**COMPANY NOTE**

Initiating Coverage

USA | Healthcare | Biotechnology

November 10, 2014

Jefferies

# Atara (ATRA)

## Targeting Unmet Needs in Muscle Wasting and Oncology - Initiate at Buy

**BUY**

Price target $35.00

Price $28.75

EQUITY RESEARCH AMERICAS

### Key Takeaway

**ATRA has a proven management team with extensive experience in licensing and developing products. We believe ATRA's two lead clinical products, PINTA 745 and STM 434, offer significant commercial opportunities with combined potential worldwide adjusted peak sales of ~$790M. Other pipeline/licensed products provide additional upside.**

*Jefferies was a co-manager in Atara's initial public offering on October 15, 2014.*

**PINTA 745 is ATRA's key value driver with a large commercial opportunity.** '745 is an anti-myostatin peptibody that is in a phase 2 study to treat protein energy wasting (PEW) in end stage renal disease (ESRD) patients on dialysis with data expected in 2H15. There are no FDA approved therapies for PEW although nutritional supplements and steroids are used off label. We estimate ~200,000 kidney dialysis patients in the US alone suffer from PEW and project ~$696M in worldwide peak adjusted sales comprising $24 of our DCF-based PT. Our favorable outlook on '745 is supported by phase 1 data in prostate cancer and initial safety data in the first 8 ESRD patients in the phase 2 study.

**STM 434 has significant potential in ovarian cancer with potential for expansion to other solid tumors.** '434 is a soluble ligand trap that binds Activin A and other ligands of the ActR2B receptor. '434 is in a phase 1 study for the treatment of ovarian and other solid tumors with data expected in 1H16. We believe '434' could be effective in ovarian cancer based on its mechanism of action and the strength of its preclinical data. We estimate ~$94M in worldwide peak adjusted sales for '434 in recurrent ovarian cancer comprising $8 of our DCF-based PT. We believe positive '434 monotherapy data in the clear cell and/or granulosa cell sub-types of ovarian cancer in the phase 1 study could potentially lead to an accelerated path to approval.

**Option agreement with Memorial Sloan Kettering for allogeneic T cell therapies represents upside.** These licensed off the shelf T-cell directed therapies to Epstein Barr Virus (EBV), Cytomegalovirus (CMV), and Wilms Tumor 1 (WT1) for the treatment of certain cancers and persistent viral infections provide significant optionality. The EBV and CMV directed T cell programs are in phase 2 trials while the WT1 targeted T cell program is in a phase 1 trial.

### Valuation/Risks

Our $35 PT is DCF-based. Risks include clinical, regulatory, competitive, commercial.

| Financial Summary | |
|---|---|
| Net Debt (MM): | $0.0 |
| Cash & ST Invest. (MM): | $74.8 |

| Market Data | |
|---|---|
| 52 Week Range: | $29.36 - $9.66 |
| Total Entprs. Value (MM): | $681.4 |
| Market Cap. (MM): | $681.4 |
| Insider Ownership: | 66.3% |
| Institutional Ownership: | 8.7% |
| Shares Out. (MM): | 23.7 |
| Float (MM): | 5.0 |
| Avg. Daily Vol.: | NA |

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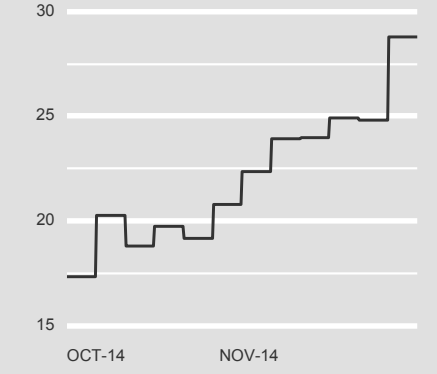
* Jefferies LLC

| USD | *Prev.* | 2013A | *Prev.* | 2014E | *Prev.* | 2015E | *Prev.* | 2016E |
|---|---|---|---|---|---|---|---|---|
| Rev. (MM) | -- | 0.0 | -- | 0.0 | -- | 0.0 | -- | 0.0 |
| **EPS** | | | | | | | | |
| Mar | -- | -- | -- | (1.02)A | -- | -- | -- | -- |
| Jun | -- | -- | -- | (0.33)A | -- | -- | -- | -- |
| Sep | -- | -- | -- | (0.39)A | -- | -- | -- | -- |
| Dec | -- | -- | -- | (0.40) | -- | -- | -- | -- |
| FY Dec | -- | (1.28) | -- | (1.34) | -- | (1.41) | -- | (2.00) |
| FY P/E | | NM | | NM | | NM | | NM |

**Price Performance**



# Atara Biotherapeutics

## BUY: $35.00 Price Target

THE LONG VIEW

### Scenarios

**Target Investment Thesis**

- We project a 40% probability of PINTA 745 approval in 2019 for PEW in ESRD patients (peak adjusted WW sales of ~$696M in 2029).
- We project a 20% probability of STM 434 approval in 2020 for recurrent ovarian cancer (peak adjusted sales reach ~$94M in 2029).
- We do not assign any value to other pipeline products or the T-cell therapies from MSK.
- DCF-based PT: $35.

**Upside Scenario**

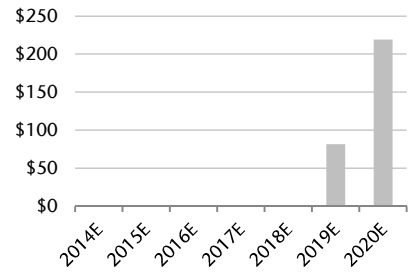
- '745 achieves higher than expected market penetration (peak adjusted WW sales of ~$836 in 2029).
- ATRA licenses the EBV T-cell therapy from MSK and is approved for EBV associated hematological malignancies in 2019 (peak adjusted sales of ~$42.8M in 2029).
- DCF-based PT: $47.

**Downside Scenario**

- '745 is not successful in its phase 3 trial.
- '434 is launched in 2020 for recurrent ovarian cancer (peak adjusted sales reach ~$94M in 2029).
- DCF-based PT: $9.

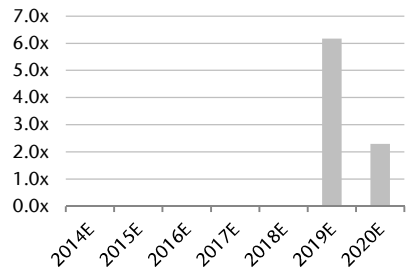
### Long Term Analysis

**Revenue (M)**




Source: Factset, Jefferies estimates

**Enterprise Value (EV)/Revenue**



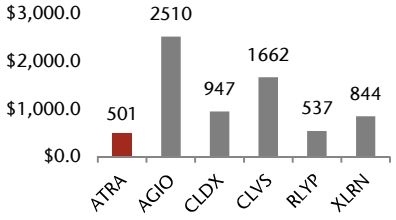

Source: Factset, Jefferies estimates

**Other Considerations**

Continued acquisition of valuable clinical stage assets by ATRA could provide additional upside to our estimates.

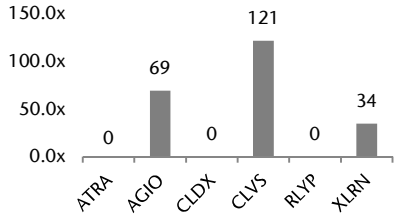
### Peer Group

**Enterprise Value (EV)**




Source: Factset

**Enterprise Value (EV)/Revenue**




Source: Factset

**Recommendation / Price Target**

| Ticker | Rec. | PT |
|---|---|---|
| **ATRA** | **Buy** | **$35** |
| AGIO | NC | NC |
| CLDX | Buy | $24 |
| CLVS | NC | NC |
| RLYP | NC | NC |
| XLRN | NC | NC |

### Catalysts

- Topline data from phase 2 trial of '745 treating PEW in ESRD patients– 2H15.
- Potential for preliminary data for phase 1 trial of '434 in OC/solid tumors – 2H15.
- Top-line data from phase 1 trial of '434 in OC/solid tumors – 1H16.
- Initial option period for MSK T-cell therapies expires –Sep. 23, 2015.

### Company Description

Atara is a US biotechnology company focused on developing a pipeline of clinical stage in-licensed assets. The key value driver for ATRA is Pinta 745, which is currently being evaluated in a phase 2 proof-of-concept trial for the treatment of protein energy wasting (PEW) syndrome in end-stage renal disease (ESRD). The second pipeline product, STM 434, has just entered the clinic in a multi-part phase 1 trial for the treatment of ovarian and other solid tumors. ATRA has also secured an option agreement with Memorial Sloan Kettering (MSK) to in-license 3 clinical-stage T-cell immunotherapies. This agreement with MSK also allows for collaborative R&D efforts for the development of other cellular immuno-therapies, such as CAR-T cells.



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# Executive Summary

**We are initiating coverage of Atara Biotherapeutics (ATRA) with a Buy rating and a YE15 price target of $35.** ATRA is a clinical stage biotech company that has a proven management team with extensive experience in licensing and developing drugs. ATRA has licensed drugs from Amgen for muscle wasting and oncology and plans to acquire or license additional assets in the future. The company's lead programs are focused on myostatin and activin, members of the TGF-beta family of proteins that have demonstrated the potential to have therapeutic benefit in a number of clinical indications. PINTA 745 is a peptibody that inhibits myostatin and is currently in a phase 2 study to treat PEW in ESRD patients while STM 434 is a soluble ActR2B receptor-IgG fusion protein that binds Activin A and other ligands of the 2B receptor that is in a phase 1 study for the treatment of ovarian and other solid tumors. ATRA also has an exclusive option agreement with Memorial Sloan Kettering (MSK) for allogeneic T cell therapies directed to EBV, CMV, and WT1.

**PINTA 745 is the key value driver for the stock with phase 2 data expected in 2H15.** PEW is a state of muscle wasting, inflammation, and malnutrition that represents a large unmet need in ESRD patients on dialysis. We estimate ~200,000 kidney dialysis patients in the US suffer from PEW that are eligible for '745 and assume ~$1.7B in worldwide peak unadjusted sales for '434 in this patient population. This was corroborated by ATRA's work with DaVita which demonstrated that PEW patients on dialysis (~54% of their patient population) had a higher mortality rate than non-PEW patients at 1 year and 3 years. Additionally, data from a phase 1 study in prostate cancer patients demonstrated significant increases in lean body mass and lower extremity muscle size. ATRA has reported that in the ongoing phase 2 study initial safety data has suggested no dose-limiting toxicities, no serious AEs, no Grade 3 or higher AEs, and no anti-drug antibodies detected within the first 8 ESRD patients dosed with '745 at 3 mg/kg. We believe '745 will be effective at improving lean body mass and muscle size in the phase 2 study in ESRD patients suffering from PEW and are also optimistic that there will be improved functional and quality of life outcomes for these patients given the optimized drug exposure through dosing, frequency of treatments and route of administration. Positive data from this study could lead to development of '745 in additional indications where muscle growth and inflammation reduction could lead to better outcomes. On the commercial side, we believe '745 will not be included in the ESRD bundle as it falls distinctly under two treatment categories that are specifically listed as unrelated to dialysis: anti-inflammatory and musculoskeletal and inclusion of a drug within the bundle requires bureaucratic action. Additionally, ATRA is conducting studies with DaVita to evaluate the cost-savings potential of a treatment for PEW in terms of reducing inpatient expenditures.

**STM 434 is a ligand trap for ovarian cancer and other solid tumors in phase 1 with data expected 1H16.** '434 is a soluble ActR2B receptor-IgG fusion protein that binds Activin A and other ligands of the 2B receptor. We believe '434 could be effective in recurrent ovarian cancer based on the strength of the preclinical data and its mechanism of action. Preclinically, ATRA and AMGN have demonstrated that '434 has had an impact on Activin A levels, tumor size (monotherapy and in combination with chemotherapy), cachexia, and survival. While there is a potential risk for bleeding based on preclinical data from a closely related compound, ATRA will be excluding patients at heightened risk for bleeding and will be closely monitoring patients for bleeding or increased risk for bleeding. We believe '434 could also potentially have an accelerated path to market with positive monotherapy data in the clear cell and granulosa cell subtypes of ovarian cancer being studied in phase 1. Data from the phase 1 study is expected in 1H16 and we assume ~$471M in worldwide peak unadjusted sales for '434 in recurrent ovarian cancer.



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**Collaboration with Memorial Sloan Kettering for T-cell therapies targeting EBV, CMV, and WT1.** We believe this exclusive option agreement for the development and commercialization of allogeneic T-cell therapies in the treatment of certain cancers and persistent viral infections provides significant optionality in the pipeline. This approach uses third party donor derived T cells targeted to either: EBV for the treatment of EBV-associated lymphoma and other malignancies, CMV for the treatment of CMV infection or persistent CMV viremia after allogeneic HSCT, or WT1 for the treatment of hematologic and solid tumors. A key advantage of this approach is that it will be an off the shelf therapy and encouragingly, data from the EBV targeted T cell program has demonstrated efficacy in patients refractory to current treatments like Rituxan. The EBV and CMV directed T cell programs are in phase 2 trials with data expected in 1H16 while the WT1 targeted T cell program is in a phase 1 trial. We do not currently assign any value to these allogeneic T cell therapies.

## Valuation

We value ATRA at $35/share using a DCF model (forecast period 2015-2029, 23.8M diluted shares outstanding and a 10% discount rate) that includes probability-adjusted WW sales for '745 (PEW in ESRD patients) and '434 (ovarian cancer). We assume '745 is launched in 2019 and estimate that it will achieve probability-adjusted (40%) peak WW sales of ~$696M in 2029. We assume '434 is launched in 2020 and achieves probability-adjusted (20%) peak sales of ~$94M in 2029. We forecast R&D expenses to grow from ~$15M in 2014 to $40M in 2017 when the pivotal trials for both '745 and '434 are projected to be ongoing. We project that R&D expenses will steadily increase until becoming capped at $70M in 2020+. We estimate SG&A expenses to increase significantly from ~$13M in 2014 to $60M in 2020 after both '745 and '434 have launched; after this we predict SG&A will grow steadily until it is capped at $80M in 2022+. We have assumed equity financings in 2016 and 2018 (~$100M and ~$150M, respectively; each raise priced at $35/share). We forecast 2020 as being the first year of profitability and a full corporate tax rate of 35% beginning in 2023.

## Risks

**Clinical Risks:** As with all companies in biotechnology that are investing in the development of clinical programs, trial failures can lead to delays in projections for market entry or possibly even discontinuation of programs. For '434 there is the possibility of bleeding risk as seen preclinically with another ligand trap (STM 217) that is closely related to '434

**Regulatory Risks:** The endpoints in a registration trial for '745 will need to be determined after the phase 2 data is obtained and after discussions with regulatory authorities. For recurrent ovarian cancer, it remains unclear if OS will be required in addition to PFS. The FDA/EMA could determine that the filings for '745/'434 are inadequate and could delay/deny approval. Any delays in approval timelines could impact our earnings estimates, price target, and/or rating

**Commercial Risks:** ATRA has never been a commercial company before and will need to build its own salesforce in the US and ex-US to sell '745/'434. Our estimates may rely on the success of the company to receive drug reimbursement from both private and public payers. Specifically, if '745 is reimbursed as part of a bundled payment for hemodialysis by Medicare and/or managed care systems, our estimates would be negatively impacted.

**Financing Risks:** We estimate that ATRA has adequate cash until 2H16, which includes the readout of topline data from both the phase 2 study of '745 and the phase 1 study for '434. We model two equity raises: $150M on 4.29M shares in 2016 and $100M on 2.86M



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shares in 2018. We project that these funds are necessary for the development and eventual commercial launch of '745/'434. ATRA may need additional dilutive financing to fund the development of the T-cell therapies with MSK and other pipeline programs.

