast cancers, additional oral treatment with a selective estrogen receptor modulation (SERM) drug such as tamoxifen or raloxifene (Evista) is often recommended. Approximately 75-80% of breast cancers are ER positive[6] (ie they grow in response to estrogen). A large-scale randomized study (IBIS-I), where over 7,000 women (aged 35-70 with elevated breast cancer risk) were randomized to five years of tamoxifen vs placebo, found that tamoxifen reduced breast cancer incidence in high-risk women by 30-50% over five years of treatment, for ER+ cancer. Despite evidence of reduced ER-positive breast cancer risk, SERM use has been limited to less than 1% of AH patients.[7] The low uptake is believed to be attributable to patients' fear of adverse effects of SERM drugs,[8] which include increased risks of thromboembolic events (including blood clots, stroke), menopausal symptoms and endometrial cancer.

The case for oral endoxifen reducing risk of recurrence results from several research groups having found that patients with deficiencies in certain cytochrome P450 enzymes (due to genetic factors, medication interactions or other factors) have an impaired ability to metabolize tamoxifen into endoxifen. Up to 15-20% of Europeans carry genetic P450 CYP2D6 variants associated with an impairment in forming anti-estrogenic tamoxifen metabolites.[9] Fox et al found that in 122 patients taking 20mg/day of tamoxifen (the standard dose), 24% had blood endoxifen levels of below 15nmol/L, and suggests that 15nmol/L of endoxifen may be the critical level needed for anticancer effect.[10] Multiple study groups (Fox, Madlensky, Saladores) have found that in patients taking tamoxifen, those with the lowest amounts of systemic endoxifen (resulting presumably from impaired tamoxifen metabolism) have higher risks of cancer recurrences (between 35% and 60% higher risk, depending on the study) than the remaining tamoxifen-treated patients.[11, 12].

Earlier attainment of steady state levels vs oral tamoxifen

As stated in our Outlook report published on 16 November 2017, in the oral endoxifen Phase I study, both the 2mg and 4mg oral treatment arms led to sustained plasma levels in excess of 30nmol/L until at least 24 hours post-administration. After 21 days of daily dosing, each of the three tested oral arms (1mg/day, 2mg/day, 4mg/day) led to plasma endoxifen levels well in excess of 30nmol/L, and the plasma concentration was dose-dependent (39.8nmol/L for the 1mg/day arm, rising to 187.8nmol/L for the 4mg/day arm). A potentially more meaningful study parameter is "steady-state" plasma endoxifen concentration after multiple doses. In February 2018, Atossa reported additional data from the Phase I study suggesting that the median time for patients in the study to reach the steady-state serum levels of endoxifen while taking daily oral endoxifen doses was seven days. Atossa reports that published literature indicates that it takes 50-200 days for patients to reach steady-state blood endoxifen levels when taking daily doses of oral tamoxifen.

Based on this, Atossa believes that oral endoxifen may provide plasma therapeutic endoxifen levels weeks or even months earlier than oral tamoxifen, which may potentially provide a more rapid onset of therapeutic effect (in terms of retarding ER+ breast cancer) than oral tamoxifen for recurrence prevention. While we believe it would be challenging to prove that the more rapid onset of steady-state blood levels leads to a statistically significant improvement in outcomes, this property, if

[6] Onitilo AA, Engel JM, Greenlee RT, et al. Clin Med Res. 2009 Jun; 7(1-2): 4–13.

[7] Waters EA, McNeel TS, Stevens WM et al. Breast Cancer Res Treat. 2012 Jul;134(2):875-80.

[8] Port ER, Montgomery LL, Heerdt AS, et al. Ann SurgOncol. 2001 Aug;8(7):580-5.

[9] Engmann NJ, Golmakani MK, Miglioretti DL et al. JAMA Oncol. 2017 Sep 1;3(9):1228-1236.

[10] Fox P, Balleine RL, Lee C, et al. Clin Cancer Res. 2016 Jul 1; 22(13):3164-71.

