EDISON

Atossa Genetics

Outlook

Seeking to prevent or treat breast cancer

Pharma & biotech

Atossa Genetics reported Phase I data on its topical endoxifen formulation and it is now developing this as a potential treatment for high mammographic breast density (MBD), which is associated with increased breast cancer risk. The firm is also developing oral endoxifen for patients refractory to tamoxifen, and its intraductal microcatheter (IDMC), combined with established cancer drug fulvestrant. After also considering the recent $5.5m equity raise (at $0.44 per share), our rNPV-derived equity valuation is $24.6m (from $9.3m previously), or $0.93 per share.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/15	0.0	(9.8)	(5.15)	0.0	N/A	N/A
12/16	0.0	(7.2)	(2.46)	0.0	N/A	N/A
12/17e	0.0	(7.8)	(0.83)	0.0	N/A	N/A
12/18e	0.0	(11.5)	(0.43)	0.0	N/A	N/A

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

Topical endoxifen targets high breast density

Oral tamoxifen, a selective estrogen receptor modulation (SERM) drug, reduces both MBD and the risk of cancer recurrence in women with breast cancer, but its adverse effects (AE) have limited its use. Endoxifen is a tamoxifen metabolite that is responsible for much of the oral drug's SERM action. Atossa believes that topical endoxifen can exert SERM effects to breast tissue and reduce MBD, with fewer significant AE. Following its Phase I study showing early safety and signs of dose-dependent absorption, Atossa plans to start a 480-patient Phase II trial in Q118.

Oral endoxifen for women refractory to oral tamoxifen

About 20% of the 300,000 US women currently taking tamoxifen (largely to prevent recurrence of breast cancer) do not achieve sufficient concentrations of endoxifen and may have increased the risk of cancer recurrence. Atossa believes that oral endoxifen can reduce recurrence risk in these patients and recently reported positive data from the oral arm of the Phase I study. A Phase II study of IDMC-fulvestrant is also underway to determine if the IDMC provides superior targeting.

Valuation: Equity valuation of $24.6m

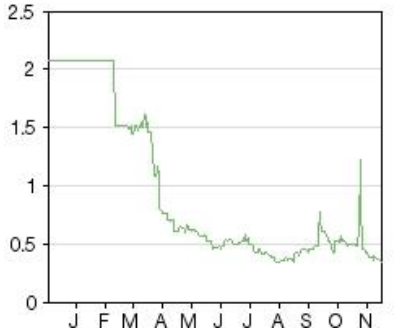
We expect Atossa will raise $10m in each of 2018 and 2019 to fund its R&D programs for endoxifen and IDMC-fulvestrant. We expect the operating cash burn rate to increase 67% in 2018 to $11.8m, due to increased clinical trial costs. Our risk-adjusted net present value (rNPV) valuation of $18.4m is up from $6.3m previously, due to us now including the topical endoxifen program, with a 5% probability of success, in our valuation for the treatment of MBD. Previously, our valuation only included the oral formulation (success probability raised to 20%, from 15% previously, due to Phase I data) and IDMC-fulvestrant (success probability of 10% vs 25% previously due to slow study recruitment). After including Q417 estimated net cash of $6.1m (factoring in the recent $5.5m equity raise), we obtain an equity valuation of $24.6m, or $0.93 per share before potential further dilution from funding requirements.

16 November 2017

Price	**US$0.34**
Market cap	**US$9m**

Estimated net cash ($m) at Q417	6.1
Shares in issue (Q417e)	26.5m
Free float	97%
Code	ATOS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(32.1)	(4.1)	(80.5)
Rel (local)	(32.4)	(7.8)	(83.4)

52-week high/low	US$2.1	US$0.3

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 topical endoxifen study	Q118
Start Phase II oral endoxifen study	Q118

Analysts

Pooya Hemami, CFA	+1 646 653 7026
Maxim Jacobs, CFA	+1 646 653 7027

healthcare@edisongroup.com

Edison profile page

Investment summary

Company description: Targeted therapies for breast cancer

Atossa Genetics initially developed medical devices and laboratory services dedicated to breast cancer and related health areas, before transitioning to drug development over the past two to three years. It started developing endoxifen, a tamoxifen metabolite intended to provide selective ER antagonism, for both topical and oral use, in the treatment of mammographic breast density and breast cancer prevention. The firm plans to start Phase II studies for both formulations in Q118. It acquired an IDMC device that is intended to selectively introduce drug to breast ducts, potentially improving drug targeting for CAR (Chimeric Antigen Receptor)-T cell and chemotherapy uses. Atossa is currently performing a Phase II study combining the IDMC with established cancer drug fulvestrant, and is in the R&D phase for delivering CAR-T cell therapy via its microcatheters.

Exhibit 1: Atossa Genetics' upcoming catalysts

Event	Timing
Start Phase II topical endoxifen study	Q118
Start Phase II oral endoxifen study	Q118
2017 financial results	March 2018

Source: Atossa Genetics reports

Valuation: Equity value of $24.6m

Our rNPV valuation of $18.4m is up from $6.3m previously. We now include the topical endoxifen program, with a 5% probability of success, in our valuation for the treatment of mammographic breast density (MBD). Previously our valuation only included the oral formulation (20% success probability, up from 15% previously) and IDMC-fulvestrant (success probability now lowered from 25% to 10% as study recruitment has been slower than expected). After including Q417 estimated net cash of $6.1m, we obtain an equity valuation of $24.6m, or $0.93 per fully diluted share. Positive clinical data and/or securing partnerships could raise our probability estimates and valuation.

Financials: Additional funding needed to complete studies

Atossa had $2.8m net cash at Q317, and on 30 October 2017 it raised $5.5m gross in an equity offering (12.5m shares placed at $0.44 per share). Our model assumes a 2018 operating cash burn rate (excluding net interest income) of $11.8m, and $6.2m in 2019. The burn rate is projected to decrease in 2019, as we expect the firm to have partnered both endoxifen programs in early 2019, which would reduce its future R&D costs. We assume that Atossa will need to raise funds before mid-2018; our model assumes Atossa will raise $10m in both 2018 and in 2019. As per our usual policy, for modeling purposes, we assign these financings to long-term debt.