# Targeting serious unmet needs in muscle wasting and oncology

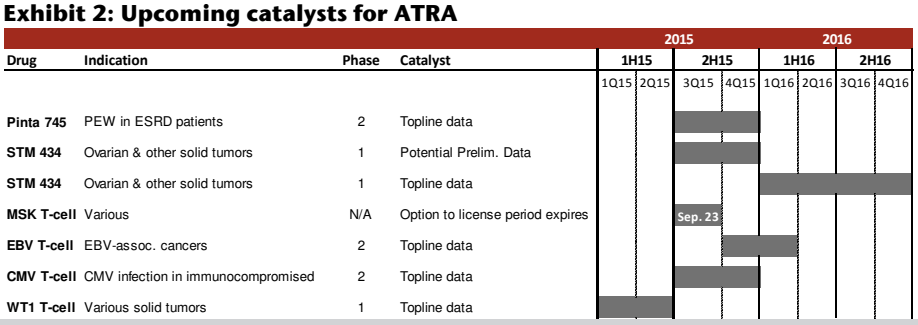
ATRA is a biotech company focused on in-licensing and developing therapies in areas of unmet medical need. The company was originally founded by the acquisition of a portfolio of biologics from Amgen that are all related to a subset of the TGFβ superfamily, called the activin system. PINTA 745 is a peptibody that inhibits myostatin and is currently in a phase 2 study to treat PEW in ESRD patients while STM 434 is a soluble ActR2B receptor-IgG fusion protein that binds Activin A and other ligands of the 2B receptor that is in a phase 1 study for the treatment of ovarian and other solid tumors. ATRA also has an exclusive option agreement with MSK for allogeneic T cell therapies directed to EBV, CMV, and WT1.

**Exhibit 1: ATRA's Activin-related portfolio**

| Drug | Target/Description | Potential Indication | Dev. stage |
|---|---|---|---|
| **PINTA 745** | Anti-myostatin peptibody | PEW, cachexia/atrophy | Ph. 2 |
| **STM 434** | ActR2B ligand trap | Ovarian/solid tumor; cachexia | Ph. 1 in 2H14 |
| **ATA 842** | Anti-Myostatin hAb | Cachexia/atrophy | Pre-clinical |
| **ATA 777** | Anti-Activin A hAb | Non-oncologic activin suppression | Pre-clinical |
| **ATA M43** | Anti-ActR2A/2B hAb | Inclusion-body myositis | Pre-clinical |
| **STM 217** | ActR2B receptor-Fc fusion | Undisclosed | Pre-clinical |
| **ActR2B5** | Soluble ActR2B receptor | Undisclosed | Pre-clinical |

**Source: Company Data**

**Exhibit 2: Upcoming catalysts for ATRA**




**Source: Jefferies estimates, company data**

The TGFβ superfamily comprises a set of hormones/cytokines that share common structural features. This superfamily has a diverse set of functions including regulation of whole-body growth, organ development, inflammation and maintenance of homeostasis. The so-called activin system of hormones/cytokines is a subset of this superfamily that all bind to the same membrane-bound receptors (i.e. activin receptors), which are categorized into two classes: type II (ActR2A & ActR2B) and type I (ActR1A, ActR1B and ActR1C). Mechanistically, the activin receptors are activated sequentially: 1) a hormone/cytokine binds to a type II receptor, and 2) the unique combination of hormone + type II receptor activates different type I receptors. This feature of activin receptor biology allows for a broad range of biological effects across tissues throughout the body. For example, both myostatin and activin A (two activin-type hormones, see below) bind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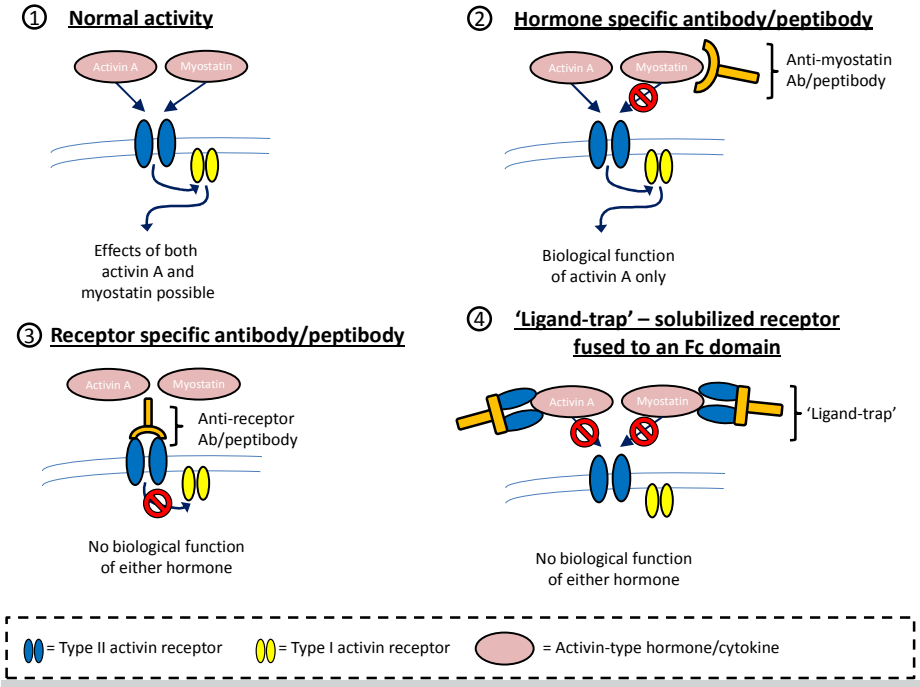
to the ActR2B receptor, but activate different type I receptors. The key players in the activin system as it relates to ATRA's portfolio are: myostatin – a potent inhibitor of muscle growth and a pro-inflammatory cytokine; activin A – a cytokine involved in tumor proliferation, wound healing and vascularization; and activin receptor type 2B (ActR2B) – important type II activin receptor that mediates the effects of both myostatin, activin A and other TGFβ-type signaling molecules.

### Therapeutics targeting the activin system

To date, there have been three basic flavors of therapeutics targeting the activin system: 1) engineered antibodies or antibody-like biologics called 'peptibodies' that bind and inhibit specific activin-type hormones/cytokines, 2) antibodies/peptibodies directed towards specific activin receptors, and 3) solubilized activin receptors fused to the Fc domain of an antibody, commonly referred to as 'ligand-traps.' Peptibodies are conjugates of a synthetic peptide and the Fc domain of human IgG's; these biologics are designed to bind targets with a high degree of specificity like antibodies, but have a much shorter half-life (~4-7 days vs. 10-14 days).

**Exhibit 3: Classes of therapeutics targeting Activin system**




**Source: Jefferies**

These categories differ in their specificity: antibodies/peptibodies targeting a hormone only inhibit the activity of that molecule, whereas antibodies/peptibodies targeting receptors and ligand-traps inhibit all downstream effects of the receptor sub-type. Obviously, the two latter approaches will have broader effects, which in some contexts may increase their efficacy (e.g. in an indication such as cachexia which is multifactorial), but may also increase the likelihood of AEs through off-target effects (e.g. nosebleeds and skin reactions in ACE-031; see table below). Most companies (including ATRA) are focusing on ActR2B and its binding partners (activin and myostatin) with target indications including atrophy, oncology and muscular dystrophy. There are some biologics targeting the ActR2A receptor and its ligands, but these are all focused on blood-disorders such as anemia and mineral imbalances.


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**Exhibit 4: Competitive landscape of activin system inhibitors**

| Name | Structure | Sponsor | Clinical Stage | Target Indication (s) | Efficacy Outcomes | Safety Outcomes | Other |
|---|---|---|---|---|---|---|---|
| ***Myostatin Inhibitors*** | | | | | | | |
| PINTA 745 | Peptibody | Atara | Ph. 2 | PEW | Increased LBM and MV | Well-tolerated; AB production | Actively recruiting |
| ATA 842 | Humanized Ab | Atara | Pre-clinical | Non-renal Cachexia/atrophy | - | - | - |
| LY2495655 | Humanized Ab | Eli Lilly | Ph. 2 | Atrophy in cancer/orthopedic | Increased MV | Well-tolerated | Actively recruiting |
| PF-06252616 | Humanized Ab | Pfizer | Ph. 1 | Unknown | - | - | Actively recruiting |
| REGN1033 | Humanized Ab | Regeneron/Sanofi | Ph. 1 | Orthopedic recovery | - | - | Recruiting not begun |
| MYO-029 | Humanized Ab | Wyeth/Pfizer | Ph. 1/2 | Muscular Dystrophy | Increased LBM; no increase in strength/function | Skin hypersensitivity | Program terminated |
| ***ActR2B Inhibitors*** | | | | | | | |
| STM 434 | Ligand trap | Atara | Ph. 1 | Ovarian/solid tumors | - | - | Initiation in 2H14 |
| ATA M43 | Humanized Ab | Atara | Pre-Clinical | Inclusion-body myositis | - | - | Targets both 2A/2B |
| STM 217 | Ligand trap | Atara | Pre-Clinical | Undisclosed | - | - | Close analog to 434 |
| ActR2B5 | Soluble receptor | Atara | Pre-Clinical | Undisclosed | - | - | Potential fusion with an Fc domain |
| ACE-031 | Ligand trap | Acceleron/Shire | Ph. 2 | Menopausal atrophy & MD | Increased LBM, MV and 6MWT | Nosebleeds and telangiectasia | Program terminated |
| BYM338 | Humanized Ab | Novartis | Ph. 2 | SIBM, COPD & sarcopenia | Increased LBM, MV, quads strength & 6MWT | Well-tolerated | Actively recruiting |
| ACE-536 | Mod. 2B ligand trap | Acceleron | Ph. 2 | Hemoglobinopathies | Increased RBC and hemoglobin | Well-tolerated | Actively recruiting; doesn't bind Activin A |
| ***Other Inhibitors*** | | | | | | | |
| ATA 777 | Anti-Activin A hAb | Atara | Pre-clinical | Non-oncologic activin inhibition | | - | - - |
| FS344 | Follistatin Gene Therapy | Milo Biotech | Ph. 1 | MD & SIBM | | - | - Actively recruiting |

*LBM = lean body mass; MV = muscle volume; AB = antibody; 6MWT = Six Minute Walk Test; SIBM = sporadic inclusion body myositis; COPD = Chronic Obstructive Pulmonary Disease; RBC = Red Blood Cells; MD = Muscular Dystrophy*

**Source: Jefferies**

# PINTA 745 - Treating Protein Energy Wasting (PEW) in End-Stage Renal Disease (ESRD)

'745 is a peptibody in-licensed from Amgen that is designed to bind-to and inhibit myostatin signaling. Myostatin is a powerful repressor of muscle growth, which when produced at high levels can lead to muscle atrophy and is linked to disease-states such as cachexia and protein energy wasting (PEW) experienced during certain cancers, chronic kidney disease (CKD) and/or end-stage renal disease (ESRD). '745 has been engineered by fusing an IgG1 Fc domain to a peptide that blocks myostatin and inhibits muscle production and maintenance. Initially, ATRA is focused on developing '745 for the amelioration of PEW in ESRD patients, but it may have broader applications in oncology and muscular dystrophy. PEW is a state of muscle wasting, inflammation, and malnutrition associated with decreased physical function and increased morbidity and mortality in patients with ESRD. '745 is currently in an ongoing phase 2 trial in ESRD patients with PEW that is expected to have topline data in 2H15. '745 was found to be safe and well tolerated across 3 phase 1 studies and demonstrated significant increases in lean body mass and lower extremity muscle size in a blinded, controlled phase 1 study in prostate cancer. We estimate '745 will be launched for PEW in ESRD patients in 2019 generating peak adjusted worldwide sales of $696M in 2029.



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# CKD/ESRD

## CKD/ESRD – etiology, prevalence and current treatments

CKD can be any condition (e.g. diabetes, hypertension, kidney stones, autoimmune disease, trauma, toxicity, or infectious disease) that causes reduced kidney function over a prolonged period of time. Clinically, CKD is diagnosed when one or both of the following occur for 3 months or greater: **1)** the glomerular filtration rate (GFR, an estimate of kidney function) remains below 60 mL/minute and/or **2)** the urine albumin-to-creatinine ratio (a measure of urine protein excretion) is over 30 mg/g. CKD is categorized into severity buckets (or staged) by GFR, ranging from stage 1 (kidney damage with normal GFR) to stage 5 (kidney failure). Earlier stages of CKD (stages 1-3), are generally treated through management of diet and comorbidities such as hypertension, acidosis (the lowering of blood pH) and mineral bone disorders (MBDs). Although the rate of progression through the stages of CKD varies throughout the population, many patients eventually deteriorate to a state of total kidney failure, known as ESRD (aka CKD stage 5). The replacement of kidney function, either through dialysis (artificial methods for filtering the blood) or transplantation, is required for patients with ESRD.

**Exhibit 5: CKD Stage and Treatment Options**

| Stage | GFR | Description | Treatment Strategies |
|---|---|---|---|
| 1 | ≥ 90 | Normal kidney function but urine or other abnormalities point to kidney disease | Observation, control blood pressure/diet |
| 2 | 60-89 | Mildly reduced kidney function and urine or other abnormalities point to kidney disease | Determine cause, plus above |
| 3 | 30-59 | Moderately reduced kidney function | As above, plus statins, bicarbonate and calcitriol/phosphate binders |
| 4 | 15-29 | Severely reduced kidney function | Plan for ESRD, explore dialysis/transplant options plus treatments above |
| 5 | ≤ 14 | Very severe, or ESRD | Dialysis or transplant is required |

**Source: Jefferies and NIDDK**

According to the CDC, it is estimated that approximately 26 million adults in the US, or roughly 1 in 10, suffer from some level of CKD. By far the most common causes of CKD are diabetes and hypertension, accounting for some 2/3 of all cases, but glomerulonephritis (kidney inflammation), inherited diseases, auto-immune disorders, kidney stones and urinary infections can also lead to CKD.

In 2011, there were ~615,000 reported patients suffering from ESRD, of which over 90,000 succumbed to their illness. Although the prognosis for ESRD patients that receive transplants is much better than that of patients on some form of dialysis, the vast majority of ESRD patients (~460K or 70%) are on dialysis due to a lack of sufficient donor kidneys.


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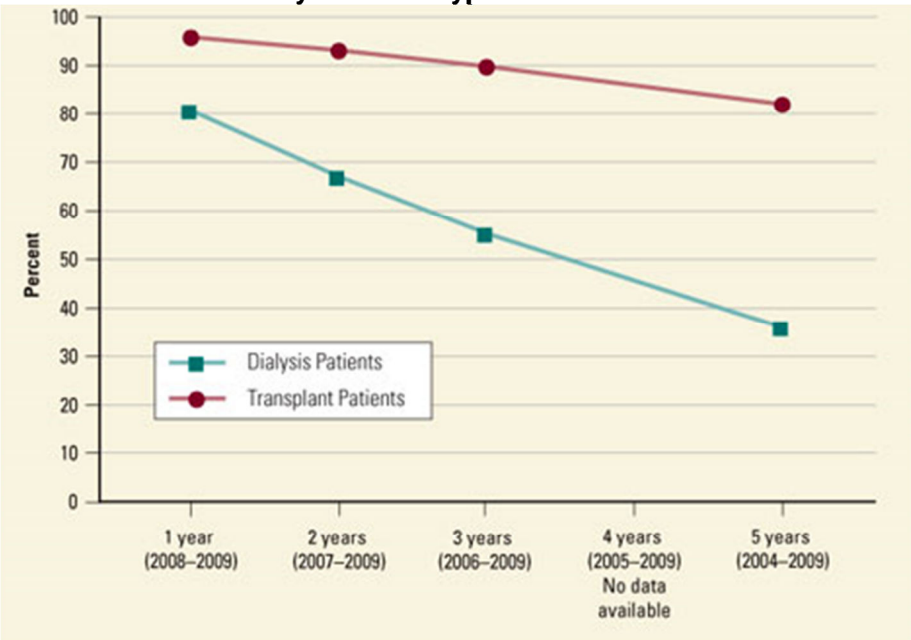
**Exhibit 6: ESRD survival by treatment type**




**Source: NIDDK**

There are two main types of dialysis: **1)** hemodialysis (HD) - the filtering of the patient's blood using an external machine called a dialyzer or 'artificial kidney' and **2)** peritoneal dialysis (PD) - blood filtering is performed by the patient's own peritoneal membrane (abdominal lining). PD may also be broken down further into continuous ambulatory peritoneal dialysis (CAPD), which is the passive infusion of a dialysis solution into the abdomen 4-6 times per day, and continuous cycler-assisted peritoneal dialysis (CCPD), which uses a machine to both infuse and drain the dialysis solution several times throughout the night. In general, HD is performed 3-4 times per week in a specialized center, whereas PD is performed several times per day by the patients within their own home. PD is preferred by most patients because it affords them more control over their schedule and maintains a degree of independence. Despite this preference, there are several very common contraindications for PD, including diabetes, advanced age and poor hygiene. Further, the overall long-term survival of at least 5 years is markedly improved in HD when compared to PD (~50% vs <10%). Given this information, nephrologists tend to prescribe HD to most ESRD patients, representing 395K in 2011 or ~92% of all dialysis patients in that year.