[11] Madlensky L, Natarajan L, Tchu S, et al. ClinPharmacolTher. 2011 May; 89(5):718-25.

[12] Saladores P, Mürdter T, Eccles D et al. The Pharmacogenomics Journal (2015) 15, 84–94.

replicated in future trials, could bolster the competitive case of endoxifen. The Phase II oral endoxifen study, planned to start in Q218, should provide more comprehensive pharmacokinetics (PK) data across a larger sample. However, the data to date from the Phase I study are encouraging, given the increased levels of plasma endoxifen shown and the dose-dependent manner of such increases.

Topical endoxifen for male breast cancer and gynecomastia

Atossa announced in March 2018 that it will be advancing its topical endoxifen for gynecomastia, and that it had started a 24-patient Phase I study of topical endoxifen in men. The objectives of the placebo-controlled, repeat-dose study in healthy male volunteers are to assess the PK, safety and tolerability of its topical endoxifen dosage forms over 28 days. The study is being conducted on behalf of Atossa by CPR Pharma Services of Australia, the same contract organization that completed its Phase I endoxifen studies in H217. A positive interim safety review was reported on 24 April 2018.

Gynecomastia is male breast enlargement and is fairly common, occurring in 50-60% of adolescents (it is often transitory in this age group), and up to 70% of men aged between 50 and 69 years.[13] Symptomatic gynecomastia, with accompanying pain, occurs much less frequently. Hence, few gynecomastia patients, as a percentage, seek treatment. Gynecomastia is often caused by a hormone imbalance where testosterone is low compared to estrogen, and can be precipitated by certain prescribed medications, including androgen deprivation therapy (to treat prostate enlargement and prostate cancer), anti-anxiety medications, and certain cancer treatments and heart medications. One of the most significant symptomatic populations are men experiencing anti-androgen treatment (such as bicalutamide or flutamide) for prostate cancer, as up to 70% of these patients experience gynecomastia.[14] About 16% of prostate cancer patients taking anti-androgen therapy discontinue their treatment primarily due to the gynecomastia[15].

There are no FDA-approved therapeutics for gynecomastia, although SERM drugs such as tamoxifen and raloxifene, and aromatase inhibitors (such as testolactone) have been used off-label. Prophylactic breast-bud radiation therapy and plastic surgery are the most common remaining treatment approaches.

Topical endoxifen can potentially provide tolerability and safety advantages compared to oral tamoxifen, given the expectation of lower systemic drug exposure. Prolonged systemic tamoxifen usage has been associated with the development of fatty liver disease in up to one-third of patients[16]. Topical endoxifen may also specific advantages for patients experiencing gynecomastia from prostate cancer therapy, as oral tamoxifen has been shown to raise serum testosterone[17], which is counterproductive and undesired given the anti-androgen therapy that is indicated for the treatment and prevention of prostate cancer. Further, just as in women, a certain percentage (5-10%) of males may have genetic variants of liver enzymes (such as P450 CYP2D6) that can impair their ability to form the tamoxifen metabolites that are believed to be involved in reducing gynecomastia.

While topical endoxifen therapy may potentially provide several benefits over current oral off-label SERM drugs such a tamoxifen, a recent review study[18] reported that less than 4% of men taking

[13] Johnson RE, Kermott CA, Murad MH. Ther Clin Risk Manag. 2011;7:145-8.

[14] Fagerlund A, Cormio L, Palangi L et al. PLoS One. 2015 Aug 26;10(8):e0136094

[15] Heidenreich A, Bastian PJ, Bellmunt J, et al. European urology 2014;65(2):467–479.

[16] US National Institutes of Health. https://livertox.nih.gov/Tamoxifen.htm

[17] Birzniece V, Sata A, Sutanto S, et al. J Clin Endocrinol Metab. 2010 Dec;95(12):5443–8.