Sensitivities: Funding, development risks, partnerships

For both the endoxifen and the IDMC-fulvestrant programs, development may hinge on future FDA guidance on whether the projects can fall under the 505(b)2 development pathway, which we assume in our model, and which reduces the breadth of required clinical data needed to support a marketing application. For topical endoxifen, commercialization success may depend on the educational and marketing efforts needed to convince at-risk patients of the benefits of local therapy for breast density. For oral endoxifen, stakeholders must be persuaded of benefits of the product vs oral tamoxifen in patients refractory to oral tamoxifen. The company must also secure the required funding to complete clinical development until it can secure partnership for its products.

Targeting breast cancer prevention and drug delivery

Atossa's strategy is to develop therapies for the prevention or treatment of breast cancer. The lead candidate is endoxifen, which is being developed in both oral and topical formulations. The firm's advancements in developing a topical endoxifen formulation have positioned it to aim to develop the topical form as a treatment for mammographic breast density (MBD), a condition associated with increased risk for the development of breast cancer. Oral endoxifen is being developed to prevent cancer recurrence in patients refractory to tamoxifen. The firm plans to start Phase II studies in Q118 in both formulations. Atossa is also involved with a 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.

Endoxifen for MBD and breast cancer prevention

In June 2016, Atossa began investigating endoxifen as a potential treatment for breast cancer. When dosed orally, tamoxifen is metabolized in the liver by enzymes (including cytochrome P450 isoforms) into multiple metabolites, yet only a few of these metabolites have an active estrogen receptor (ER) antagonist effect (blocking estrogen from binding to its receptors). The most significant of these metabolites (in terms of ER antagonism contribution and plasma concentration in patients with normal tamoxifen metabolism) are endoxifen (4-hydroxy-N-desmethyltamoxifen) and, to a lesser extent, afimoxifene (4-hydroxytamoxifen).[1,2]

Atossa has since secured drug manufacturing supply, developed topical and oral formulations and filed composition of matter and methods of treatment patent applications (with patent lives potentially into 2036). The company now sees two separate cancer-prevention opportunities for endoxifen as a treatment to prevent cancer recurrence in patients refractory to tamoxifen; and, more recently, as a topical treatment to reduce mammographic breast density (MBD).

Topical treatment could provide targeted efficacy with lower 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.

Atossa believes that the optimal potential market for topical therapy (to delivery ER inhibition with less AE risk than oral drug) would be for the 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. For most women, breasts become less dense with age. 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.

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

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.

Tamoxifen is the only known approved prescription product that has been unequivocally shown to reduce breast density,[3] but due in part to the risks for AE (including thromboembolic complications), it has not generally been employed for this purpose. 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] and, further, prolonged oral use can cause longer-term side effects so these products may not be recommended for women to help reduce their breast cancer risk.[5]

Recent studies link high breast density with cancer risk

A topical treatment with tamoxifen-like effects for reducing MBD and possibly few side effects could have a meaningful chemo-preventative market, given that a recent US study following over 202,000 women found that MBD is a significant independent predictor for increased breast cancer risk.[6] The study examined multiple criteria in addition to MBD, including first-degree family history of breast cancer, body mass index, history of benign breast biopsy, and age at first childbirth. Among these, the study found MBD was the most prevalent risk factor for both premenopausal and postmenopausal women. It 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 September 2017, Atossa reported positive results from the topical administration arm of its Phase I safety study conducted in Australia on endoxifen. In addition to assessing safety and tolerability, the placebo-controlled, repeat-dose, 28-day study on healthy female volunteers (aged between 18 and 65) evaluated the pharmacokinetics (PK) of both an oral and a topical endoxifen formulation. The study consisted of six cohorts (comprising eight patients each; where six would take the treatment and two would take placebo), with the first three cohorts (totaling 24 patients) receiving a topically-administered endoxifen formulation (in the form of a single-dose “sachet”) applied to the breast daily (dose arms of 1mg, 3mg, and 5mg/breast). The subsequent three cohorts (also totaling 24 patients) received an oral endoxifen capsule formulation.

The topical arm of the study was successful as there were no clinically significant adverse safety events in all tested dose treatment arms, and the product was tolerated at each dose level and for the duration utilized in the study. In all arms, there were no safety signals observed in weekly assessments of blood chemistry, coagulation or hematology parameters, or urinalysis, cardiac signs or other physical exam. There were no serious AE, but one subject in the placebo arm and one in the treatment arm experienced a treatment emergent AE of moderate severity and possibly drug-related (relating to headache and/or nausea).

In terms of tolerability, a self-assessment of local tolerance was performed daily (24 subjects for 28 days for a total of 672 daily assessments) where each participant would self-assess for five tolerability parameters (redness, burning, pain, itching and irritation) on a four-point scale (none, mild, moderate or severe). Based on these assessments, 97.3% of the self-reported measures were suggestive of no tolerability issues, 1.8% reflected mild and 0.2% moderate issues (there were no severe readings, and 0.6% of measures were N/A).

When examining the participants who did report at least one episode of a mild or moderate tolerability event (none of the patients had reported a severe event), both the low and medium dose cohorts reported fewer patients having experienced at least one episode than the placebo arm; this suggests that these doses were well tolerated. Only in the higher treatment arm was the total

[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] University of Adelaide press release, 24 January 2017. www.adelaide.edu.au/news/news90207.html

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

number of subjects having a tolerability event (4/6 or 67%) higher than those in the placebo arm (3/6 or 50%).