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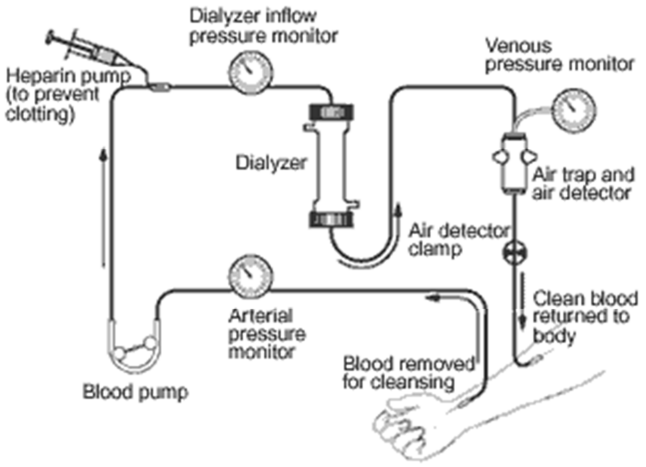
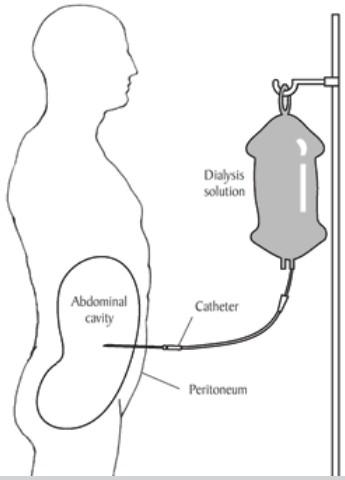
**Exhibit 7: Hemodialysis**




Source: NIDDK

**Exhibit 8: Peritoneal Dialysis**




Source: NIDDK

### Protein Energy Wasting (PEW) in ESRD patients

Shortly after the widespread application of hemodialysis for the treatment of kidney failure in the 1960's, it became clear to physicians that some ESRD patients were at a much higher risk for negative outcomes. At first, physicians were not able to clearly identify risk-factors, but were able to accurately predict patient outcomes. For example, when asked a simple question 'would you be surprised if this patient died in the next year,' physicians routinely predicted the patient population with the highest mortality. Anecdotally, doctors also noted patients who were suffering from a 'protein-related malnutrition syndrome,' and further that these patients were the ones not faring as well. Despite this recognition, the exact cause or even appropriate characterization of this syndrome were not determined due to wide variability in clinical and diagnostic measures used. In recognition of these problems, both US and international nephrology organizations created consensus criteria, such as the Kidney Disease Quality Outcomes Initiative (KDOQI) and the Kidney Disease: Improving Global Outcomes (KDIGO), which established a framework to reliably diagnose CKD/ESRD patients and to identify patients at risk for poorer outcomes. As a result, clinicians were able to identify several risk factors contributing to poorer outcomes, including some that were obvious, such as existing cardiovascular disease and declining GFR, but also identified the suite of factors that are now collectively referred to as protein energy wasting (PEW) syndrome. Clinically, patients suffering from PEW present with a general state of catabolism (i.e. 'wasting'), often greater than can be explained by reduced dietary intake alone. It is generally accepted that PEW is actually a confluence of several biological insults specific to ESRD patients, including anorexia, inflammation, infection and generalized catabolism.



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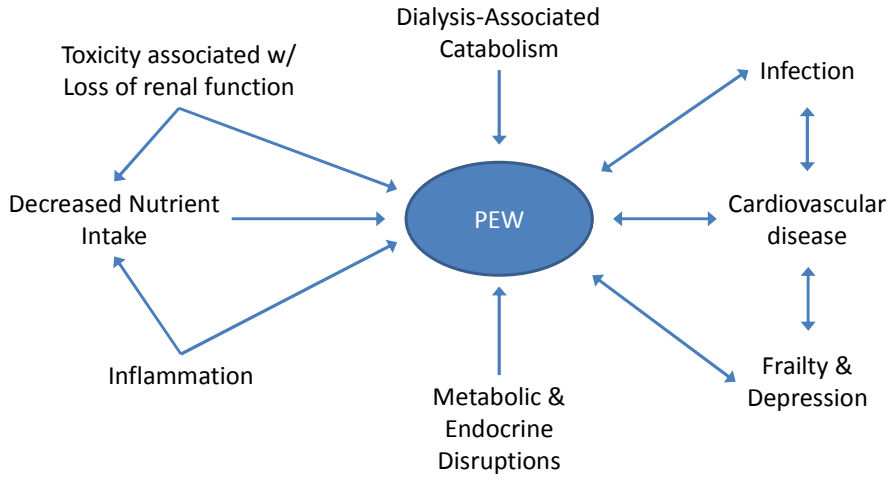
**Exhibit 9: Etiology of PEW**




**Source: Jefferies**

Epidemiological reports have placed the mortality risk in PEW patients from 25 - 47% above that of ESRD patients without the syndrome. In a 2013 paper from the *Journal of the American Society of Nephrologists*, Kim *et al* report that elderly patients suffering from PEW experience several negative consequences in addition to increased mortality, including: poorer quality of life, impaired physical functioning, impaired socialization, and depression. Studies have also shown that PEW increases the risk of infections, cardiovascular disease, and other complications and a higher survival rate was observed in patients who lost overall body weight but gained muscle mass. Many dialysis patients with PEW experience a lower quality of life due to poor limb strength, low endurance and impaired muscle power. Worsening of walking speed and grip strength, associated with loss of muscle mass, have been shown to be effective predictors of mortality. There are no currently approved treatments specifically for PEW, but these patients are often given appetite stimulants, anabolic steroids, anti-inflammatory glucocorticoid regimens and nutritional supplementation. Consensus guidelines recommend dietary supplements containing 10g or more of protein per day. None of these treatments have reliably relieved the symptoms of PEW, but recent reports suggest that frequent nutritional supplementation may reduce hospitalization rates in PEW patients. Dietary changes or nutritional supplementation have not led to long term stabilization of lean body mass, muscle mass or serum albumin levels in patients showing symptoms of PEW or related conditions such as cancer cachexia.

### Diagnosis of PEW

According to the International Society of Renal Nutrition and Metabolism (ISRNM, the leading international society of academic nephrologists), PEW is diagnosed if characteristics from three of the four following categories are present: serum chemistry (low serum levels of albumin/pre-albumin, or cholesterol), reduced body mass (total body or fat mass), reduced muscle mass (muscle wasting or sarcopenia) and anorexia (reduced total energy intake or protein intake). The criteria suggested in the ISRNM guidelines are not widely adopted due to problems with the reliability of their measurement or confounds with their interpretation. For example, dietary energy/protein intake often requires patient recollection which is notoriously unreliable in ESRD patients. Further, BMI may actually be high in some patients suffering from PEW due to a paradoxical concomitant increase in obesity.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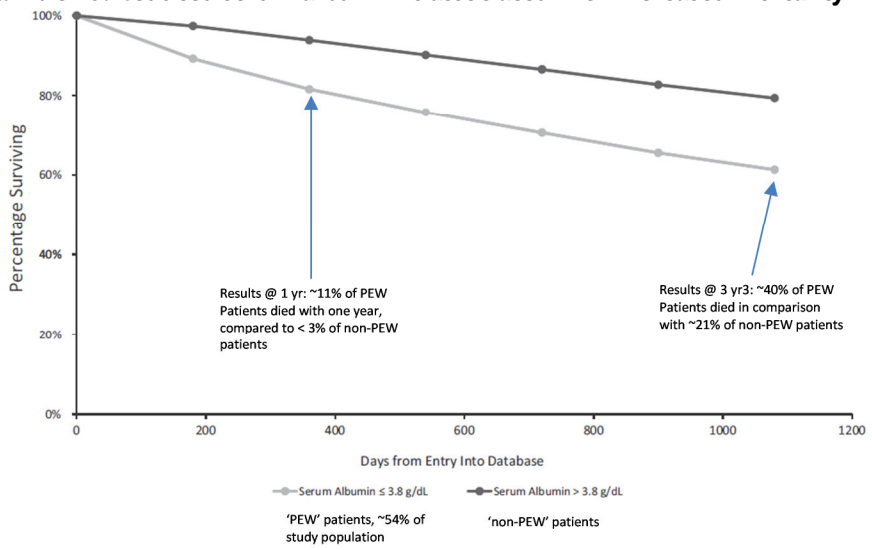
Despite the scientific rationale behind the inclusion of all the categories listed above for the diagnosis of PEW, in practice, physicians within a dialysis unit prefer to use hypoalbuminemia (reduced serum albumin) as a surrogate for PEW diagnosis. Physicians view serum albumin as a 'canary in the coal-mine' for ESRD patients. Reduced serum albumin itself is not the deleterious cause or consequence of PEW and its increased mortality and morbidity, but rather is an easily observable and regularly monitored sign of the overall anabolic/catabolic state. Albumin is the most abundantly produced protein in the human body, and its levels are extraordinarily preserved except in the case of severely negative health states. Further, using hypoalbuminemia as a diagnostic for PEW is well justified because serum albumin levels below 3.8 g/dL have been consistently associated with the same increases in mortality and morbidity as PEW in studies performed both by ATRA and outside academic epidemiologists.

### Collaborative study of PEW in dialysis patients with DaVita

ATRA and DaVita, one of the largest hemodialysis providers in the US, conducted a collaborative study to better understand both the prevalence of PEW and clinical outcomes for these patients. As a normal business practice, DaVita has created a database with clinical information on over 130,000 patients in order to increase the understanding of the pathology and clinical course of kidney disease. In a retrospective, epidemiological study, ATRA/DaVita identified 56,350 dialysis patients who began their treatment at DaVita from 2009-2012 and had received at least 6 months of dialysis. Data from these patients were evaluated from the time they entered the database for 1,200 days or until they died or were lost to follow-up. 54% of these patients had PEW, as defined by having serum albumin levels ≤ 3.8 g/dL after 6 months of dialysis. It was found that patients suffering from PEW had higher mortality rates compared to non-PEW patients (serum albumin > 3.8 g/dL) at both one year (~11% vs. <3%) and at 3 years (~40% vs. ~21%). ATRA/DaVita believe that patients with PEW represent a significant burden on the health care system, and as a follow-up to this study are planning and conducting economic impact studies of this disorder.

**Exhibit 10: Reduced serum albumin is associated with increased mortality**




**Source: Adapted from Company Data**



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## Myostatin biology and PEW

**Exhibit 11: Myostatin knockout bull ('Belgian Blue')**

**Source: Wikimedia Commons**

Myostatin was initially discovered due the observation that certain breeds of cattle (e.g. 'Belgian Blue') and dogs (e.g. 'Bully Whippets'), were extremely muscular. This phenotype is attributed to a loss of function mutation within the gene that encodes for myostatin, *Mstn*. Functionally, myostatin is a repressor of myocyte (muscle cell) hypertrophy and myoblast (muscle stem cells) differentiation and proliferation. Myostatin binds to ActR2B, which results in both the suppression of the transcription of genes necessary for muscle growth and the suppression of IGF-1 signaling required for muscle-related protein synthesis. Additionally, myostatin can promote the production of pro-inflammatory cytokines, such as IL-6 and TNFα. Interestingly, these same pro-inflammatory cytokines appear to upregulate myostatin production within myocytes, resulting in a 'feed-forward' loop. Therefore, in PEW, myostatin promotes muscle atrophy, increases catabolism and increases inflammatory signaling, which in and of itself sustains myostatin production.



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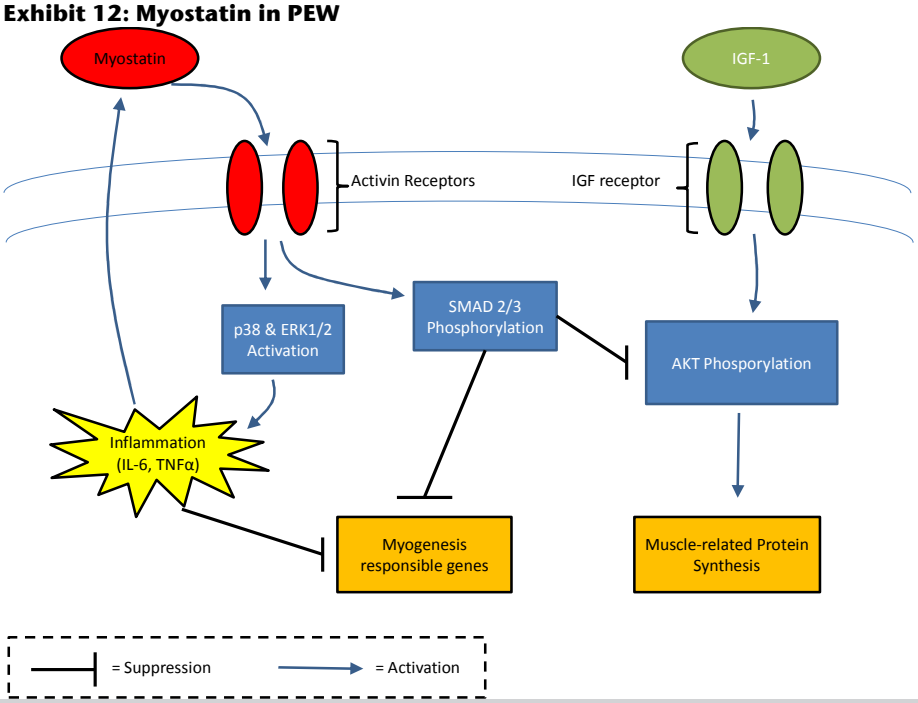
**Exhibit 12: Myostatin in PEW**




**Source: Jefferies**

### Pre-clinical studies with '745

Amgen previously tested the efficacy of a mouse-specific version of '745 (PINTA 745/s) at reversing muscle atrophy and pro-inflammatory signaling in a mouse model of ESRD (5/6$^{th}$ nephrectomy model), and reported the results in the *FASEB Journal* in 2011. To create the mouse model, the majority of the kidneys (100% of the left and 70% of the right) from each mouse was surgically removed, and they were then fed a high protein diet to mimic the physiological consequences of ESRD (e.g. uremia, hypoalbuminemia and muscle atrophy). These nephrectomized mice which have a condition mimicking ESRD are referred to as CKD mice. These CKD mice received subcutaneous injections of '745 (5mg/kg) every other day for 7-28 days. Within this study, it was demonstrated that '745/s was highly specific to myostatin, with no detectable suppression of activin A signaling. More importantly, administration of '745/s significantly increased not only total body weight, but also muscle mass in the CKD mice which increased significantly after 7 days and persisted for over 28 days. Muscle mass was also increased in the tibialis anterior and the gastrocnemius after 7 days and persisted for over 28 days. '745/s was also shown to increase protein synthesis, limit protein degradation, and reduce inflammation (cytokine levels) in these mice.