[18] Wibowo E, Pollock PA, Hollis N et al. Andrology. 2016 Sep;4(5):776-88.

oral tamoxifen for gynecomastia stopped taking the drug for toxicity reasons. The review study assessed tamoxifen use in men across 14 randomized clinical trials and 39 non-randomized studies found that the most common AEs in men from tamoxifen therapy were gastrointestinal, cardiovascular issues and psychiatric disorders.

IDMC advancing with fulvestrant and TRAP CAR-T

Atossa continues its Phase II trial using its proprietary intraductal microcatheter (IDMC) to deliver fulvestrant, an approved metastatic breast cancer drug marketed by AstraZeneca, to treat ductal carcinoma in situ (DCIS), and potentially other breast cancers. Fulvestrant (marketed as Faslodex by AstraZeneca) is FDA-approved for ER+ metastatic breast cancer (with $941m in global 2017 sales, up 14% y-o-y) and is normally administered by intramuscular (IM) injection (to the buttocks), usually consisting of a monthly dose of two injections (costing $10,000-14,000 a month in the US).

In March 2016, Atossa initiated a 30-patient, open-label Phase II study on IDMC-administered fulvestrant, and transferred the study site from Columbia University Medical Center to the Montefiore Medical Center in New York City in early 2017. The company has not provided guidance as to when it expects to complete recruitment.

The firm is also investigating the use of its IDMC to deliver potential chimeric antigen receptor T-cell therapies (CAR-T therapies) directly to the site of breast cancer, through a process it refers to as Transpapillary CAR-T Delivery (TRAP CAR-T). Atossa believes that its IDMC could potentially provide preferential and more targeted delivery of CAR-T therapies to the breast ducts, the site of the majority of early-stage breast cancers, and thereby potentially improve efficacy while reducing off-site and systemic toxicity (such as “cytokine storms” associated with therapy). Atossa is still in the research stage of the TRAP CAR-T platform and will need to partner with a developer of CAR-T immunotherapy, as its involvement will be primarily at the drug delivery level, while relying on the pharmacological and immunology expertise of a would-be partner for the “active treatment” component of the planned TRAP CAR-T therapies.

Under a proposed CAR-T therapy, immune T-cells are removed from a patient and modified through recombinant processes (to form CAR T-cells) so that they express receptors specific to cells expressed by the patient's particular breast cancer. These CAR T-cells, designed to recognize and attack the cancer cells, are reintroduced into the patient’s breast ducts using IDMC. The company is in the research phase and intends to develop a partnership in 2018 with a developer of CAR-T therapies to assess a TRAP CAR-T (combination of the CAR-T therapy with its IDMC) platform.

Review of financials

Atossa reported Q417 results on 8 March 2018, with a Q417 net loss of $2.0m and an operating cash burn rate of $1.7m for the quarter. The FY17 net loss (excluding a $2.6m dividend attributable to preferred shareholders in Q217[19]) was $8.1m, and the operating cash burn rate was $6.6m. 2017 R&D costs were $2.3m, lower than our prior $3.1m forecast, and were mostly attributable to the Phase I oral and topical endoxifen study costs. We continue to expect R&D costs to increase in 2018 as the company proceeds with larger Phase II studies on topical and oral endoxifen (recruitment sizes still unknown), as well as the recently started Phase I study on topical endoxifen in men.

[19] Atossa Genetics had issued convertible preferred shares and warrants as part of a Q217 equity financing initiative, and the accounting treatment of the attached warrants prompted the issuance of a $2.6m deemed dividend to the preferred shareholders. All of the convertible preferred shares attached to the financing were converted to common equity by the end of Q317.

Given that R&D costs were lower than anticipated in 2017 and that the Phase II studies for endoxifen have been pushed back to start in Q218 (vs previous guidance of Q118), we have lowered our 2018 R&D expense forecast to $7.0m from $7.6m previously. Given recent trends in G&A expenses, we have also raised our 2018 G&A forecast to $4.2m, up from $3.8m previously.