Exhibit 3: Atossa Genetics Phase I topical endoxifen study tolerability data

Dose cohort	Dose (mg per breast)	Number of participants reporting at least one tolerability event*
Low (n=6)	1	2 (33%)
Medium (n=6)	3	1 (17%)
High (n=6)	5	4 (67%)
All receiving placebo (n=6)	N/A	3 (50%)

Source: Atossa Genetics reports. Note: *Consisting of mild or moderate occurrences over the 28-period of itching, pain, redness, burning or irritation. None of the participants reported a severe score on any of these symptoms at any point in the study

In addition, each dose arm and all patients receiving placebo were asked on a weekly basis, whether the tolerability side effects (such as the five mentioned parameters) experienced through the use of the topical product had bothered the patient in an in-person interview.

Exhibit 4: Topical Phase I interview data on whether patients felt bothered by product

Dose cohort	Not at all	A little bit	Somewhat	Very much
Low	100% (6/6)	0%	0%	0%
Medium	100% (6/6)	0%	0%	0%
High	50% (3/6)	2/6 (33%)	1/6 (17%)	0%
Placebo	83% (5/6)	1/6 (17%)	0%	0%

Source: Atossa Genetics reports

In the low (1mg/breast) and intermediate (3mg/breast) treatment arms, all participants (six for each arm) reported “not at all” across the measures. In the high treatment arm (5mg/breast), 50% of participants consistently reported “not at all” but two out of six (33%) reported being “a little bit” bothered by the adverse events, and one of six (16.7%) reported being “somewhat” bothered by such effects.

Across the placebo arm (n=6), five out of six (83%) reported “not at all” consistently, and one participant (16.7%) reported “a little bit” bothered. Overall, the tolerability data in the study appear very favorable for the low and intermediate arms, as these arms appear to perform equally or comparably to placebo on tolerability scales. The high arm could be trending to a slightly lower level of overall tolerability, although it is premature to speculate as to whether this would have an impact on this dose’s overall suitability in future studies.

Early pharmacokinetic (PK) data suggestive of dose-response effect

The Phase I 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. The therapeutic premise would be that the formulation would be placed on the skin surface and penetrate afterwards, with endoxifen reaching breast tissue and exerting a therapeutic effect by binding ER (retarding the potential for cancer cell growth and/or reducing density growth) in the region, with some proportion of the endoxifen being absorbed by the vascular structure and reaching systemic circulation. Hence, measures on whether plasma endoxifen would rise after topical administration could be a reference marker for the ability to reach local breast tissue.

The company reported that each of the patients (in treatment and placebo arms) 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 level of plasma endoxifen was measured at or above 2ng/mL. In the placebo arm, as expected, there were no measures reaching this threshold; in the treatment arms, there was 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 arm.

However, from this data 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 has not been established at all.

Normally 2ng/mL systemically would not be significant enough to have a meaningful treatment effect for an orally dosed product (studies have shown that 15nmol/L or about 6ng/mL, is the ideal dose level for anti-cancer effect for oral product). However, the principle here is that the product will reach local breast tissue before reaching systemic circulation, so this measure may not be clinically meaningful for a topical administration.

Phase II endoxifen study planned for Q118

Atossa plans to initiate a Phase II study on endoxifen in Q118 at the Stockholm South General Hospital in Sweden (affiliated with the Karolinska Institute). Atossa recently submitted an application with the Swedish regulatory authority. The placebo-controlled, double-blinded study intends to enroll up to 480 subjects, and the primary endpoint is MBD reduction, which will be measured after six and 12 months of dosing, as well as safety and tolerability. Patients with BI-RADS grades B, C and D will be included in the study.

The larger study size (compared to the Phase I) will entail higher R&D costs for Atossa in 2018 (we estimate $3.0m in costs for the Phase II topical endoxifen study), and we expect completion in early 2019. We assume that upon study completion, Atossa will out-license the endoxifen program (both the topical and oral forms) and be entitled to 20% royalties on net sales.

As tamoxifen has a long-established history of systemic use, and as endoxifen is a metabolite of this drug (and with a similar "active moiety"[7]), we expect that Atossa (or the eventual endoxifen licensee) would be able to pursue FDA approval through the 505(b)2 registration pathway, whereby the extent of efficacy data needed for registration is less substantive or onerous than through a traditional New Drug Application, or 505(b)1, pathway. This should shorten the amount of time needed for a registration study. We expect the pharmaceutical partner (licensee of endoxifen) would then fund the pivotal study (to start in H119), and that topical endoxifen would, in a best case scenario, achieve commercial approval and start sales in 2021.

Initial forecasts for topical endoxifen

The premise for a topical treatment with few AE to reduce MBD could potentially represent a significant market if it shows efficacy, given the relationship between MBD and cancer risk. As over 95% of breast cancers occur in women above age 40, and 65% of these have a mammogram every two years (as per US Centers for Disease Control data), we estimate that 10% of this collective group will fall within the highest category of MBD (BI-RADS grade D) and would represent the potential treatment target market. The firm plans to also assess topical endoxifen in lower grades of MBD (namely BI-RADS grades B and C), but our forecasts assume that it will primarily be used in grade D; the extension of commercial product use to patients with lower (less dense) MBD categories could provide upside to our estimates. Based on our preliminary discussions with management, and our view of a realistic or feasible treatment protocol, we assume that a potential endoxifen therapy would require a course of daily therapy for up to several months (after which MBD would be reduced for a certain period). Afterwards, we assume a course of MBD reduction therapy may need to be repeated every five years (as MBD may re-develop gradually once treatment is discontinued).

[7] The FDA defines "active moiety" as the part of "the molecule or ion" (excluding certain appended portions or other non-covalent attachments) "responsible for the physiological or pharmacological action of the drug substance".

Based on the above assumptions, and assuming a peak market share of 10% of the target market, in the year of peak sales (2025), about 160,000 women would obtain therapy. We assume a starting net price per treatment cycle of $2,400 (consistent with our existing yearly oral endoxifen estimate) in 2021, and thus total US sales in 2026 of $523m (and worldwide sales of $922m). Assuming a 20% royalty rate to Atossa, this translates to royalties of $184m in 2026.