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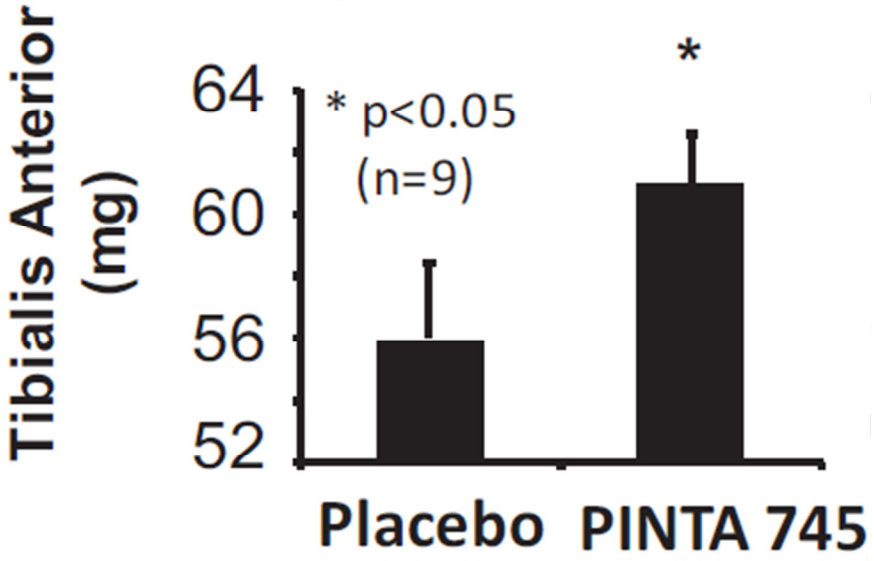
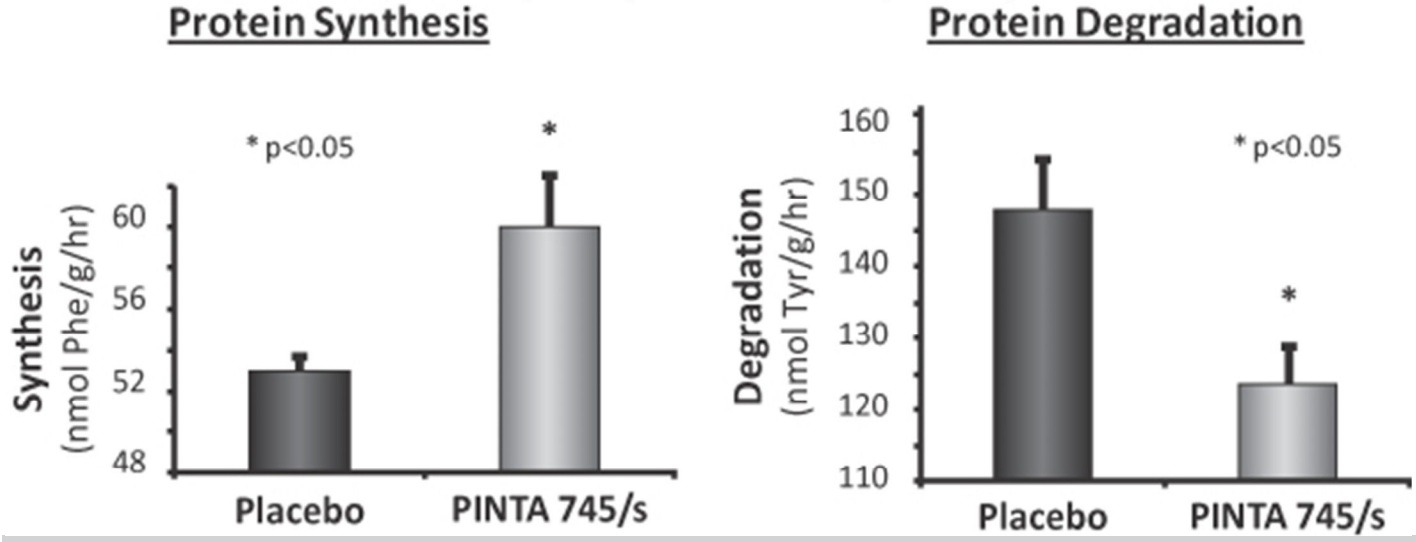
**Exhibit 13: '745/s significantly increased muscle mass in a CKD mouse model**




Source: Company Data

**Exhibit 14: '745/s simultaneously increased protein synthesis and reduced protein degradation in a CKD mouse model**




Source: Company Data

## Clinical Development for '745

Amgen conducted three phase 1 studies of '745 – two of which were in healthy volunteers and one in prostate cancer patients. 151 subjects were enrolled across all three studies including 48 at the highest 3mg/kg subcutaneous dose with no treatment related serious adverse events reported. In the two healthy volunteer studies, adverse events were mild in severity and similar to those observed in the placebo control group.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### Phase 1 study of '745 in Prostate Cancer Patients

This phase 1 study, performed by Amgen, was a randomized, double-blind, placebo controlled trial evaluating the efficacy and safety of subcutaneously administered '745 in prostate cancer patients undergoing androgen deprivation therapy (ADT). ADT is associated with decreased lean body mass, muscle size, fatigue and increased obesity in this patient population. During the initial dose escalation portion of the study, 16 patients were randomized in a 3:1 fashion to '745 (8 patients in both the 0.3mg/kg and 1 mg/kg dose cohorts) or placebo. Once safety was confirmed, 38 patients were randomized in a 1:1 fashion to either 3 mg/kg '745 or placebo. All doses of '745 were given weekly for 4 weeks. Safety, tolerability and PK were assessed at all dose levels. Efficacy of '745 in the 3 mg/kg cohort was also evaluated (at the end of the study [EOS] and at a 1 month follow-up [FUP]) via total body composition (lean body mass via DEXA scan and fat body mass), lower extremity muscle size (CT scans) and physical function (1 rep-maximum knee extension and short physical performance battery [SPPB]).

In the 3 mg/kg dose cohort, '745 was effective at improving total body composition (increase of lean body mass and decrease in total body fat) and increasing lower extremity muscle size, but had no detectable effect on physical function by the EOS. Most effects were durable, as both lean body mass and muscle size increases were detected at the FUP. Historical control patients lost as much as 4% of muscle mass over a 12 month period.

**Exhibit 15: Efficacy of '745 in Prostate Cancer Patients**

| | Lean Body Mass | Whole Body Fat | Lower-extremity Muscle Size |
|---|---|---|---|
| *Percent change from baseline to EOS* | | | |
| '745 (3mg/kg) | 1.5% | -1.70% | 1.20% |
| Placebo | -0.7% | 0.80% | -0.70% |
| Between-group | 2.2% | -2.50% | 1.90% |
| p-value | **0.008** | **0.021** | 0.065 |
| *Percent change from baseline to FUP* | | | |
| '745 (3mg/kg) | 1.90% | -1.50% | 2.70% |
| Placebo | 0.20% | 0.50% | -0.10% |
| Between-group | 1.70% | -2.00% | 2.80% |
| p-value | **0.023** | 0.183 | **0.007** |

**Source: Company Data**

'745 was well tolerated, with treatment emergent AEs experienced by 2 or more subjects limited to diarrhea, fatigue, contusion and injection site bruising. One serious adverse event of syncope was reported from a patient receiving the 3 mg/kg dose; this was associated with an ECG change of moderate severity. This SAE occurred 19 days after the final dose was given, and the patient had a history of AV block and syncopal episodes. One patient discontinued '745 after the second 3 mg/kg dose due to erythema (redness) of the abdomen that was considered to be related to the investigational drug. Anti-'745 antibodies were detected in 2/54 (3.7%) patients that received the drug at any dose. PK data demonstrated that the time to maximum ($T_{max}$) exposure of '745 occurred 24-72 hours after each dose, and '745 had a circulating half-life of 3-6 days.


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**Exhibit 16: AEs experienced by 2 or more patients**

| | Placebo | 0.3 mg/kg '745 | 1 mg/kg '745 | 3 mg/kg '745 | All '745 |
|---|---|---|---|---|---|
| | (n = 23) | (n = 6) | (n = 6) | (n = 19) | (n = 31) |
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| Fatigue | 1 (4) | 0 (0) | 1 (17) | 3 (16) | 4 (13) |
| Inj. Site Bruising | 1 (4) | 1 (17) | 0 (0) | 1 (15) | 2 (6) |
| Diarrhea | 2 (9) | 0 (0) | 0 (0) | 4 (21) | 4 (13) |
| Contusion | 0 (0) | 0 (0) | 0 (0) | 3 (16) | 3 (10) |

**Source: Company Data**

### Phase 2 trial in ESRD patients with PEW

The ongoing phase 2 trial is planning on enrolling a total of 48 ESRD patients that have been on maintenance HD for at least 6 months in an outpatient setting. Patients will be enrolled at 6 sites including academic sites and those associated with DaVita and Fresenius. Additionally, all patients must have serum albumin below 3.8 g/dL, the validated biomarker for PEW. Treatment with appetite stimulants (e.g. medical marijuana), anabolic steroids or growth hormone is not allowed during the trial. Patients will be randomized in a 3:1 ('745 to placebo) fashion. Initially, ATRA planned to evaluate two doses of '745 in a dose escalation fashion: 3 mg/kg and 10 mg/kg given weekly IV for 3 months. However, PK data from the first 8 patients in the 3 mg/kg cohort suggested a longer half-life and therefore higher drug exposure in ESRD patients when compared to prostate cancer/healthy subjects. Drug exposure levels in these patients at 3 mg/kg were similar to those predicted for 10 mg/kg based on the prior phase 1 experience. Additionally, the PK data also demonstrated that steady state levels of '745 could be rapidly achieved with a schedule comprising loading doses followed by maintenance doses in these patients. In response, ATRA amended the protocol as follows: add a cohort of 20 patients that will receive 3 weekly infusions of a loading dose (3 mg/kg) followed by weekly infusions of a lower 'maintenance' dose (1 mg/kg) for the following 9 weeks and; add a cohort of 20 patients that will receive 3 weekly infusions of a loading dose (6 mg/kg) followed by weekly infusions of a lower 'maintenance' dose (2mg/kg) for the following 9 weeks. At the conclusion of treatment with '745 for 3 months, patients will be followed for an additional 2 months to assess the durability of changes in muscle and inflammation. ATRA has reported that there have been no dose-limiting toxicities, no serious AEs, no Grade 3 or higher AEs, and no anti-drug antibodies detected within the first 8 ESRD patients dosed with '745. AEs possibly related to '745 were grade 1 or 2 in severity and the most common treatment related AE was myalgia.

The primary endpoints for the study are safety and percent changes in lean body mass from baseline to the end of the treatment period. Secondary endpoints of the study include two physical function tests (stair climbing power test and the 6 minute walk test) and changes in muscle composition (lean body mass, appendicular lean mass and mid upper arm muscle circumference). The secondary endpoints will be assessed during both the treatment period (weeks 5 and 9) and a 2 month follow-up period (weeks 16 and 20). ATRA will also be evaluating quality of life assessments in these patient (KDQOL, fatigue and anorexia scales and effects on the duration of use and dose intensity of supportive care drugs), which may prove to be important for reimbursement. Serum mysotatin levels will be assessed in the phase 2 trial to determine its utility as a biomarker in predicting which patients respond best to treatment with '745. Topline data is expected in 2H15.


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**Exhibit 17: Differences between '745 clinical trials**

| | Phase 1 (Prostate) | Phase 2 (PEW) | Significance |
|---|---|---|---|
| Duration of therapy | 1 month | 3 months | Longer duration increases drug exposure time for safety/efficacy assessment |
| Dose of '745 | 0.3, 1.0 and 3.0 mg/kg | 3 and 6 mg/kg loading doses with 1 and 2 mg/kg maintenance doses | Higher doses increase drug exposure; may increase both efficacy and AE rates |
| Duration of follow-up | 1 month | 2 month | Longer follow-up allows assessment of effect durability |
| Route of administration | Subcutaneous | IV | IV increases overall drug exposure, but may limit risk for allergic reactions |
| Physical function assessment | 1RM-KE; SPPB | Stair climbing; 6MWT | New functional tests are well validated efficacy outcomes |

**Source: Company Data and Jefferies**

We expect '745 to be effective at improving lean body mass and muscle size in ESRD patients suffering from PEW, as this has been shown previously (albeit in a different patient population). We are also optimistic that there will be improved functional and QOL outcomes for these patients given the optimized drug exposure through dosing, frequency of treatments and route of administration. Positive data from this study could lead to development of '745 in additional indications where muscle growth and inflammation reduction could lead to better outcomes (e.g. orthopedic indications; inflammation and inflammatory disease; age-related sarcopenia; and cancer cachexia).

# Commercial Opportunity for '745

### The Costs of ESRD and the 'dialysis bundle'

The treatment of ESRD is an enormous burden on US healthcare spending, accounting for approximately $50B in 2011. $34B of this spending came from Medicare, covering 82% of all ESRD patients. Of this Medicare spending in 2011, costs per patient per year (PPPY) differed substantially by treatment modality: $87,945 for HD, $71,630 for PD and $32,922 for transplant.


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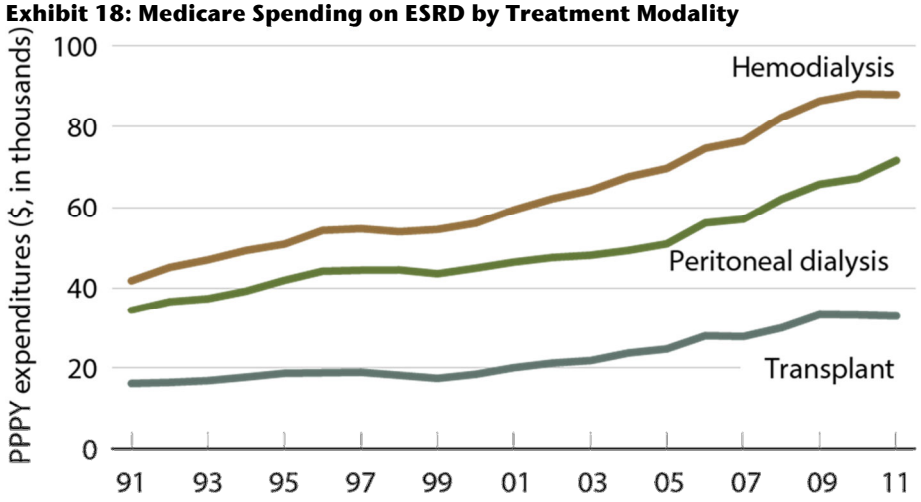
**Exhibit 18: Medicare Spending on ESRD by Treatment Modality**




**Source: USRDS**

Despite the highest cost PPPY coming from HD treatment, these costs actually declined for the very first time in 2011. Academic economists and the United States Renal Data System (USRDS) attribute this decline in costs to the newly implemented 'End-Stage Renal Disease Prospective Payment System,' the so-called 'dialysis bundle' or just 'bundle.' The bundle is a fixed Medicare payment to out-patient facilities for dialysis treatment and related services, and was specifically designed to control spending on treatments for ESRD, with a particular emphasis on HD. The base rate for each dialysis treatment in the bundle is ~$240, which translates to a PPPY payment of approximately $50,000. The remaining ~$38K PPPY (or ~40%) of Medicare payments for ESRD is comprised of treatments specifically excluded from the bundle (e.g. excluded drugs/biologics and hospitalizations). According to the Centers for Medicare and Medicaid Services (CMS), drugs and biologics that are currently outside of the bundles payment system include 'categories of drugs [and biologics] that may be furnished by a dialysis center, but are not considered to be ESRD-related.' These treatments that fall outside of the bundle are reimbursed to the dialysis center at the standard ASP + 6%, with a 20% co-payment by the ESRD patient.


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**Exhibit 19: Categories of drugs/biologics excluded from the ESRD bundle**

| Drug Category | Rationale for Exclusion |
|---|---|
| Anticoagulant | Drugs labeled for non renal dialysis conditions and not for vascular access |
| Antidiuretic | Used to prevent fluid loss |
| Antiepileptic | Used to prevent seizures |
| Anti-inflammatory | May be used to treat kidney disease (glomerulonephritis) and other inflammatory conditions |
| Antipsychotic | Used to treat psychosis |
| Antiviral | Used to treat viral conditions such as shingles |
| Cancer management | Includes oral, parenteral and infusions. Cancer drugs are covered under a separate benefit category |
| Cardiac management | Drugs that manage blood pressure and cardiac conditions |
| Cartilage | Used to replace synovial fluid in a joint space |
| Coagulants | Drugs that cause blood to clot after anti-coagulant overdose or factor VII deficiency |
| Cytoprotective agents | Used after chemotherapy treatment |
| Endocrine/metabolic management | Used for endocrine/metabolic disorders such as thyroid or endocrine deficiency, hypoglycemia and hyperglycemia |
| Erectile dysfunction management | Androgens were used prior to the development of ESAs for anemia management and currently are not recommended practice. Also used for hypogonadism and erectile dysfunction |
| Gastrointestinal management | Used to treat gastrointestinal conditions such as ulcers and gallbladder disease |
| Immune system management | Anti-rejection drugs covered under a separate benefit category. |
| Migraine management | Used to treat migraine headaches and symptoms |
| Musculoskeletal management | Used to treat muscular disorders such as prevent muscle spasms, relax muscles, improve muscle tone as in myasthenia gravis, relax muscles for intubation and induce uterine contractions |
| Pharmacy handling for oral anti-cancer, anti-emetics and immunosuppressant drugs | Not a function performed by an ESRD facility |
| Pulmonary system management | Used for respiratory/lung conditions such as opening airways and newborn apnea |
| Radiopharmaceutical procedures | Includes contrasts and procedure preparation |
| Unclassified drugs | Should only be used for drugs that do not have a HCPCs code and therefore cannot be identified |
| Vaccines | Covered under a separate benefit category |

**Source: Federal Register Vol. 75(155)**

Since its initial proposal in 2007, there has been considerable debate regarding the overall payment rate, and more germane to '745, what drugs/biologics should be included within this payment bundle. In general, patient advocacy groups and drug developers have argued that stifling innovation through cost-controlling measures is detrimental to ESRD patients and their families. In response, CMS has proposed a Quality Incentive Plan (QIP, or a system to incentivize ESRD facilities based upon patient outcomes), and has reiterated that categories of treatments they consider to be not directly related to ESRD, yet necessary for improved patient health and quality of life, will remain outside of the bundle. Additionally, the exclusion of treatments from the bundle appears to be sensitive to commercial interest: Amgen lobbyists have recently been successful in extending the exclusion of oral ESRD drugs (such as Sensipar) until 2024. Finally, to our knowledge, the 11 drugs that are currently included in the bundle have not changed since the initial proposal in 2007. This suggests that the inclusion of a drug within the bundle is not automatic, but rather an active decision, and appears to be a slow and inefficient process.