We now assume an operating cash burn rate (excluding net interest income) of $11.5m in 2018 and $7.0m in 2019, versus our prior estimates of $11.8m and $6.2m respectively. We believe the burn rate will decrease in 2019, as we expect the company to have partnered the endoxifen programs (oral and topical) in H119, which would reduce its R&D expense needs.

Atossa had $7.3m net cash at year-end 2017. On 19 April 2018, Atossa common shares underwent a 12:1 reverse stock split. In December 2017 it completed a $1.4m ($1.2m net after all expenses) equity offering where it sold 0.44m shares at $3.24 per share (on a post-share consolidation basis). Concurrent to this equity offering was the provision of warrants to purchase 0.883m shares (on a post-consolidation basis) at an exercise price of $3.78 per share warrant to the same purchasers involved with the equity offering. We expect Atossa's current funds on hand (excluding any possible exercise from the outstanding warrants) to last into late Q318.

Rights offering underway

On 23 April 2018 Atossa released an S1/A registration statement with the US Securities and Exchange Commission (SEC), explaining it is pursuing a shareholder rights offering to obtain new financing to extend its financial runway. Shareholders of record by 9 May 2018 as well as holders of the company's warrants (0.883m outstanding) from the December 2017 financing, will each be provided a non-transferable subscription right to purchase one unit, at a subscription price of $1,000 per unit, consisting of one share of newly issued SBCPS with a face value of $1,000 (and immediately convertible into 284 shares of common stock at a conversion price of $3.52 per share) and 284 common-share purchase warrants with an exercise price of $4.05, exercisable for up to four years. Given that Atossa had 2.652m shares outstanding (as of 20 April 2018) and 0.883m warrants, it expects to grant 3.535m subscription rights. However, it has capped the number of subscriptions it will accept to 20,000 units (corresponding to a maximum issuance of 20,000 SBCPS and 5.68m new share purchase warrants). The maximum gross proceeds from the offering will be $20m (or $18.4m net, after all expenses) and will only require 0.6% of issued subscription rights to be exercised to reach this maximum. If more than 20,000 unit subscription requests are received, the S1/A filing states:

"If exercises of basic subscription rights exceed the number of units available in the rights offering, we will allocate the available units pro-rata among the record holders exercising the basic subscription rights in proportion to the number of shares of our common stock each of those record holders owned on the record date (including shares of common stock issuable upon exercise of the December 22, 2017 warrants), relative to the number of shares owned on the record date by all record holders exercising the basic subscription right."

The anticipated subscription period of the rights offering is between 10 May 2018 and 24 May 2018. In general, while traditional shareholder rights offerings provide participating shareholders an opportunity to purchase additional equity in a firm to maintain their ownership percentages and avoid dilution, the Atossa rights plan is structured such that the theoretical purchase commitment can be substantially higher than the market value of current shares held. For instance, a shareholder who owns 100 shares of Atossa's common stock (with a market value of approximately $350-400) can theoretically commit to purchase 100 SBCPS for $100,000, which would be convertible to 28,400 common shares. The actual allotment would be unknown until the end of the subscription period and could be significantly less than 100 SBCPS (thus depending on how many

subscription requests are received by Atossa). Atossa's S1/A filing also states "The exercise of subscription rights is irrevocable and may not be cancelled or modified."

Given that this rights offering is still open and it is unknown how many unit subscription requests will be received by Atossa or exercised in full, we have not included it in our forecasts or valuation model. However, if the rights offering is exercised in full (with 20,000 SBCPS issued) and assuming full conversion of these SBCPS into 5.68m common shares, Atossa's current shares outstanding (and without considering the exercise of any warrants) would increase by 214% to 8.332m common shares, and we estimate that Atossa's operating cash runway would be extended well into 2020.

We plan to update our model once the rights offering has concluded (and the SBCPS are issued). Our forecasts continue to assume that Atossa will need to raise funds before Q418; our model assumes Atossa will raise $10m in both 2018 and 2019. As per our usual policy, for modeling purposes, we assign these financings to long-term debt. However, as reflected by the recent S1 statement, the company is seeking to issue equity instead through the rights offering.