Exhibit 5: Topical endoxifen revenue forecasts

Year-end 31 December	2021	2022	2023	2024	2025	2026
US market						
Estimated population of women above age 40 (000)*	92,915	94,141	95,561	97,003	98,466	99,952
High breast density proportion (%)**	10	10	10	10	10	10
Proportion with mammography test in past 2 years (%)	65	65	65	65	65	65
Estimated number of years between treatment cycle	5	5	5	5	5	5
Market share (%)	1.1	2.5	4.9	8.3	12.6	15.0
Number of patients undergoing treatment at year-end	12,683	30,777	61,069	104,094	160,871	194,906
Net price per treatment cycle ($)	2,400	2,479	2,528	2,579	2,630	2,683
Total topical endoxifen revenue ($000)	7,724	76,377	154,529	268,628	423,360	522,911
Royalty rate (%)	20	20	20	20	20	20
Net revenue to Atossa ($000)	1,545	15,275	30,906	53,726	84,672	104,582
Europe and ex-US markets						
Total topical endoxifen revenue ($000)	5,902	58,360	118,076	205,261	323,493	399,560
Royalty rate (%)	20	20	20	20	20	20
Net revenue to Atossa ($000)	1,180	11,672	23,615	41,052	64,699	79,912
Worldwide topical endoxifen sales ($000)	13,625	134,737	272,605	473,889	746,853	922,471
Worldwide topical endoxifen royalties to Atossa ($000)	2,725	26,947	54,521	94,778	149,371	184,494

Source: Edison Investment Research. Note: *Based on US Census data.**Estimated prevalence of BI-RADS Class D is over 7% in patients above age 40 according to Sprague BL, Gangnon RE, Burt V, et al. *J Natl Cancer Inst.* 2014 Oct; 106(10). We assume a proportion of patients within BI-RADS Class C may also be considered as having high MBD. This explains our assumption that 10% of women above age 40 (who undergo periodic mammography testing) could be potential MBD treatment candidates.

Oral endoxifen aims to reduce 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[8] (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. IBIS-I found that after a median follow-up of 16 years, tamoxifen-treated patients had a 7.0% risk of developing breast cancer, versus 9.8% in the placebo group. The reduction in ER-positive invasive breast cancer was maintained for at least 11 years after cessation of tamoxifen.[9] US clinical practice guidelines now recommend consideration of adjuvant tamoxifen therapy for 10 years.[10,11,12] Tamoxifen is approved in both pre-menopausal and post-menopausal cancers, and raloxifene, a newer SERM drug,[13] is only approved for use in post-menopausal women.

Despite evidence of reduced ER-positive breast cancer risk, SERM use has been limited to less than 1% of AH patients.[14] The low uptake is believed to be attributable to patients' fear of adverse effects (AE) of SERM drugs,[15,16]which include increased risks of thromboembolic events (including

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

9 Cuzick J, Sestak I, Cawthorn S, et al. *Lancet*Oncol 16 (1): 67-75, 2015.

10 Davies C, Pan H, Godwin J, et al. *Lancet.* 2012.

11 Davies C, Pan H, Godwin J, et al. *Lancet.* 2013;381: 805-816.

12 Burstein HJ, Temin S, Anderson H, et al. *J ClinOncol*. 2014;32: 2255-2269.

13 Vogel VG, Costantino JP, Wickerham DL, et al. *JAMA*. 2006 Jun 21; 295(23):2727-41.

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

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

blood clots, stroke), menopausal symptoms, and endometrial cancer. Chemoprevention use (the use of drugs to reduce cancer risk) remains low even though raloxifene, a newer oral SERM approved by the FDA in 2007, has a more advantageous AE profile vs tamoxifen.[17,18]

Oral endoxifen intended to benefit patients refractory to tamoxifen

Several research groups 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, and that up to 15-20% of Europeans carry genetic P450 CYP2D6 variants associated with an impairment in forming anti-estrogenic tamoxifen metabolites.[6] 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.[19] Lyon *et al*[20] suggest that 20nmol/L reflects a therapeutic plasma level of endoxifen. 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 remaining tamoxifen-treated patients.[21,22] These studies form a basis for dosing oral endoxifen directly in such patients.

Oral Phase I data show safety and dose-dependent PK

Results from the 24-patient oral arm of the Phase I study testing doses of 1mg, 2mg and 4mg/day were released on 25 October 2017. Healthy females (eight patients per arm, with six receiving drug and two receiving placebo) received drug for 28 days. Safety and tolerability was favorable as there were no serious AEs in any arm, and no safety signals (using the same parameters assessed in the topical arm) were identified. AEs deemed probably related to study drug were infrequent and included vomiting, delayed menstruation and hot flush, but there were no differences in the frequencies of such AEs in the study dose (and AEs also occurred in the placebo arm). Tolerability was assessed using a questionnaire on whether patients were bothered by treatment, using a five-point scale. Tolerability responses were similar at all dose levels and comparable with placebo, although one of the six patients in the 1mg arm reported a 5 out of 5 in her level of “bother” at day 21 (no other patient, across all treatment arms, reported a level above 3 out of 5 at any reported period).

In terms of PK, Atossa believes that 30nmol/L is an ideal minimum target level of plasma endoxifen to ensure possible therapeutic effect. Exhibit 6 shows 24-hour plasma endoxifen levels after a single oral administration (for all oral dose arms and placebo). Both the 2mg and 4mg oral doses led to sustained plasma levels in excess of 30nmol/L until at least 24 hours post-administration. A more important study parameter is “steady-state” plasma endoxifen concentration after multiple doses, which is shown in Exhibit 7. These data show that after 21 days of daily dosing, all three treatment arms 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 larger Phase II oral endoxifen study, planned by Atossa to start in Q118, should provide more comprehensive PK data across a larger sample, but the PK 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.