It should also be noted that the bundle seems to have shifted the balance of dialysis treatments towards in-home PD slightly. Prior to the bundle, incentives for dialysis centers were skewed towards HD in the out-patient centers; now with the bundle, incentives for the centers are skewed towards cost savings. One strategy to cut-costs is to increase the number of patients receiving in-home PD. This may potentially impact '745 in that IV administration of the drug will be less likely in the home setting. Despite this, we view the shift towards PD unlikely to change the market potential for '745, because the patients with PEW, and thus worse off, are more likely to remain on HD in the outpatient setting.


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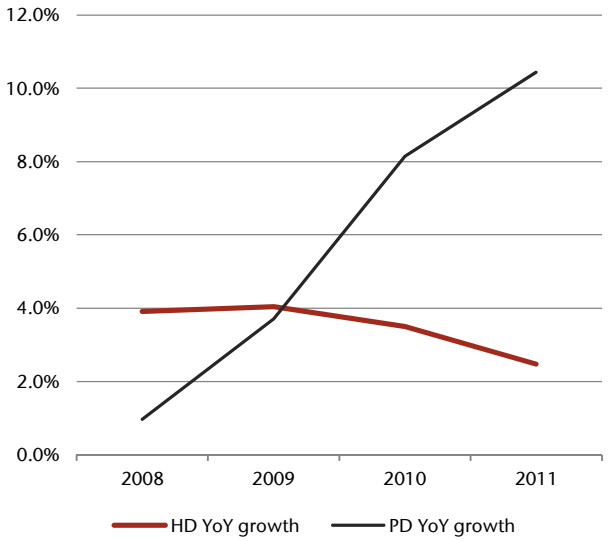
**Exhibit 20: Dialysis utilization by modality**

| | 2008 | 2009 | 2010 | 2011 |
|---|---|---|---|---|
| Center hemodialysis | 353,327 | 367,628 | 380,503 | 389,922 |
| *YoY Growth* | *3.9%* | *4.0%* | *3.5%* | *2.5%* |
| Total PD | 26,595 | 27,583 | 29,830 | 32,944 |
| *YoY Growth* | *1.0%* | *3.7%* | *8.1%* | *10.4%* |
| **Total Dialysis** | **384,705** | **400,754** | **416,738** | **430,273** |
| ***YoY Growth*** | ***3.8%*** | ***4.2%*** | ***4.0%*** | ***3.2%*** |

**Source: USRDS and Jefferies**

**Exhibit 21: YoY growth of dialysis by modality**




**Source: Jefferies**

### '745 and reimbursement

We believe that '745 is positioned favorably for reimbursement from both Medicare and private payers. For Medicare patients, we believe that '745 may not be included in the ESRD bundle for two key reasons: **1)** given the mechanism of action of '745, it falls distinctly under two treatment categories that are specifically listed as unrelated to dialysis: anti-inflammatory and musculoskeletal, and **2)** inclusion of a drug within the bundle requires bureaucratic action, a process that has proven to be inefficient and sensitive to commercial interests. Despite the potential favorable exclusion from the bundle, we expect the need for co-payment assistance programs given the potential substantial burden on the largely fixed-income Medicare patient population.

'745 also has the potential to make a cost-savings value proposition to both Medicare and private-payers by reducing overall dollars spent on ESRD patients. Approximately 40% of all Medicare dollars spent on ESRD patients are not directly related to dialysis, but rather are related to complications and co-morbidities of ESRD, with the most expensive consequence being hospitalizations. In fact, CMS estimated that 38% of all ESRD expenditures were on inpatient services in 2010. ATRA is conducting studies with DaVita to evaluate the cost-savings potential of a treatment for PEW in terms of reducing inpatient expenditures.

### Competitive landscape

There are no currently approved therapies for PEW in ESRD patients, and to our knowledge there are no drugs other than '745 that are being developed specifically for this indication. However, as stated above, there are many other candidates being developed that inhibit the activin system that could theoretically be applied to this indication.

### '745 market model

At this time, ATRA plans to commercialize '745 by itself in the US and ex-US. Because all patients eligible for '745 will be receiving HD from a specialized center, we believe ATRA could utilize a relatively lean salesforce to target the major centers and/or leverage their existing relationships with both DaVita and Fresenius dialysis providers. We assume '745 will launch in 2019 at a price of $13,000/patient ($180/treatment, 3X a week for 6



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months) and assume patent expiration in 2035 for both US and ex-US. We estimate that there are currently ~440,000 patients on HD in the US, and that this population will continue to grow at the current YoY growth rate of 2.6%. We believe that ~40% of these patients suffer from PEW based upon the midpoint estimate from various academic epidemiological reports. We assume '745 can achieve a peak market penetration of 30% in this treatable population in 2023 with unadjusted peak US sales of ~$1.1B in 2029. Assuming a 40% probability of success we estimate peak adjusted US sales in 2029 of ~$444M. We assume '745 will launch in 2019 ex-US and achieve sales that are ~65% of those in the US. After assuming ~5% royalty payout to Amgen, we forecast peak unadjusted worldwide sales of ~$1.7B and peak adjusted sales of ~$696M in 2029.

# STM 434 for the treatment of ovarian cancer and other solid tumors

'434 is a soluble ActR2B receptor-IgG fusion protein, or ligand-trap that was acquired from Amgen. Ligand-traps bind and inhibit all of the ligands (or binding partners) for the target receptor; in this case '434 binds Activin A, myostatin and other TGFβ family members that normally interact with the 2B receptor. Activin A has been linked to the proliferation and growth of ovarian and other solid tumors and its upregulation is correlated with poorer prognoses. It is therefore hypothesized that inhibiting Activin A will slow the progression of these tumors and potentially make them more responsive to chemotherapies. Initially, ATRA is focused on developing '434 for the treatment of ovarian cancers, but may also have therapeutic applications in many other solid tumor types such as breast, gastric, pancreatic and colorectal cancers. ATRA could seek breakthrough designation from the FDA if monotherapy data is positive in the clear cell and granulosa cell sub-types of ovarian cancers. '434 is in the first part (dose escalation) of a recently initiated phase 1 trial as a monotherapy for ovarian cancer and other solid tumors, with initial results expected in 1H16. We estimate '434 will be launched for recurrent ovarian cancer in 2020 generating peak adjusted worldwide sales of $94M.

## Ovarian cancer

### Incidence, prevalence and current treatments

Ovarian cancers (OCs) are one of the most common types of gynecologic malignancies, with an estimated prevalent population in 2011 of ~188k women in the US. According to the SEER statistics, it is estimated that there will be 21,980 new cases of ovarian cancer, and approximately 14,270 deaths from this disease in 2014. The prognosis for OC is relative to the stage at which it is diagnosed: OCs that are diagnosed early have a high 5-year survival rate of approximately 92%. However, due to the lack of early diagnostic and screening tools, most OCs present at an advanced stage and have dismal 5-year survival rates (~22% for stage 3 and ~5% for stage 4).

First-line treatment for OC is typically surgery when it is confined to the ovary or a cyto-reductive debulking surgery (e.g. a hysterectomy and oophorectomy), followed by a regimen of platinum-based chemotherapy when it has escaped the ovary. Despite the high initial response rate to these therapies (70-80%), only ~15% of women achieve a cure. The remaining women develop incurable recurrent disease with very low odds of survival. The treatment strategy for this recurrent population is to prolong survival time and ameliorate symptoms and involves a number of other chemotherapy options including liposomal doxorubicin, topotecan, and gemcitabine. Platinum-based chemotherapy resistant OC has a median survival of ~13 months.


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## Sub-types of Ovarian Cancers

OCs are generally classified into 3 main sub-types based upon the type of malignant cells: epithelial (the lining of the outside of the ovary), germ cells (the 'egg-producing' cells) and sex cord stromal (a.k.a. granulosa cells, or the connective tissue that holds the ovary together). Epithelial cell tumors are by far the most common, ~90% of all OCs, but this is typically broken down further by histopathology (e.g. clear-cell or serous cells). Of the sub-types, serous cell tumors have the highest response rate to existing platinum-based chemotherapies (~70-75%), whereas other sub-types, such as clear-cell and granulosa cell tumors, have a much lower response rate (~10-20%).

**Exhibit 22: Sub-types of Ovarian Cancers**

| | | Extrapolation from SEER population | |
|---|---|---|---|
| | % of total OCs | Prevalence | Incidence |
| *Epithelial Cell* | 91.7% | 172396 | 20156 |
| Serous | 56.7% | 106596 | 12463 |
| Endometrioid | 9.7% | 18236 | 2132 |
| Clear-cell | 5.2% | 9776 | 1143 |
| Other/unspecified | 20.1% | 37788 | 4418 |
| *Germ cell* | 5.9% | 11092 | 1297 |
| *Granulosa* | 2.5% | 4700 | 550 |

**Source: NIH SEER statistics & Jefferies**

## The Role of Activins in Cancer

Activins were initially studied for their role in the modulation of reproduction (particularly through the control of follicle stimulating hormone production and secretion), and more recently have been studied in the context of wound-healing and malignancies. It is becoming clear that activins have a role in both immunomodulation and cellular proliferation, processes that are integral to the pathogenesis and progression of malignancies. Despite this clear relationship, it appears that the consequence of activin signaling is tissue/tumor specific. For example, activins can have a growth-inhibitory effect on breast, liver, prostate and pancreatic cancers and a mitogenic (or 'tumor promoting') effect on ovary, testicular and bone metastases. Mechanistically, the pro-malignant effects of activins appear to be primarily from the proliferation of fibroblasts, angiogenesis, and suppression of the immune system in the tumor microenvironment. When Activin A binds to the ActR2B receptor it initiates a cascade of gene transcription that leads to abnormal cell proliferation, cell migration, blood vessel formation and inhibition of programmed cell death.


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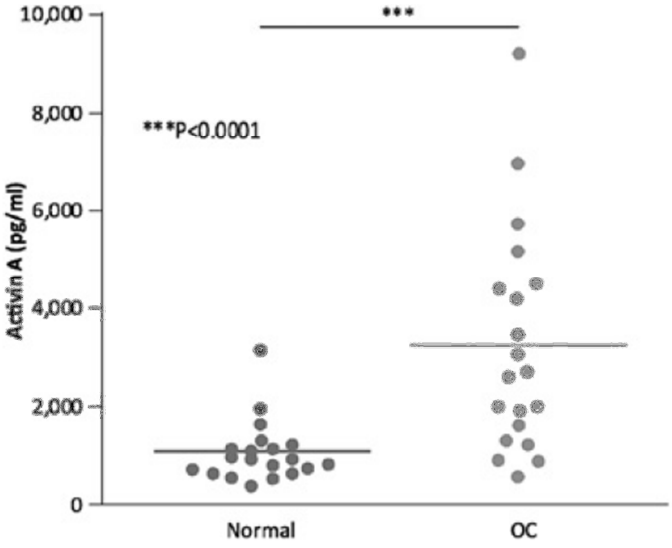
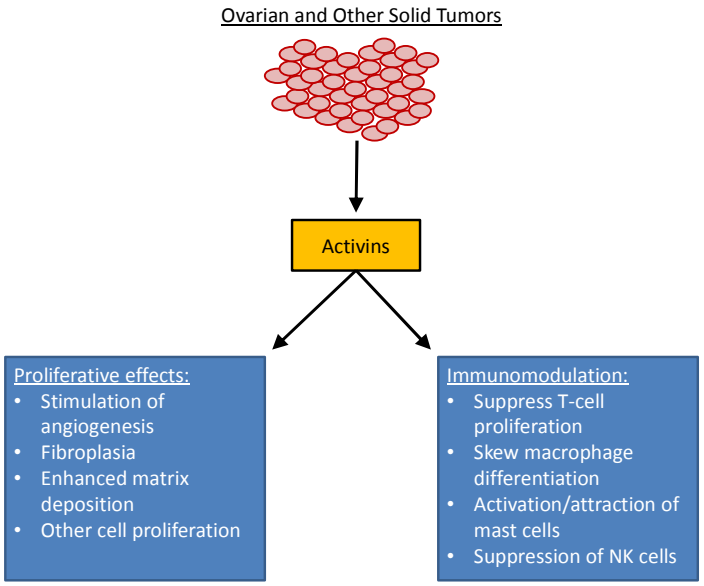
**Exhibit 23: Activin A is higher in Women with OC**




Source: Company Data

**Exhibit 24: The role of activins in cancer**




Source: Jefferies

In addition to activins, other binding partners of the ActR2B receptor also appear to play a role in tumor progression. In mouse xenograft tumor models, up-regulation of follistatin (the endogenous 'functional-analogue' to '434) prevented the metastasis into bone greater than the effects of inhibiting Activin A alone. These results have been supported by clinical findings, in that follistatin levels are inversely related to tumor spread and progression in patients with breast and prostate cancers.

### Pre-clinical studies with '434

Preclinical studies of STM 434 were carried out with a close analog ligand trap, STM 217 (STM 434/s) in two different mouse models. In monkeys, '434 had a half-life of 1-2 weeks, which ATRA suggests supports dosing once every 4 weeks and would fit in nicely with the current chemotherapy protocols in first and second line ovarian cancer.

In the TOV-21G mouse xenograft model of ovarian cancer (transfected with clear cell tumor cells and carrying ARID1A mutations that drive upregulation in the signaling cascade triggered by the ActR2B receptor), weekly infusions of '434/s significantly reduced tumor volume (31% reduction as a monotherapy or 73% in conjunction with chemotherapy [5-FU]) and reversed cancer related cachexia manifested in increased body weight of the mice. These results suggest that '434 has effects beyond its antitumor impact, with the reversal of cachexia likely mediated through myostatin antagonism as seen in '745 above.