Valuation: rNPV increases to $24.7m

Our rNPV valuation continues to include the prospects of the company's topical and oral endoxifen programs for women, and its IDMC-fulvestrant program. Given the early stage of its men's topical endoxifen program, with no human proof-of-concept data thus far in gynecomastia and with certain studies suggesting that oral tamoxifen use in men does not result in substantial treatment discontinuations when used (albeit off-label) for gynecomastia, we prefer to wait for further advancement in this program before including it in our valuation.

Our revenue assumptions for topical and oral endoxifen, as well as IDMC-fulvestrant, are unchanged from our 16 November 2017 Outlook note. We assume that Atossa will out-license the oral and topical endoxifen programs in H119, on the conclusion of the currently planned Phase II studies, and will be entitled to 20% royalties on net sales. Following a subsequent pivotal study (to be funded by the partner), topical endoxifen could be launched in 2021. We continue to estimate that the potential target market for topical endoxifen for MBD prevention is 10% of women above age 40 (this collective group will fall in the highest category of MBD, BI-RADS grade D) and that peak market share would be 15% of the target market, such that in the year of peak sales (2026) about 195,000 US women would be obtaining therapy, leading to US sales of $523m (worldwide sales of $922m), and worldwide net royalties of $184m (in 2026).

For oral endoxifen, we continue assume a potential launch in 2020, and that the target market will be 20% of the 300,000 US women (and approximately one million women worldwide) currently taking tamoxifen and who we estimate do not achieve sufficient plasma endoxifen concentrations. Of these, we assume a peak market share of 50% of this group, which would be attained by 2025, with peak net sales of $91m in the US ($161m worldwide), which leads to global net royalties to Atossa of $32m in 2025. For IDMC-fulvestrant we continue to assume a potential launch in 2023, with worldwide peak sales (consisting of the IDMC device and separate from the cost of fulvestrant) of $182m in 2026, with royalties to Atossa of $36.5m (20% assumed royalty rate).

We assume Atossa will spend $3.6m on R&D on the topical female endoxifen program (primarily for the planned Phase II study) between Q218 and Q219. We assume it will spend $2.9m on R&D for oral endoxifen over the same period before partnering it. We assume that Atossa will spend $2.8m in R&D costs on the IDMC-fulvestrant program between Q218 and H219 before also partnering this program.

We continue to apply a 20% probability of success estimate for the oral endoxifen program, a 5% probability for topical endoxifen in MBD (since proof-of-concept in terms of MBD reduction has not been shown and our forecasts depend on building significant support and recognition among

patients, physicians and stakeholders of the benefits of treating MBD as a preventative approach to lowering cancer risk), and a 10% probability for the IDMC-fulvestrant program.

Exhibit 3: Atossa Genetics rNPV assumptions

Product contributions (net of R&D costs)	Indication	rNPV ($m)	rNPV/share ($)	Probability of success	Launch year	Peak US market share	Peak WW sales (US$m)
Topical endoxifen	High breast density	22.0	8.31	5.0%	2021	15%	922 in 2026
Oral endoxifen	Breast cancer	23.3	8.77	20.0%	2020	12.5% of patients taking tamoxifen	161 in 2025
Intraductal microcatheter (for fulvestrant)	Breast cancer	8.0	3.01	10.0%	H222	25%	182 in 2026
Corporate costs & expenses							
SG&A expenses		(21.7)	(8.19)				
Net capex, NWC & taxes		(6.9)	(2.58)				
Total rNPV		24.7	9.33				
Net cash (Q118e)		5.2	1.97				
Total equity value		30.0	11.30				
FD shares outstanding (000) (*)		2,652					

Source: Edison Investment Research. Note: *as per S1/A filing dated 23 April 2018

We continue to apply a 12.5% discount rate. After rolling forward our estimates, we now obtain an rNPV valuation of $24.7m, up from $18.4m previously. After including Q118 estimated net cash of $5.2m, we obtain an equity valuation of $30.0m (vs $24.6m previously), or $11.30 per fully diluted (FD) share (before considering any potential dilution from funding requirements).