---

16 Taylor R, Taguchi K. *Ann Fam Med*. 2005 May-Jun;3(3):242-7.

17 Vogel VG, Costantino JP, Wickerham DL, et al. *JAMA*. 2006 Jun 21; 295(23):2727-41.

18 Melnikow J, Paterniti D, Azari R, et al. *Cancer*. 2005 May 15; 103(10):1996-2005.

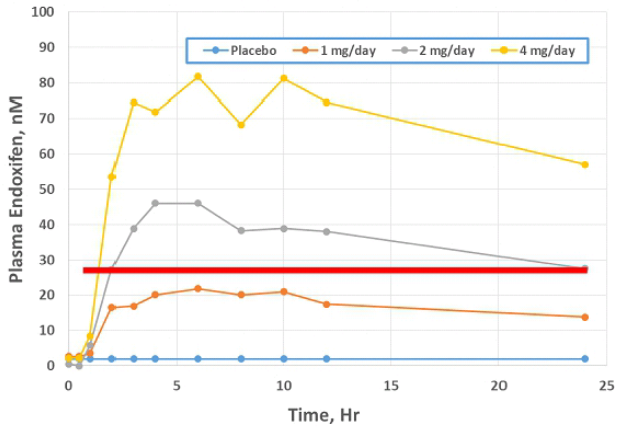
19 Fox P, Balleine RL, Lee C, et al. *Clin Cancer Res*. 2016 Jul 1; 22(13):3164-71.

20 Lyon E, Gastier FJ, Palomaki GE, et al. *Genet Med.* 2012 Dec; 14(12):990-1000.

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

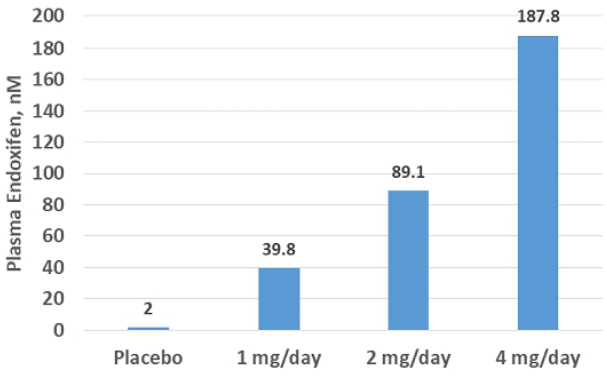
22 Saladores P, Mürdter T, Eccles D et al. *The Pharmacogenomics Journal* (2015) 15, 84–94.

Exhibit 6: Single-dose pharmacokinetics (Oral study)



Source: Company reports

Exhibit 7: Pseudo-steady state levels: 21-day sample



Source: Company reports

Pivotal oral study under 505(b)2 could start in H119

As with topical endoxifen, we believe the oral formulation would also be eligible for the 505(b)2 registration pathway and, as such, a Phase III trial demonstrating oral endoxifen's efficacy in reducing cancer recurrence may not be necessary for approval. Beyond the currently planned Phase II study, we assume that an additional (pivotal) study would be required for approval of the oral drug, and we believe it would start in Q418 or H119, and could lead to approval in 2020. We believe Atossa will partner its oral and topical endoxifen formulation with a pharma company in 2019and we model that it will be entitled to 20% in net royalties. In terms of product safety and possible interactions, we note that some researchers have found that endoxifen, due to its effects on the protein kinase C (PKC) signaling system, can potentially have a therapeutic effect for treating patients with mania or bipolar disorder.[23] Other groups have found similar effects with tamoxifen[24] as it also inhibits PKC; hence we do not believe the PKC effect is likely to hinder endoxifen's commercial or regulatory prospects.

NCI/Mayo Clinic group activity on endoxifen could provide competition

A team of investigators at Mayo Clinic (Matthew Goetz, Matthew Ames and collaborators) and the National Cancer Institute (NCI) is studying its own formulation of endoxifen hydrochloride in treating patients with ER+ breast cancer (but negative for HER receptors). While Atossa is filing patents for its own endoxifen formulations and methods of treatment, there is a material risk that competing studies from the Mayo/NCI investigators, should they lead to registration or commercialization-stage end products, could lead to intellectual property (IP) related competition challenges to Atossa's eventual endoxifen product.

Oral endoxifen peak revenue assumptions unchanged

Based on findings from Madlensky and Fox, we continue to assume that 20% of the 300,000 US women (and approximately one million women worldwide) currently taking tamoxifen[25] do not achieve sufficient plasma endoxifen concentrations, and thus reflect the potential target market for Atossa's oral endoxifen (thus 60,000 persons in the US), and that peak market share for Atossa's

[23] Ahmad A, Sheikh S, Shah T et al. *ClinTransl Sci*. 2016 Jun 27. doi: 10.1111/cts.12407

[24] Talaei A1, Pourgholami M, Khatibi-Moghadam H, et al. *J ClinPsychopharmacol*. 2016 Jun;36(3):272-5. doi: 10.1097/JCP.0000000000000492

[25] Waters EA, McNeel TS, Stevens WM et al. "Use of tamoxifen and raloxifene for breast cancer chemoprevention in 2010" (2012). Cancer Prevention Faculty Publications. Paper 6. http://digitalcommons.wustl.edu/canpre_pubs/6.

product would be 50% of this group, which would be attained within five years of launch (2025). There may also be a market for patients who refuse oral tamoxifen due to the drug's side effects, but we do not factor this into our forecasts (as it is still unknown whether oral endoxifen would have fewer significant AEs than oral tamoxifen). As we model a starting net price of $200/month for the drug on launch (in 2020), we expect peak sales in 2025 of $91m and $161m in the US and worldwide, respectively, which, at our 20% assumed royalty rate, leads to global net royalties of $32m to Atossa in 2025.

We reiterate that there is the potential for some variability in our market size estimates. A study[26] on 279 Polish women taking tamoxifen found that nearly 60% of these had endoxifen concentrations below the predefined threshold of therapeutic efficacy.

IDMC-fulvestrant forecasts pushed back

Atossa's intraductal microcatheter (IDMC) intends to deliver therapeutics for breast cancer and/or precancerous conditions, with potentially higher local exposure and lower systemic exposure vs established therapies or delivery approaches. The current IDMC clinical program is designed to irrigate and deliver fulvestrant (marketed as Faslodex by AstraZeneca) to each of the five to seven breast ducts. Fulvestrant is FDA-approved for estrogen receptor-positive (ER+) metastatic breast cancer (with $830m in global 2016 sales, up 18% 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).