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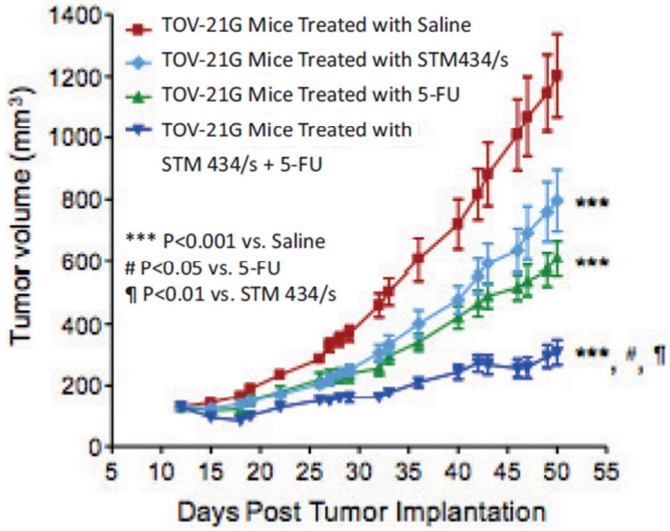
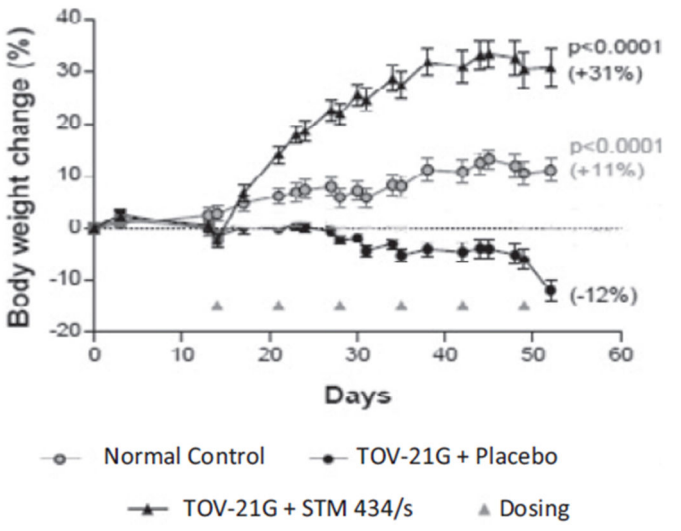
**Exhibit 25: '434/s anti-tumor effect as monotherapy and with chemotherapy in TOV-21G mice**




Source: Company Data

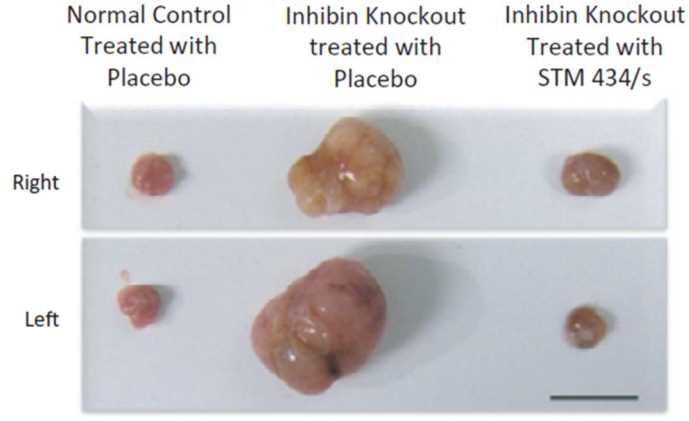
**Exhibit 26: '434/s reversed cancer-related cachexia in TOV-21G mice**




Source: Company Data

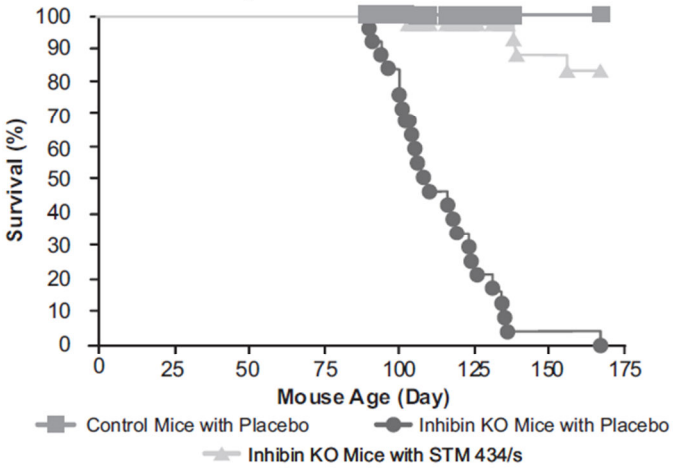
Additionally, using an inhibin knockout mouse-model (high activin levels), which is phenotypically similar to granulosa cell tumors in humans, '434/s monotherapy at 30 mg/kg significantly reduced serum Activin A levels and tumor size vs. control mice. '434/s also drastically improved overall survival vs. untreated control mice (90% alive vs. 96% dead at 133 days).

**Exhibit 27: '434/s reduces ovarian tumor size in inhibin KO mice**




Source: Company Data

**Exhibit 28: '434/s improves survival in a inhibin KO mice**




Source: Company Data

In July of this year, ATRA received a pre-clinical report from Amgen detailing an 8 week pharmacology study of STM 434/s in neutered male cynomolgus monkeys. The aim of the study was to determine the ability of '434/s to reverse the effects of androgen deprivation (AD). In the study reported, '434/s was given in two weekly doses at either 3 mg/kg or 10 mg/kg. The study found that '434/s was effective at reversing the effects of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AD on muscle and bone loss; however, there were also reports of 'muzzle bleeding' (the monkey equivalent of a nosebleed) and one monkey with a lesion on its buttock. It should be noted that ACE-031, Acceleron/Shire's ActR2B ligand trap, was discontinued from development in muscular dystrophy and menopausal atrophy due to a similar issue with nosebleeds. As a result of this history and the additional findings, ATRA performed subsequent *in vitro* studies of both '434 and '434/s to determine a potential cause for this increased bleeding. Data from the additional *in vitro* studies suggest that neither compound affects platelet function, a necessary blood constituent for clotting. However, these studies did reveal that both compounds bound BMP-9, a factor involved in bleeding and blood vessel development, which ATRA believes is the likely mechanism for the increased potential for bleeding. ATRA believes this risk is minimal, particularly given the clinical experience with Avastin, another angiogenesis inhibitor. Despite this, ATRA has altered the ongoing phase 1 study to exclude patients at heightened risk of bleeding and enhance the monitoring of patients for bleeding or increased risk for bleeding. Additionally, all of this information and heightened vigilance has been shared with the FDA.

### Ongoing Phase 1 trial

In October, ATRA dosed the first patient in an open-label phase 1 study evaluating '434 in up to 66 patients with ovarian and other solid tumors. The study is designed in 3 distinct parts (each with monthly dosing): **1)** an initial dose escalation study in patients with advanced solid tumors (1/3$^{rd}$ ovarian and 2/3$^{rd}$ other); dosing will be initiated at 0.25 mg/kg up to the MTD and if no MTD is reached, ascending doses of 0.5, 1.0, 2.0 and 4.0 mg/kg will be tested. **2)** '434 as a monotherapy at the optimal dose determined in part 1 in patients with advanced ovarian cancer including clear and granulosa cell tumors. **3)** '434 in combination with liposomal doxorubicin chemotherapy or current standard of care in ovarian cancer patients who have received prior treatment.

Additionally, ATRA plans to measure baseline Activin A and FSH levels (activin negatively regulates FSH) in order to potentially validate them as biomarkers for future studies. Patients will also be tested for ARID1A and FOXL2 mutations associated with tumor proliferation. As mentioned above, ARID1A gene mutations found in clear cell ovarian tumors lead to an upregulation in the signaling cascade triggered by the ActR2B receptor similar to increased activin levels. The FOXL2 mutation is reported to be widely present in granulosa cell ovarian tumors as a result of which follistatin, a natural activin inhibitor, is not turned on. ATRA also hopes to have sufficient clinical data to obtain FDA breakthrough designation for '434 in certain sub-types of OC (namely clear-cell and granulosa cell tumors). This would come with several advantages, including an accelerated path to approval (which could be as early as 2019 for '434) and close guidance from the FDA on trial design.

Given the strength of the pre-clinical data and the mechanism of action of '434, we expect Activin A levels to be strongly related to response to therapy. In other solid tumor types, the link between activin A and tumor progression is less clear, and we therefore expect the focus of the '434 program to be on ovarian cancer. Lastly, because '434 is a ligand-trap and binds myostatin as well, we expect '434 to improve cancer-related co-morbidities such as atrophy/cachexia. Initial data is expected by 2H16.

### Avastin in recurrent ovarian cancer

Avastin (bevacizumab), a VEGF-A antibody developed by Genentech/Roche, is currently approved as an angiogenesis inhibitor in the treatment of glioblastoma, metastatic colorectal cancer, non-small cell lung cancer and metastatic kidney cancer. Avastin was also recently evaluated in combination with liposomal doxorubicin for the treatment of recurrent, platinum-resistant ovarian cancer in the Phase III AURELIA study. This study enrolled a total of 361 OC patients who had received ≤ 2 previous treatments. Results


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from this trial demonstrated that Avastin + chemotherapy significantly increased progression free survival (PFS) by 52% when compared to chemotherapy alone (median PFS: 6.7 months vs. 3.4 months; Hazard Ratio [HR] = 0.48, p <0.001). However, there was no significant improvement in overall survival (OS; 16.6 months vs. 13.3 months; HR = 0.85, p = 0.174). As a result of this study, a sBLA was submitted for Avastin + chemotherapy, which the FDA accepted and granted priority review. The PDUFA date for this review is November 19, 2014. At this time, it is unclear whether or not the FDA will accept PFS as demonstrating a clinical benefit for recurrent ovarian cancer, as no other drugs have been approved in this setting. In August of this year, the EU approved Avastin + chemo for recurrent ovarian cancer based upon these same data.

PARP inhibitors are another class of drugs being evaluated in a subset of recurrent ovarian cancers. Mechanistically, these small molecules suppress a cell's ability to utilize a DNA repair pathway which appears to have particular utility in OC with BRCA genetic mutations. It is estimated that < 10% of ovarian cancers have these mutations. There are several PARP inhibitors in Phase 3 trials evaluating their safety and efficacy in treating BRCA+ ovarian cancers, including Lynparza (AstraZeneca), Rucaparib (Clovis) and Niraparib (Tesaro). Recently, Lynparza received a positive opinion by CHMP, and could be approved in the EU by YE14; however, Lynparza did receive a negative AdComm vote earlier this year, with the FDA PDUFA date on January 3, 2015.

### Market Model for '434

As with '745, ATRA plans to commercialize '434 by itself in the US and ex-US. Again, since all patients eligible for '434 (patients with recurrent ovarian cancer) will be receiving care from a specialized center, we believe ATRA could utilize a relatively lean salesforce to target the major centers. We assume '434 will launch in 2020 at a price of $85,000 per patient with a modest 3% growth rate each year. We assume patent expiration in 2035 for both US and ex-US. We assume that the prevalent ovarian cancer population in the US is ~22,000, and that this population will continue to shrink at the current YoY rate of -1%. We estimate that ~80% of these patients are identified in any given year, and that 70% fail their first line of therapy. '434 can achieve a peak market penetration of 25% in this treatable population in 2023 with unadjusted peak US sales of ~$294M in 2029. Assuming a 20% probability of success we estimate peak US sales in 2029 of ~$59M. We assume '434 will launch in 2020 ex-US and achieve sales that are ~65% of those in the US. After assuming ~3% royalty payout to Amgen, we forecast peak unadjusted worldwide sales of ~$471M and peak adjusted sales of ~$94M in 2029.

# T-cell therapies from Memorial Sloan Kettering (MSK)

In September, ATRA entered into an exclusive option agreement with MSK for the exclusive, worldwide license rights to clinical-stage T-cell therapies directed towards three targets: **1)** Epstein Barr Virus (EBV) – the virus that causes mononucleosis in otherwise healthy individuals and lymphomas in immunocompromised patients; **2)** cytomegalovirus (CMV) – a virus that can cause blindness, illness or death, depending on the tissues affected and the health-status of the patient; **3)** Wilms Tumor 1 (WT1) – an antigen expressed at abnormally high levels in a variety of hematological cancers and solid tumors (e.g. myeloma, AML, ovarian). Both the EBV and CMV therapies are in phase 2 clinical trials and the WT1 therapy is currently in a phase 1 trial. In exchange for the option to license these technologies, ATRA paid $1.25M and issued ~60,000 shares to MSK. The initial option period is for 12 months, but ATRA may extend this period up to 27


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months by paying an additional ~$0.6M. ATRA will work with MSK during the option period to submit information to the FDA in support of a pivotal trial for the EBV targeted T cell therapy. If ATRA decides to license these technologies, they will make an upfront payment of $4.5M, additional developmental/commercial milestones totaling up to $33M and undisclosed royalties off of net sales. In addition to these specific technologies, ATRA and MSK have agreed to collaborate on further research to develop other cellular therapies, which may include T-cells directed against other antigens and/or chimeric antigen receptor-modified (CAR) T-cells.

### Technology for T-cell therapies

Although each T-cell therapy is directed against different target antigens, they are all created using a common technology. Briefly, peripheral blood mononuclear cells (PBMCs) are collected from donors, from which T-cells are enriched. The T-cells are then exposed to the antigen (e.g. an inactivated/irradiated EBV) along with various necessary pro-inflammatory cytokines necessary for T-cell activation. Once activated, the T-cells go through further quality control (selected for specific cell-surface markers), and immunogenicity towards the target is confirmed. The final selected T-cells are then stored in a library of similar T-cells from many donors, which is representative of a wide variety of human leukocyte antigen (HLA) genotypes. HLA are the specific cell surface markers that our immune system uses to recognize 'self,' and is also the determining factor of whether an organ donor is a 'match' for transplant recipients. As a final step, patients receiving the therapies are partially HLA-matched to a T-cell therapy in the library, and then infused with those cells. Importantly, because there is a large library of HLA-genotypes represented in the respective libraries, this is essentially an off-the-shelf product that can be given to the patient within a few days (rather than ~1-4 weeks with other current cellular-based therapies such as Provenge and CAR-T cells).


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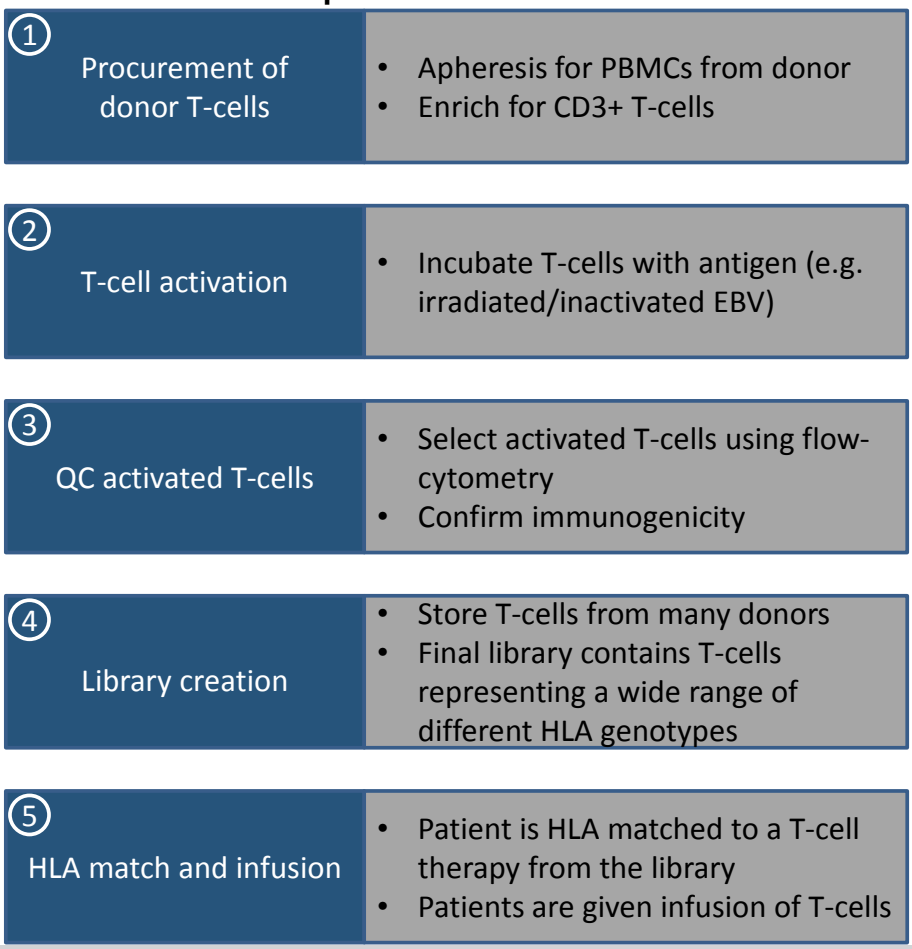
**Exhibit 29: MSK T-cell therapies**




**Source: Jefferies, company data**

### EBV targeted T-cell therapy

EBV is a member of the herpes family of viruses, and is one of the most common amongst humans; it is best known as the cause of infectious mononucleosis ('mono' or 'the kissing disease'). In immunocompromised individuals, such as those infected with HIV, EBV can also cause a variety of malignancies: Hodgkin's lymphoma, Burkitt's lymphoma, nasopharyngeal carcinoma, hairy leukoplakia and post-transplant lympho-proliferative disorders (PTLDs).

*Phase 1 trial in PTLD patients*

In an open-label phase 1 trial, 49 patients with biopsy confirmed PTLD were given an infusion of either total leukocytes (i.e. white blood cells) or EBV-targeted T-cells that were HLA-matched to the recipient (the technology described above). Overall, the results were impressive, with ~67% (33/49) of the patients achieving a complete response (CR); perhaps more telling, is that 55% (11/20) patients that were refractory to Rituxan also achieved a CR. Graft versus host disease (GVHD) was only observed in 14% of patients that received infusions of total leukocytes and was not observed in patients that received the EBV-targeted T-cells.