Exhibit 4: Financial summary

US$(000)	2015	2016	2017	2018e	2019e	2020e
31-December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	2	0	0	0	0	5,590
Cost of Sales	(132)	0	0	0	0	(0)
General & Administrative	(9,996)	(6,176)	(4,730)	(4,200)	(3,000)	(3,060)
Research & Development	(2,360)	(770)	(2,328)	(7,000)	(4,000)	(1,000)
EBITDA	(9,484)	(6,946)	(7,058)	(11,200)	(7,000)	1,530
Depreciation	(273)	(303)	(129)	(56)	(59)	(63)
Amortization	0	0	0	0	0	0
Operating Profit (before exceptionals)	(9,756)	(7,250)	(7,187)	(11,256)	(7,059)	1,466
Exceptionals	0	881	(935)	0	0	0
Other	(3,002)	0	0	0	0	0
Operating Profit	(12,758)	(6,369)	(8,123)	(11,256)	(7,059)	1,466
Net Interest	0	0	0	49	(113)	(188)
Profit Before Tax (norm)	(9,756)	(7,250)	(7,187)	(11,208)	(7,173)	1,279
Profit Before Tax (FRS 3)	(12,758)	(6,369)	(8,123)	(11,208)	(7,173)	1,279
Tax	0	0	0	0	0	0
Profit After Tax and minority interests (norm)	(9,756)	(7,250)	(9,756)	(11,208)	(7,173)	1,279
Profit After Tax and minority interests (FRS 3)	(12,758)	(6,369)	(10,691)	(11,208)	(7,173)	1,279
Average Number of Shares Outstanding (m)	0.2	0.2	1.0	2.7	2.7	2.7
EPS - normalised ($)	(61.78)	(29.52)	(10.01)	(4.23)	(2.70)	0.48
EPS - normalised and fully diluted ($)	(61.78)	(29.52)	(10.01)	(4.23)	(2.70)	0.48
EPS - (IFRS) ($)	(80.78)	(25.93)	(10.97)	(4.23)	(2.70)	0.48
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	1,948	890	266	280	297	319
Intangible Assets	1,701	640	76	76	76	76
Tangible Assets	248	249	190	204	222	243
Current Assets	4,295	3,255	7,898	6,342	9,151	10,409
Short-term investments	275	55	55	55	55	55
Cash	3,716	3,028	7,217	5,661	8,471	7,868
Other	304	172	626	626	626	2,486
Current Liabilities	(2,502)	(1,047)	(1,225)	(891)	(891)	(891)
Creditors	(2,502)	(1,047)	(1,225)	(891)	(891)	(891)
Short term borrowings	0	0	0	0	0	0
Long Term Liabilities	0	0	0	(10,000)	(20,000)	(20,000)
Long term borrowings	0	0	0	(10,000)	(20,000)	(20,000)
Other long term liabilities	0	0	0	0	0	0
Net Assets	3,742	3,097	6,939	(4,269)	(11,442)	(10,163)
CASH FLOW						
Operating Cash Flow	(13,953)	(5,375)	(6,594)	(11,535)	(7,000)	(330)
Net Interest	0	0	0	49	(113)	(188)
Tax	0	0	0	0	0	0
Capex	(131)	(9)	0	(70)	(77)	(85)
Acquisitions/disposals	(158)	0	0	0	0	0
Financing	9,457	4,696	10,783	0	0	0
Net Cash Flow	(4,785)	(688)	4,190	(11,556)	(7,190)	(603)
Opening net debt/(cash)	(8,501)	(3,991)	(3,083)	(7,272)	4,284	11,474
HP finance leases initiated	0	0	0	0	0	0
Other	275	(220)	0	0	(0)	0
Closing net debt/(cash)	(3,991)	(3,083)	(7,272)	4,284	11,474	12,077

Source: Edison Investment Research, Atossa Genetics reports

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