Atossa in early 2017 transferred the site of its ongoing 30-patient, open-label Phase II study on IDMC administered fulvestrant to the Montefiore Medical Center in New York City, from the Columbia University Medical Center where it had been initiated in March 2016. Patient recruitment has been slower than expected, both prior to and following the shift in clinic site. The company is no longer providing guidance for when the study will complete recruitment (compared to its prior estimate of August 2017).

The IDMC-fulvestrant study is comparing the safety, tolerability and pharmacokinetics following the IDMC instillation of fulvestrant (n=24), compared to intramuscular (IM) administration (n=6), in a neoadjuvant setting[27] in patients with breast cancer or ductal carcinoma in situ (DCIS) who are scheduled for mastectomy or lumpectomy. The primary outcome measure is the number and severity of adverse events at four weeks using the National Cancer Institute's CTCAE v4.0 protocol. The study will also measure changes in the expression of Ki-67[28] as well as estrogen and progesterone receptors, between biopsies taken prior to fulvestrant therapy, and post-treatment surgical specimen.

Projecting IDMC-fulvestrant potential launch in 2023 (vs H121 previously)

We continue to believe that after the current IDMC-fulvestrant trial, a larger (200- to 400-patient) pivotal study will be needed before approval, under the FDA 505(b)2 process. We expect the company to partner the IDMC-fulvestrant program with an oncology-experienced medical devices and/or pharma firm before or in parallel to starting this pivotal study, with Atossa entitled to 20% royalties on net IDMC sales.

---

[26] Hennig EE, Piatkowska M, Karczmarski J, et al. *BMC Cancer*. 2015 Aug 1;15:570.

[27] A neoadjuvant treatment refers to a therapy provided as a first step to shrink or control a tumor before the main (or more involved) treatment, usually surgery, is provided. In the ongoing Phase II IDMC-fulvestrant trial, the neoadjuvant treatment (fulvestrant by IM or IDMC administration) is provided 30-45 days before surgery.

[28] Ki-67 is a protein marker for cellular proliferation whose density level correlates with cancer growth and progression.

While we previously modeled that the pivotal study could start in H218, given the push back in expected recruitment completion for the ongoing study and lack of guidance, we now model that the pivotal study would start in H219 at the earliest, which is now when we also expect the product to be partnered. This pushes back our potential launch forecast to H222 (from H121 previously). We continue to estimate that the IDMC single-use device will be sold at launch at $3,500 per monthly application.

We assume that IDMC-fulvestrant will be used in the neoadjuvant setting in the treatment of ER+ breast cancers. The American Cancer Society (ACS) estimates that about 252,710 new cases of invasive breast cancer will be diagnosed in women per year. Approximately 75-80% of such breast cancers are ER+[29] (ie they grow in response to estrogen).

We expect that IDMC-fulvestrant will be used in a peak case of 25% of neoadjuvant treatment scenarios (reflecting only up to 40% of diagnosed ER+ breast cancers, primarily those at Stage II and III). We expect commercialization through 2030, when the IDMC technology's core patents expire.

We have not changed our peak penetration forecasts (25%), but given the push back in our launch timeline, we slightly lowered our post-launch pricing increase assumptions, but maintained our estimate for peak sales in 2026. We now assume peak global IDMC-fulvestrant product sales (consisting of the IDMC device and separate from the cost of the fulvestrant drug) of $182m in 2026 (from $191m); this translates to peak royalties to Atossa of $36.5m in 2026.

Exhibit 8: IDMC-fulvestrant revenue assumptions

Year-end 31 December	2022	2023	2024	2025	2026
US market					
Estimated Breast cancer incidence (000)	274.8	278.9	283.1	287.3	291.6
Estrogen-receptor positive proportion (%)	75.0	75.0	75.0	75.0	75.0
Neoadjuvant therapy eligible proportion (%)	40.0	40.0	40.0	40.0	40.0
IDMC-Fulvestrant market share (%)	0.9	6.7	16.3	24.1	25.0
Number of IDMC-Fulvestrant units sold	776	5,604	13,811	20,746	21,874
Average IDMC selling price ($)	3,500	3,675	3,859	4,052	4,254
Total IDMC-Fulvestrant product revenues ($000)	2,717	20,594	53,292	84,056	93,057
Royalty rate (%)	20.0	20.0	20.0	20.0	20.0
Net revenue to Atossa ($000)	543	4,119	10,658	16,811	18,611
Europe and ex-US markets					
Total IDMC-Fulvestrant product revenues ($000)	2,604	19,739	51,080	80,567	89,194
Royalty rate (%)	20.0	20.0	20.0	20.0	20.0
Net revenue to Atossa ($000)	521	3,948	10,216	16,113	17,839
Worldwide IDMC-Fulvestrant sales ($000)	5,321	40,332	104,372	164,622	182,251
Worldwide IDMC-Fulvestrant royalties to Atossa ($000)	1,064	8,066	20,874	32,924	36,450

Source: Edison Investment Research

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

Valuation

Our rNPV valuation continues to include the prospects of the company's oral endoxifen and the IDMC-fulvestrant programs. Given the reported Phase I data and the firm's plans and strategy for developing a topical formulation to treat MBD, we now include the topical endoxifen program in our valuation.

We assume Atossa will spend $4.0m on R&D on the topical endoxifen program (primarily for the planned 480-patient Phase II study) between Q417 and Q119. We assume it will spend $3.5m on oral endoxifen R&D over the same period before partnering it as well. We assume that Atossa will spend $3.2m in R&D on the IDMC-fulvestrant program between Q417 and H219 before partnering it.

Given the slower than expected pace of recruitment for the Phase II study, we now apply a 10% probability for the IDMC-fulvestrant program (vs 25% previously). For the oral endoxifen program, given the positive top-line Phase I data, we have increased our probability of success to 20% (from 15% previously). For the topical endoxifen program, we apply a 5% probability of success. This is because proof-of-concept for the reduction of MBD with topical endoxifen has not yet 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 breast cancer risk (as it is much more challenging to create a solid market for a preventative treatment, than to treat an established ailment).