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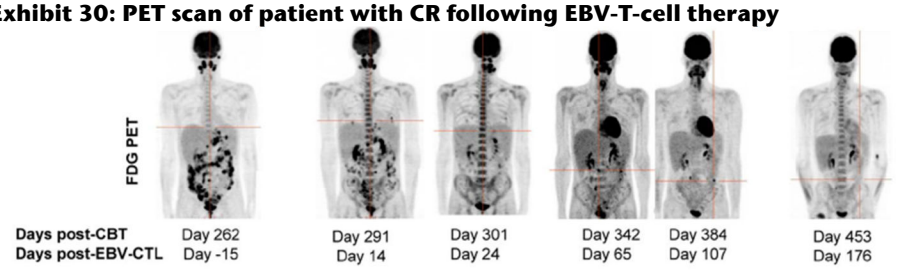
**Exhibit 30: PET scan of patient with CR following EBV-T-cell therapy**




**Source: Company Data**

*Ongoing Phase 2 trial*

MSK is currently conducting an open-label phase 2 trial evaluating the EBV T-cell therapy in ~112 patients with an EBV-associated lymphoproliferative disorder in two arms: patients that have received bone marrow transplants or patients that have received a whole organ transplant. In both arms, patients will receive 3 weekly doses of 2 X $10^6$ normally matched or partial-HLA matched third party T-cells/kg. The primary endpoint of the study is overall response rate at 3 weeks post-treatment; the secondary endpoint is duration of response, assessed at 6 months. Data is expected from this trial potentially by YE15/1H16.

### CMV targeted T-cell therapy

In an earlier phase I trial involving 13 post autologous stem cell transplant patients with persistent CMV infection with current standard of care, 12/13 patients showed complete resolution of the viral infection with the CMV targeted T-cell therapy. In an ongoing open-label phase II trial, MSK is evaluating 3 weekly doses of 1X$10^6$ donor CMV targeted T-cells/kg in ~80 patients with persistent CMV infections. The primary efficacy outcome of the study is the clearance of CMV infection 3-7 weeks following the final CMV T-cell therapy dose received. Topline data from this trial is expected potentially in 2H15.

In one of its ASH abstracts, MSK will present data on 38 patients post autologous stem cell transplant who have either overt CMV disease (n = 12) or CMV viremia (n = 26); 5 patients were not evaluable due to concomitant treatment with anti-retroviral therapies. Responses were considered complete (CR) if all detectable CMV viremia and disease resolved and partial if patients became asymptomatic. For viremia alone, a complete resolution of viremia was considered a CR and a PR if the viral load reduced by 2 logs. Of the 25 evaluable patients with viremia alone 5 (20%) achieved CR and 9 (36%) PR; 5 patients had a reduction of viral load less than 2 logs and 6 patients had progression of their disease. Of the 8 patients treated for disease 2 (25%) achieved a CR, 3 (38%) a PR, 1 had SD and 2 progressed. Of the total 38 patients enrolled, 9 eventually died due to their infection. There was no evidence of de novo GvHD or flares of prior GvHD.

In another ASH abstract, MSK has disclosed that they have created over 132 CMV targeted T-cell lines, and that these lines have been successfully HLA matched (by at least one relevant allele) in 52/56 cases requested. This serves to validate the 'off-the-shelf' nature of these technologies, which will allow ATRA/MSK to treat a large proportion of patients that present with CMV viremia/disease.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### Clinical development of WT1 T-cell therapy

MSK is currently conducting an open-label phase I trial evaluating six escalating doses of the WT1 T-cell therapy as a treatment for patients with $WT1^+$ leukemias or other hematological malignancies that have relapsed following an allogeneic stem cell transplant or persistent minimal residual disease. The primary endpoint for the study will be safety of the treatment doses; secondary endpoints include the efficacy of treatment on disease progression and the survival/proliferation of the adoptive T-cells. The study plans to enroll ~36 patients, with data expected potentially in 1H15.

## Intellectual Property

ATRA in-licensed a number of issued patents related to the compounds from AMGN: ATRA has 4 issued patents for '745 (both composition of matter and method of use) in the US and 1 issued patent in the EU, which together, have expected expirations ranging from 2023-2035. ATRA also holds 3 issued patents related to '434 in the US, with expected expiration dates ranging from 2026 to 2035. ATRA also notes that they have filed numerous other patent applications, and that their issued patents may be eligible for extensions.

## Financials

We project ATRA will have ~$75M in cash after the recent initial public offering that was priced at ~$11/share, in which they raised $58.8M. ATRA plans to use the proceeds primarily for the development of both '745 and '434. The remainder of funds will be used for other pipeline products, working capital and other corporate financial purposes.

## Management

**Isaac E. Ciechanover, M.D., President and Chief Executive Officer**: previously the Executive Director for Business Development at Celgene. At Celgene, he led the company's venture capital efforts and led licensing and acquisition activities with an aggregate transaction value of more than $6.7 billion. Those efforts included licensing and partnership transactions with cancer therapeutics companies Agios Pharmaceuticals, Inc., Acceleron Pharma Inc. and PTC Therapeutics Inc. Prior to founding Atara, Dr. Ciechanover was a Partner with Kleiner Perkins Caufield & Byers, a leading venture capital firm.

**Christopher Haqq, M.D., Ph.D., Chief Medical Officer**: previously Vice President for Clinical Research and Development at Cougar Biotechnology, which was acquired by Johnson & Johnson in 2009. At Cougar Biotechnology, he was the lead clinician for a pivotal prostate cancer study leading to market approval for Zytiga (abiraterone acetate). He has served as medical monitor for more than ten clinical trials and has contributed to drug development programs for a wide range of molecules, and served as an attending oncology physician and director of a translational laboratory at the University of California, San Francisco.

**Mitchall G. Clark, Chief Regulatory and Quality Officer**: previously Senior Vice President of Global Regulatory Affairs at Abraxis Bioscience, Inc., or Abraxis, where he submitted and managed five INDs for oncology and cardiovascular drugs including Abraxane (nanoparticle albumin-bound paclitaxel).


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**Gad Soffer, Chief Operating Officer**: previously held various roles at Celgene, including most recently Global Project Leader for Abraxane following Celgene's acquisition of Abraxis, where he led successful regulatory submissions for pancreatic cancer and non-small cell lung cancer.

**John F. McGrath, Jr., Chief Financial Officer**: previously Executive in Residence and Operating Partner at Kleiner Perkins Caufield & Byers. Prior to that time, he served as Vice President and Chief Financial Officer for Network Equipment Technologies, Inc., a publicly traded company. He has served on the board of directors of the Presidio Fund, a publicly traded mutual fund, and on the boards of directors and as Audit Committee chairman of publicly traded companies Actel Corporation and Endwave Corporation.



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**Exhibit 31: ATRA Income Statement: 2013A-2020E ($M)**

| *(In Millions, except per share data)* | 2013A | 1Q14A | 2Q14A | 3Q14A | 4Q14E | 2014E | 2015E | 2016E | 2017E | 2018E | 2019E | 2020E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Revenues** | | | | | | | | | | | | |
| PINTA 745 WW Sales (prob. adjusted) | | | | | | | | | | | 81.3 | 185.3 |
| STM 434 WW Sales (prob. adjusted) | | | | | | | | | | | - | 15.8 |
| EBV T-cell WW sales (prob. adjusted) | | | | | | | | | | | - | - |
| **Total Revenues** | **-** | **-** | **-** | **-** | **-** | **-** | **-** | **-** | **-** | **-** | **81.3** | **201.1** |
| **Operating Expenses** | | | | | | | | | | | | |
| COGS | | | | | | | | | | | 12.2 | 30.2 |
| *% of sales* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *15%* | *15%* |
| R&D | 4.9 | 3.0 | 3.2 | 4.0 | 4.5 | 14.7 | 16.0 | 25.0 | 40.0 | 55.0 | 65.0 | 70.0 |
| *% of sales* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *80%* | *35%* |
| Direct R&D costs | 4.3 | 3.0 | 2.1 | 4.0 | 4.5 | 13.6 | 16.0 | 25.0 | 40.0 | 55.0 | 65.0 | 70.0 |
| R&D costs paid to Amgen | 0.6 | - | 1.1 | - | - | 1.1 | - | - | - | - | - | - |
| In process R&D acquired from Amgen | | | | | | - | - | - | - | - | - | - |
| SG&A | 3.8 | 4.1 | 1.4 | 3.5 | 3.5 | 12.5 | 12.5 | 16.0 | 20.0 | 35.0 | 50.0 | 60.0 |
| *% of sales* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *N/A* | *62%* | *30%* |
| Milestone payments | | | | | | | | 8.0 | | 10.0 | 20.0 | |
| **Total Operating expenses** | **8.6** | **7.1** | **4.5** | **7.5** | **8.0** | **27.1** | **28.5** | **49.0** | **60.0** | **100.0** | **147.2** | **160.2** |
| **Net Operating Income (Expense)** | **(8.6)** | **(7.1)** | **(4.5)** | **(7.5)** | **(8.0)** | **(27.1)** | **(28.5)** | **(49.0)** | **(60.0)** | **(100.0)** | **(65.9)** | **40.9** |
| **Other Income (Expense)** | | | | | | | | | | | | |
| Interest income | 0.0 | 0.0 | - | - | - | 0.0 | - | - | - | - | - | - |
| **Total Other Income (Expense)** | **0.0** | **0.0** | **-** | **-** | **-** | **0.0** | **-** | **-** | **-** | **-** | **-** | **-** |
| Income before taxes | (8.6) | (7.0) | (4.5) | (7.5) | (8.0) | (27.1) | (28.5) | (49.0) | (60.0) | (100.0) | (65.9) | 40.9 |
| Taxes | 0.2 | (0.0) | - | - | - | (0.0) | - | - | - | - | - | - |
| *Tax Rate* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* | *0%* |
| **Net Income (Loss)** | **(8.8)** | **(7.0)** | **(4.5)** | **(7.5)** | **(8.0)** | **(27.1)** | **(28.5)** | **(49.0)** | **(60.0)** | **(100.0)** | **(65.9)** | **40.9** |
| Basic EPS | (1.28) | (1.02) | (0.33) | (0.39) | (0.40) | (1.34) | (1.41) | (2.00) | (2.45) | (3.66) | (2.40) | 1.49 |
| Diluted EPS | (1.28) | (1.02) | (0.33) | (0.33) | (0.34) | (1.14) | (1.20) | (1.75) | (2.14) | (3.24) | (2.13) | 1.32 |
| Shares outstanding (Basic) | 6.9 | 6.9 | 13.7 | 19.4 | 20.2 | 20.2 | 20.2 | 24.5 | 24.5 | 27.4 | 27.4 | 27.5 |
| Shares outstanding (Diluted) | 6.9 | 6.9 | 13.7 | 23.0 | 23.7 | 23.7 | 23.8 | 28.0 | 28.0 | 30.9 | 31.0 | 31.0 |

**Source: Jefferies estimates, company data**



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**Exhibit 32: ATRA Balance Sheet: 2013A-2020E ($M)**

| *(In Millions)* | 2013A | 1Q14A | 2Q14A | 3Q14A | 4Q14E | 2014E | 2015E | 2016E | 2017E | 2018E | 2019E | 2020E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Assets** | | | | | | | | | | | | |
| Current assets: | | | | | | | | | | | | |
| Cash and cash equivalents | 51.6 | 39.8 | 31.8 | 24.1 | 74.8 | 74.8 | 62.9 | 167.9 | 112.2 | 116.5 | 55.1 | 100.2 |
| Short-term available-for-sale investments | - | 22.3 | 24.7 | 24.7 | 24.7 | 24.7 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Prepaid expenses and other current assets | 0.2 | 0.3 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.7 | 0.7 | 0.7 |
| Total current assets | 51.8 | 62.3 | 57.1 | 49.4 | 100.1 | 100.1 | 63.7 | 168.7 | 113.0 | 117.4 | 56.0 | 101.1 |
| Property and equipment, net | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.2 | 0.3 |
| Other assets | 0.0 | 0.6 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.4 | 1.5 | 1.5 | 1.5 |
| Total assets | 51.8 | 62.9 | 58.5 | 50.8 | 101.5 | 101.5 | 65.1 | 170.2 | 114.6 | 119.0 | 57.7 | 102.9 |
| | | | | | | | | | | | | |
| **Liabilities, convertible preferred stock and stockholders' deficit** | | | | | | | | | | | | |
| Current liabilities: | | | | | | | | | | | | |
| Accounts payable | 0.6 | 1.4 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.7 | 0.7 |
| Accrued compensation | 0.3 | 0.2 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.5 | 0.5 |
| Income tax payable | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | - | - | - | - | - | - |
| Other accrued liabilities | 0.4 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.3 | 1.4 | 1.6 | 1.7 | 1.9 | 2.0 |
| Total current liabilities | 1.5 | 2.8 | 2.1 | 2.1 | 2.1 | 2.1 | 2.2 | 2.4 | 2.6 | 2.8 | 3.0 | 3.2 |
| Other long-term liabilities | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.3 | 0.3 | 0.4 | 0.4 | 0.5 |
| Total liabilities | 1.8 | 3.0 | 2.3 | 2.3 | 2.3 | 2.3 | 2.4 | 2.7 | 2.9 | 3.2 | 3.4 | 3.6 |
| | | | | | | | | | | | | |
| Approximate value of convertible preferred stock | 61.1 | 74.6 | - | - | - | - | - | - | - | - | - | - |
| Series A convertible preferred stock | 19.9 | 19.9 | | | | | | | | | | |
| Series A-1 convertible preferred stock | 2.8 | 2.8 | | | | | | | | | | |
| Series B convertible preferred stock | 38.4 | 51.9 | | | | | | | | | | |
| Stockholders' equity (deficit) | | | | | | | | | | | | |
| Common stock | 0.0 | - | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Additional paid-in capital | 2.2 | 5.5 | 84.5 | 84.5 | 84.5 | 84.5 | 84.7 | 84.9 | 85.1 | 85.3 | 85.5 | 85.7 |
| Notes receivable from stockholder | (0.3) | - | - | - | - | - | - | - | - | - | - | - |
| Accumulated other comprehensive loss | - | (0.0) | - | - | - | - | - | - | - | - | - | - |
| Accumulated deficit | (12.9) | (19.9) | (28.3) | (35.8) | (43.8) | (43.8) | (72.2) | (121.2) | (181.2) | (281.2) | (347.1) | (306.2) |
| Total stockholders' equity (deficit) | (11.0) | (14.4) | 56.2 | 48.7 | 99.2 | 99.2 | 62.7 | 167.5 | 111.6 | 115.8 | 54.3 | 99.3 |
| Total liabilities, convertible preferred stock and stockholders' equity | 51.8 | 63.2 | 58.5 | 51.0 | 101.5 | 101.5 | 65.1 | 170.2 | 114.6 | 119.0 | 57.7 | 102.9 |

**Source: Jefferies estimates, company data**



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**Exhibit 33: ATRA Cash Flow Statement: 2013A-2020E ($M)**

| *(In Millions)* | 2013A | 1Q14A | 2Q14A | 3Q14A | 4Q14E | 2014E | 2015E | 2016E | 2017E | 2018E | 2019E | 2020E |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Operating activities** | | | | | | | | | | | | |
| Net income (loss) | (8.8) | (7.0) | (4.5) | (7.5) | (8.0) | (27.1) | (28.5) | (49.0) | (60.0) | (100.0) | (65.9) | 40.9 |
| Adjustments to reconcile net cash used in operating activities: | | | | | | | | | | | | |
| In-process research and development acquired from Amgen | - | - | - | - | - | - | - | - | - | - | - | - |
| Depreciation expense | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.2 | 0.2 | 0.3 | 0.3 |
| Investment premium amortization, net | - | 0.0 | 0.1 | 0.1 | 0.1 | 0.4 | 0.5 | 0.6 | 0.8 | 0.9 | 1.0 | 1.2 |
| Stock-based compensation expense | 1.7 | 3.3 | 0.5 | 0.5 | 0.5 | 4.9 | 4.9 | 5.0 | 5.0 | 5.1 | 5.1 | 5.2 |
| Interest accrued on notes receivable from stockholder | (0.0) | (0.0) | (0.0) | (0.0) | (0.0) | (0.0) | - | - | - | - | - | - |
| Changes in operating assets and liabilities: | | | | | | | | | | | | |
| Other assets | 0.0 | 0.0 | - | - | - | 0.0 | - | - | - | - | - | - |
| Prepaid expenses and other current assets | (0.2) | 0.0 | (0.3) | (0.3) | (0.3) | (0.9) | (0.9) | (1.0) | (1.0) | (1.1) | (1.1) | (1.2) |
| Accounts payable | 0.5 | 0.4 | (0.5) | (0.5) | (0.5) | (0.9) | (1.0) | (1.0) | (1.1) | (1.1) | (1.2) | (1.2) |
| Income tax payable | 0.1 | (0.1) | - | - | - | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (0.1) | (0.6) |
| Other accrued liabilities | 0.3 | 0.6 | (0.2) | (0.2) | (0.2) | (0.0) | - | - | - | - | - | - |
| Accrued compensation | 0.3 | (0.1) | 0.2 | 0.2 | 0.2 | 0.3 | 0.4 | 0.4 | 0.4 | 0.5 | 0.5 | 0.5 |
| Net cash used in operating activities | (6.0) | (2.9) | (4.7) | (7.7) | (8.2) | (23.4) | (24.6) | (44.9) | (55.8) | (95.6) | (61.4) | 45.1 |
| **Investing activities** | | | | | | | | | | | | |
| Sale (Purchase) of short-term investments | - | (22.4) | (2.6) | - | - | (25.0) | 24.5 | - | - | - | - | - |
| Purchase of property and equipment | (0.0) | (0.0) | (0.0) | - | - | (0.0) | (0.0) | (0.0) | (0.0) | (0.0) | (0.1) | (0.1) |
| Net cash used in investing activities | (0.0) | (22.4) | (2.6) | - | - | (25.0) | 24.5 | (0.0) | (0.0) | (0.0) | (0.1) | (0.1) |
| **Financing activities** | | | | | | | | | | | | |
| Proceeds from sale of common stock | - | - | - | - | 58.8 | 58.8 | 0.1 | 150.0 | 0.1 | 100.0 | 0.1 | 0.1 |
| Repayment of notes receivable from stockholder | - | 0.0 | 0.3 | - | - | 0.3 | - | - | - | - | - | - |
| Proceeds from sale of unvested restricted stock | - | - | - | - | - | - | - | - | - | - | - | - |
| Proceeds from sale of convertible preferred stock | 53.6 | 13.5 | - | - | - | 13.5 | - | - | - | - | - | - |
| Offering costs for sale of convertible preferred stock | (0.2) | (0.0) | - | - | - | (0.0) | - | - | - | - | - | - |
| Offering costs incurred in anticipation of initial public filing | - | (0.0) | (1.0) | - | - | (1.1) | - | - | - | - | - | - |
| Net cash provided by financing activities | 53.4 | 13.5 | (0.7) | - | 58.8 | 71.6 | 0.1 | 150.0 | 0.1 | 100.0 | 0.1 | 0.1 |
| Increase (decrease) in cash and cash equivalents | 47.4 | (11.9) | (8.0) | (7.7) | 50.7 | 23.1 | (0.0) | 105.0 | (55.7) | 4.3 | (61.4) | 45.1 |
| Cash and cash equivalents-beginning of period | 4.2 | 51.6 | 39.8 | 31.8 | 24.1 | 39.8 | 62.9 | 62.9 | 167.9 | 112.2 | 116.5 | 55.1 |
| Cash and cash equivalents-end of period | 51.6 | 39.8 | 31.8 | 24.1 | 74.8 | 62.9 | 62.9 | 167.9 | 112.2 | 116.5 | 55.1 | 100.2 |

**Source: Jefferies estimates, company data**

**Exhibit 34: ATRA DCF Analysis**

| *(In Millions)* | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| WW Product Sales ($M) | - | - | - | - | 81 | 201 | 367 | 515 | 646 | 668 | 691 | 715 | 739 | 764 | 790 |
| Operating expenses | 28 | 49 | 60 | 110 | 147 | 160 | 195 | 222 | 234 | 230 | 226 | 221 | 224 | 226 | 229 |
| EBIT | (28) | (49) | (60) | (110) | (66) | 41 | 172 | 293 | 412 | 438 | 465 | 493 | 515 | 538 | 561 |
| (Taxes) | - | - | - | - | | - | 12 | 44 | 144 | 153 | 163 | 173 | 180 | 188 | 197 |
| EBIAT | (28) | (49) | (60) | (110) | (66) | 41 | 160 | 249 | 268 | 285 | 302 | 321 | 335 | 350 | 365 |
| PV of CF | (28) | (45) | (50) | (83) | (45) | 25 | 90 | 128 | 125 | 121 | 117 | 112 | 107 | 101 | 96 |

**Source: Jefferies estimates, company data**



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**Exhibit 35: PINTA 745 Market Model**

| | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **PINTA 745** | | | | | | | | | | | |
| Total US Hemodialysis Patients | 498,633 | 511,598 | 524,899 | 538,547 | 552,549 | 566,915 | 581,655 | 596,778 | 612,294 | 628,214 | 644,547 |
| Patients with PEW | 199,453 | 204,639 | 209,960 | 215,419 | 221,020 | 226,766 | 232,662 | 238,711 | 244,918 | 251,286 | 257,819 |
| PINTA 745 penetration | *5%* | *11%* | *19%* | *25%* | *30%* | *30%* | *30%* | *30%* | *30%* | *30%* | *30%* |
| # PINTA 745 patients | 9,973 | 22,510 | 39,892 | 53,855 | 66,306 | 68,030 | 69,799 | 71,613 | 73,475 | 75,386 | 77,346 |
| Price/pt/yr ($) | $ 13,000 | $ 13,130 | $ 13,261 | $ 13,394 | $ 13,527 | $ 13,663 | $ 13,799 | $ 13,937 | $ 14,077 | $ 14,217 | $ 14,360 |
| **PINTA 745 US Sales ($M)** | **$ 130** | **$ 296** | **$ 529** | **$ 721** | **$ 897** | **$ 929** | **$ 963** | **$ 998** | **$ 1,034** | **$ 1,072** | **$ 1,111** |
| ***Prob. Adj. PINTA 745 US Sales ($M)*** | ***$ 52*** | ***$ 118*** | ***$ 212*** | ***$ 289*** | ***$ 359*** | ***$ 372*** | ***$ 385*** | ***$ 399*** | ***$ 414*** | ***$ 429*** | ***$ 444*** |
| **PINTA 745 Ex-US Sales ($M) as % of US** | **$ 84** | **$ 192** | **$ 344** | **$ 469** | **$ 583** | **$ 604** | **$ 626** | **$ 649** | **$ 672** | **$ 697** | **$ 722** |
| ***Prob. Adj. PINTA 745 Ex-US Sales ($M)*** | ***$ 34*** | ***$ 77*** | ***$ 138*** | ***$ 188*** | ***$ 233*** | ***$ 242*** | ***$ 250*** | ***$ 260*** | ***$ 269*** | ***$ 279*** | ***$ 289*** |
| **PINTA 745 WW Sales ($M)** | **$ 214** | **$ 488** | **$ 873** | **$ 1,190** | **$ 1,480** | **$ 1,534** | **$ 1,589** | **$ 1,647** | **$ 1,707** | **$ 1,768** | **$ 1,833** |
| **PINTA 745 WW Sales excluding Amgen royalty (5%)** | **$ 203** | **$ 463** | **$ 829** | **$ 1,131** | **$ 1,406** | **$ 1,457** | **$ 1,510** | **$ 1,565** | **$ 1,621** | **$ 1,680** | **$ 1,741** |
| ***Prob. Adj. PINTA 745 WW Sales ($M)*** | ***$ 81*** | ***$ 185*** | ***$ 332*** | ***$ 452*** | ***$ 562*** | ***$ 583*** | ***$ 604*** | ***$ 626*** | ***$ 648*** | ***$ 672*** | ***$ 696*** |

Source: Jefferies estimates

**Exhibit 36: STM 434 Market Model**

| | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 |
|---|---|---|---|---|---|---|---|---|---|---|
| **STM 434** | | | | | | | | | | |
| # pts with ovarian cancer (incidence) | 20,729 | 20,522 | 20,317 | 20,113 | 19,912 | 19,713 | 19,516 | 19,321 | 19,128 | 18,936 |
| # pts on first line therapy | 16,583 | 16,417 | 16,253 | 16,091 | 15,930 | 15,771 | 15,613 | 15,457 | 15,302 | 15,149 |
| # of recurent patients (failing first line therapy) | 11,608 | 11,492 | 11,377 | 11,264 | 11,151 | 11,039 | 10,929 | 10,820 | 10,712 | 10,604 |
| STM 434 penetration | *5%* | *11%* | *19%* | *25%* | *25%* | *25%* | *25%* | *25%* | *25%* | *25%* |
| Price/pt/yr ($) | $85,000 | $87,550 | $90,177 | $92,882 | $95,668 | $98,538 | $101,494 | $104,539 | $107,675 | $110,906 |
| **STM 434 US Sales ($M)** | **$ 49** | **$ 111** | **$ 195** | **$ 262** | **$ 267** | **$ 272** | **$ 277** | **$ 283** | **$ 288** | **$ 294** |
| **Prob. Adj. STM 434 US sales ($M)** | **$ 10** | **$ 22** | **$ 39** | **$ 52** | **$ 53** | **$ 54** | **$ 55** | **$ 57** | **$ 58** | **$ 59** |
| **STM 434 Ex-US Sales ($M) as % of US** | **$ 32** | **$ 72** | **$ 127** | **$ 170** | **$ 173** | **$ 177** | **$ 180** | **$ 184** | **$ 187** | **$ 191** |
| **Prob. Adj. STM 434 Ex-US Sales ($M)** | ***$ 6*** | ***$ 14*** | ***$ 25*** | ***$ 34*** | ***$ 35*** | ***$ 35*** | ***$ 36*** | ***$ 37*** | ***$ 37*** | ***$ 38*** |
| **STM 434 WW Sales ($M)** | **$ 81** | **$ 183** | **$ 322** | **$ 432** | **$ 440** | **$ 449** | **$ 458** | **$ 467** | **$ 476** | **$ 485** |
| **STM 434 WW Sales excluding Amgen royalty (3%)** | **$ 79** | **$ 177** | **$ 312** | **$ 419** | **$ 427** | **$ 435** | **$ 444** | **$ 453** | **$ 461** | **$ 471** |
| ***Prob. Adj. STM 434 WW Sales ($M)*** | ***$ 16*** | ***$ 35*** | ***$ 62*** | ***$ 84*** | ***$ 85*** | ***$ 87*** | ***$ 89*** | ***$ 91*** | ***$ 92*** | ***$ 94*** |

Source: Jefferies estimates



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## Company Description

Atara Biotherapeutics, Inc. is a clinical stage biopharmaceutical company focused on developing novel therapeutics for serious unmet medical needs, with an initial focus on muscle wasting conditions and oncology. Its product candidates are biologics targeting myostatin and activin, members of the transforming growth factor-beta, protein superfamily, which play roles in the growth and maintenance of muscle and many other body tissues. The company's product candidate includes PINTA 745, STM 434 and ATA 842. Atara Biotherapeutics was founded by Isaac E. Ciechanover on August 22, 2012 and is headquartered in Brisbane, CA.

## Analyst Certification:

I, Ryan Martins, certify that all of the views expressed in this research report accurately reflect my personal views about the subject security(ies) and subject company(ies). I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views expressed in this research report.

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## Company Specific Disclosures

For Important Disclosure information on companies recommended in this report, please visit our website at https://javatar.bluematrix.com/sellside/Disclosures.action or call 212.284.2300.

## Meanings of Jefferies Ratings

Buy - Describes stocks that we expect to provide a total return (price appreciation plus yield) of 15% or more within a 12-month period.

Hold - Describes stocks that we expect to provide a total return (price appreciation plus yield) of plus 15% or minus 10% within a 12-month period.

Underperform - Describes stocks that we expect to provide a total negative return (price appreciation plus yield) of 10% or more within a 12-month period.

The expected total return (price appreciation plus yield) for Buy rated stocks with an average stock price consistently below $10 is 20% or more within a 12-month period as these companies are typically more volatile than the overall stock market. For Hold rated stocks with an average stock price consistently below $10, the expected total return (price appreciation plus yield) is plus or minus 20% within a 12-month period. For Underperform rated stocks with an average stock price consistently below $10, the expected total return (price appreciation plus yield) is minus 20% within a 12-month period.

NR - The investment rating and price target have been temporarily suspended. Such suspensions are in compliance with applicable regulations and/or Jefferies policies.

CS - Coverage Suspended. Jefferies has suspended coverage of this company.

NC - Not covered. Jefferies does not cover this company.

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## Valuation Methodology

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**Jefferies Franchise Picks**

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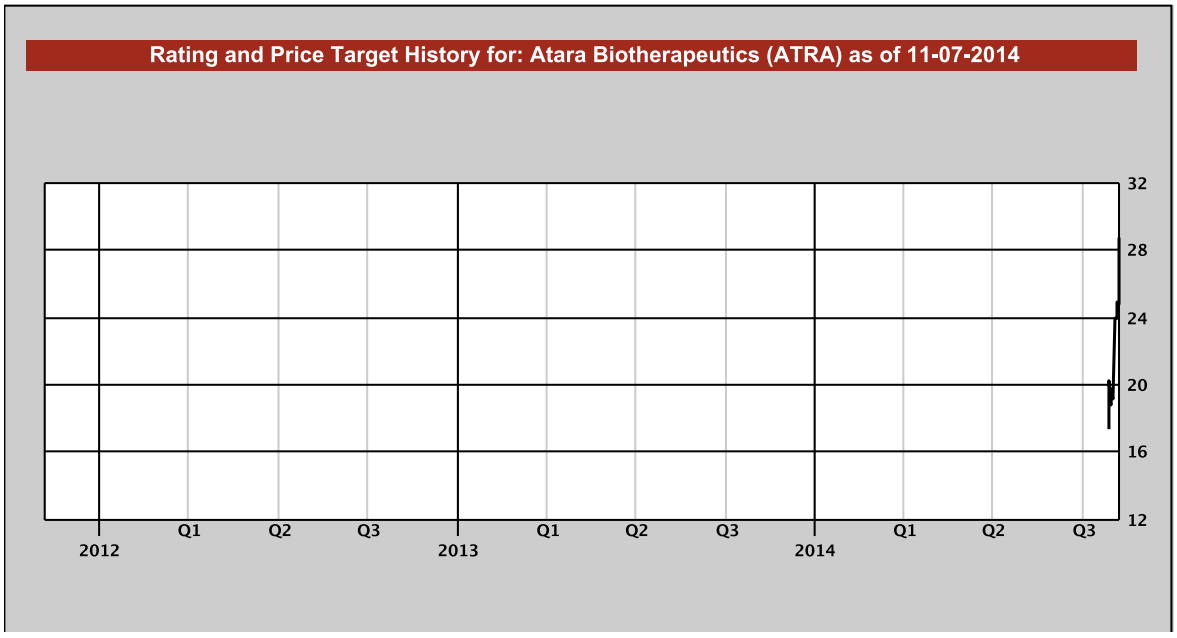
## Other Companies Mentioned in This Report

- Amgen, Inc. (AMGN: $160.25, BUY)
- Celldex Therapeutics, Inc. (CLDX: $13.42, BUY)
- DaVita, Inc. (DVA: $74.49, BUY)
- Eli Lilly & Co. (LLY: $66.60, HOLD)
- Fresenius Medical Care (FME GR: €57.21, UNDERPERFORM)
- Fresenius SE (FRE GR: €41.10, BUY)
- Novartis AG (NOVN VX: CHF88.65, BUY)
- Pfizer, Inc. (PFE: $29.92, BUY)
- Regeneron Pharmaceuticals, Inc. (REGN: $377.84, HOLD)
- Roche (ROG VX: CHF282.40, BUY)
- Sanofi (SAN FP: €72.97, HOLD)
- Shire (SHP LN: p4,171.00, BUY)
- Shire (SHPG: $198.58, BUY)




## Distribution of Ratings

| Rating | Count | Percent | IB Serv./Past 12 Mos. Count | IB Serv./Past 12 Mos. Percent |
|---|---|---|---|---|
| **BUY** | 1009 | 52.09% | 264 | 26.16% |
| **HOLD** | 789 | 40.73% | 143 | 18.12% |
| **UNDERPERFORM** | 139 | 7.18% | 5 | 3.60% |



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