Exhibit 9: 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	20.1	0.76	5.0%	2020	15%	922 in 2026
Oral endoxifen	Breast cancer	21.4	0.81	20.0%	2021	12.5% of patients taking tamoxifen	161 in 2025
Intraductal Microcatheter (for Fulvestrant)	Breast cancer	7.2	0.27	10.0%	H222	25%	182 in 2026
Corporate costs & expenses							
SG&A expenses		(24.0)	(0.90)				
Net capex, NWC & taxes		(6.4)	(0.24)				
Total rNPV		**18.4**	**0.70**				
Net cash (Q417e)		6.1	0.23				
Total equity value		**24.6**	**0.93**				
FD shares outstanding (000s) (Q417e)		26,522					

Source: Edison Investment Research

Given the contribution of the topical endoxifen program, we now obtain an rNPV of $18.4m (up from $6.3m previously). After including Q417 estimated net cash of $6.1m, we obtain an equity valuation of $24.6m, or $0.93 per fully diluted share (before considering any potential dilution from funding requirements).

Sensitivities

Development and regulatory risk: To gain approval, endoxifen and IDMC-fulvestrant must be shown to be safe without any notable safety concerns. To be commercially successful they must also show signals of therapeutic efficacy. The development strategies for both programs also depend on whether the FDA agrees to the firm's proposed regulatory pathway (505(b)2), rather than the standard (505(b)1) NDA application process, or PMA for IDMC-fulvestrant. Should the FDA require the standard application processes (needing more exhaustive clinical data), the additional resource and time requirements could have an impact on the firm's ability to continue such programs and/or weigh on our valuation. The potential for drug transference risk (gel rubbing off on

clothing and the possible risk of topical endoxifen exposure to family members) may also be considered by the regulators.

Commercial and competition risk: Even if endoxifen obtains regulatory approval, much of its success will hinge on the marketing capabilities of a would-be partner. Currently tamoxifen's share for breast cancer prevention in at-risk patients remains very low, due to concerns of systemic side effects. Endoxifen's success will depend largely on the marketing and educational efforts of the partner to persuade healthcare providers and patients of the drug's potential uses and benefits (and in the case of topical endoxifen, of the benefit of reducing MBD). Further, the product will need to compete with other preventative cancer products, most notably aromatase inhibitors in post-menopausal women, as well as other potential emerging products. Commercial success will depend on relative performance (in reduction of recurrence rates, safety, etc).

Partnership risk: We believe that Atossa will require development partners to advance endoxifen or IDMC-fulvestrant through pivotal studies and to support the marketing activities required to raise a sufficient profile for these products. Challenges to securing viable partnerships could lead to unnecessary development delays and/or unfavorable terms.

Financing risk: Atossa's current funds on hand are expected to only be sufficient into late Q118. We are modeling that the company will need to raise $10m in each of the next two years (2018 and 2019). After this point, we expect partners to fund the therapeutic programs in endoxifen and fulvestrant. While our model accounts for these financings as long-term debt, the firm most likely will need to issue equity instead, at pricing that may not be favorable for current shareholders and could lead to significant dilution. For instance, raising $10m in equity at today's market price could dilute our equity valuation (inclusive of net cash) from $0.93 per share to approximately $0.62 per share.

Intellectual property and litigation risk: The success of Atossa's programs will depend on its ability to defend the intellectual property (IP) assets surrounding its technologies. For oral endoxifen, different research groups are developing oral formulations and there may be IP challenges should these groups' advancements lead to approved commercial products. The IDMC-fulvestrant program may also need to contend with legal challenges from AstraZeneca, if it does not support or enter a partnership with Atossa on IDMC-fulvestrant. AstraZeneca could perceive the IDMC-fulvestrant program as a competitive threat and could seek legal action to impede its development.

Financials

Atossa reported Q317 results on 13 November 2017, with a net loss of $2.2m ($0.18 per share given 12.4m average Q317 shares outstanding), and an operating cash burn rate of $1.7m. Q317 R&D costs were $0.74m, and were mostly attributable to the Phase I oral and topical endoxifen study costs. We expect R&D costs in 2018 to increase as the company proceeds with a 480-patient topical endoxifen Phase II study and the oral endoxifen study (recruitment size still unknown).

Atossa had $2.8m net cash at Q317, and on 30 October 2017 it completed a $5.5m (gross) underwritten equity offering where it sold 12.5m shares at $0.44 per share. We estimate the Q417 operating cash burn rate will be $2.1m, accounting for the completion of the oral and topical arms of the endoxifen Phase I, and the firm's preparations for starting Phase II studies on both topical and oral endoxifen in Q118. Our model assumes a 2018 operating cash burn rate (excluding net interest income) of $11.8m and $6.2m in 2019. The burn rate is projected to decrease in 2019, as we expect the company to have partnered the endoxifen programs (oral and topical) in early 2019, which would reduce its R&D expenses.

We assume that Atossa will need to raise funds before mid-2018; 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, the company may need to issue equity instead, at pricing that may not be favorable for current shareholders and could lead to significant dilution. For instance, raising $20m in equity at today's market prices could dilute shareholders by about 70%. Further, in the event the company is unable to raise the required funds, we believe it may need to delay or deprioritize one of its programs. This would have a negative effect on the pipeline valuation.

Exhibit 10: Financial summary

US$(000)	2014	2015	2016	2017e	2018e	2019e
31-December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	40	2	0	0	0	0
Cost of Sales	0	(132)	0	0	0	0
General & Administrative	(8,360)	(9,996)	(6,176)	(4,576)	(3,800)	(3,000)
Research & Development	(1,110)	(2,360)	(770)	(3,111)	(7,600)	(3,200)
EBITDA	(6,943)	(9,484)	(6,946)	(7,687)	(11,400)	(6,200)
Depreciation	(388)	(273)	(303)	(136)	(128)	(119)
Amortization	0	0	0	0	0	0
Operating Profit (before exceptionals)	(7,331)	(9,756)	(7,250)	(7,823)	(11,528)	(6,319)
Exceptionals	(2,352)	0	881	(491)	0	0
Other	(2,487)	(3,002)	0	0	0	0
Operating Profit	(12,171)	(12,758)	(6,369)	(8,314)	(11,528)	(6,319)
Net Interest	0	0	0	10	18	(126)
Profit Before Tax (norm)	(7,331)	(9,756)	(7,250)	(7,813)	(11,511)	(6,445)
Profit Before Tax (FRS 3)	(12,171)	(12,758)	(6,369)	(8,303)	(11,511)	(6,445)
Tax	0	0	0	0	0	0
Profit After Tax and minority interests (norm)	(7,331)	(9,756)	(7,250)	(10,381)	(11,511)	(6,445)
Profit After Tax and minority interests (FRS 3)	(12,171)	(12,758)	(6,369)	(10,871)	(11,511)	(6,445)
Average Number of Shares Outstanding (m)	1.6	1.9	2.9	12.5	26.5	26.5
EPS - normalised ($)	(4.57)	(5.15)	(2.46)	(0.83)	(0.43)	(0.24)
EPS - normalised and fully diluted ($)	(4.57)	(5.15)	(2.46)	(0.83)	(0.43)	(0.24)
EPS - (IFRS) ($)	(7.59)	(6.73)	(2.16)	(0.87)	(0.43)	(0.24)
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	2,424	1,948	890	655	602	565
Intangible Assets	1,887	1,701	640	561	561	561
Tangible Assets	537	248	249	94	40	4
Current Assets	9,340	4,295	3,255	6,306	4,468	8,059
Short-term investments	0	275	55	55	55	55
Cash	8,501	3,716	3,028	6,090	4,252	7,843
Other	839	304	172	161	161	161
Current Liabilities	(2,263)	(2,502)	(1,047)	(1,072)	(691)	(691)
Creditors	(2,263)	(2,502)	(1,047)	(1,072)	(691)	(691)
Short term borrowings	0	0	0	0	0	0
Long Term Liabilities	(2)	0	0	0	(10,000)	(20,000)
Long term borrowings	0	0	0	0	(10,000)	(20,000)
Other long term liabilities	(2)	0	0	0	0	0
Net Assets	9,498	3,742	3,097	5,889	(5,622)	(12,067)
CASH FLOW						
Operating Cash Flow	(10,555)	(13,953)	(5,375)	(7,061)	(11,780)	(6,200)
Net Interest	0	0	0	10	18	(126)
Tax	0	0	0	0	0	0
Capex	(5)	(131)	(9)	(5)	(75)	(83)
Acquisitions/disposals	(339)	(158)	0	0	0	0
Financing	13,156	9,457	4,696	10,117	0	0
Net Cash Flow	2,257	(4,785)	(688)	3,062	(11,838)	(6,409)
Opening net debt/(cash)	(6,327)	(8,501)	(3,991)	(3,083)	(6,145)	5,693
HP finance leases initiated	0	0	0	0	0	0
Other	(83)	275	(220)	(0)	0	0
Closing net debt/(cash)	(8,501)	(3,991)	(3,083)	(6,145)	5,693	12,102

Source: Edison Investment Research, Atossa Genetics reports

Contact details	Revenue by geography
107 Spring Street Seattle, WA 98104 US 866-893-4927 www.atossagenetics.com	N/A

Management team

Chairman and CEO: Steven C Quay, MD, PhD	Chief financial officer and counsel/secretary: Kyle Guse, CPA
Dr Quay has served as CEO, president and chairman since the firm was incorporated in April 2009. Before joining Atossa, Dr Quay was chairman, president and CEO of MDRNA (now Marina Biotech), a biotechnology company focused on the development and commercialization of RNAi-based therapeutic products, from 2000 through 2008. Dr Quay is certified in anatomic pathology with the American Board of Pathology, completed both an internship and residency in anatomic pathology at Massachusetts General Hospital, and is a former faculty member of the Department of Pathology, Stanford University School of Medicine. Dr Quay is a named inventor on 76 US patents. He received an MD in 1977 and a PhD in 1975 from the University of Michigan Medical School. He also received his BA degree in biology, chemistry and mathematics from Western Michigan University in 1971.	Mr Guse has served as chief financial officer, general counsel and secretary since January 2013. His experience includes more than 20 years of counselling life sciences and other rapid growth companies through all aspects of finance, corporate governance, securities laws and commercialization. Mr Guse has practiced law at several international law firms, including from January 2012 through January 2013 as a partner at Baker Botts LLP, and from October 2007 to January 2012 as a partner at McDermott Will & Emery LLP. Mr Guse began his career as an accountant at Deloitte &Touche and is a licensed Certified Public Accountant in the state of California. Mr Guse earned a BS in business administration, an MBA from California State University, Sacramento, and a JD from Santa Clara University School of Law.
Vice president, regulatory affairs and quality: Janet Rose Rea	
Ms Rea has nearly 35 years of industry leadership experience in regulatory affairs and quality. She obtained her BS degree in microbiology from the University of Washington and was conferred a master's of science of public health from the same institution. Her career in the healthcare industry started with Miami, FL-based Dade Division of the American Hospital Supply Corporation (now Baxter), followed by Genetic Systems, and Immunex Corporation. She held positions with MDS Pharma, Targeted Genetics, and executive positions with AVI BioPharma (now Sarepta), Poniard Pharmaceuticals and Protein Sciences Corporation (Meriden, CT) and Therapeutic Proteins International (Chicago, IL).	

Principal shareholders	(%)
Iroquois Capital Management LLC	8.7
Empery Asset Management	8.7
Renaissance Technologies	1.3
Ensisheim	1.1
Vanguard Group	0.8

Companies named in this report

AstraZeneca

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
295 Madison Avenue, 18th Floor
10017, New York
US

Sydney+61 (0)2 8249 8342
Level 12, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia