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April 14, 2014

Stock Rating Overweight Industry View In-Line

### Akebia Therapeutics Inc

### Compelling, Large Anemia Opportunity; Init OW, PT \$90

We see Akebia's lead asset, AKB-6548, as having \$2+bn WW sales potential in its first indications.

AKB-6548, the lead Akebia asset, is targeting the large and underserved CKD anemia patient population. We see this asset as having a) a novel approach for anemia, b) \$2+bn potential in its lead indications, c) generated good, albeit early, proof of concept data, and d) lower overall risk than the Street assigns.

Novel Approach: AKB-6548 (and the earlier stage AKB-6899) target the HIF pathway and increase the lifespan, and thus activity, of HIF proteins. The HIF pathway is activated as a person goes to higher altitudes. This leads to physiologic changes including increasing the production and "efficiency" of RBC's the cells which are low in anemia. We view this as a potentially more physiologic approach to anemia correction vs. the current standard of care using large doses of erythropoietin and/or iron.

Large Market: We expect Akebia, and HIF competitors (see inside for competitor discussion), to start targeting the CKD and dialysis markets as unmet need is high (2+mn anemic patients) and the data for the class to date have primarily been generated in these patients. Specifically in CKD, the current IV/SC options are not viewed as optimal and have not deeply penetrated. We see the potential for a safer to dose drug that has a steady impact on anemia correction as significant.

Data: The Ph 2a data (n=93) showed AKB-6548 was safely able to raise hgb levels by ~1+ gm/dL – a meaningful change. The drug was easily dose titrated to avoid hgb overshooting (a regulatory concern). We look to the ~200 patient, 20 wk Ph 2b data at YE14 to confirm Ph 2a data and increase confidence in Ph 3.

**Risks:** There are few key risks that we think will mostly be mitigated by the time of Ph 3 start in '15. 1) Safety -The drug has been safe to date, but in a relatively small patient set. The Ph 2b data should help confirm safety in CKD patient population, which is known to be on the sicker side. 2) Ph 3 – While the FDA, and to a degree EMEA, have become more risk averse in CKD/dialysis anemia setting, we expect a Ph 3 design that stays within FDA's comfort area of Hgb levels should be negotiable and achievable for the drug. 3) Competition There likely will be other HIF drugs on the market and there are ongoing IP challenges. We are optimistic Akebia will be competitive on all fronts.

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#### **Key Ratios and Statistics**

Reuters: AKBA.O Bloomberg: AKBA US Biotechnology / United States of America

\$90.00 Shr price, close (Apr 11, 2014) \$16.86 \$341 Mkt cap, curr (mm) 52-Week Range \$28.50-16.41

Fiscal Year ending	12/13	12/14e	12/15e	12/16e
ModelWare EPS (\$)	(126.94)	(2.36)	(3.33)	(3.19)
P/E	NM	NM	NM	NM
Consensus EPS (\$)§	-	-	-	-
Div yld (%)	-	-	-	-

Unless otherwise noted, all metrics are based on Morgan Stanley ModelWare framework (please see explanation later in this note).

§ = Consensus data is provided by Thomson Reuters Estimates. e = Morgan Stanley Research estimates

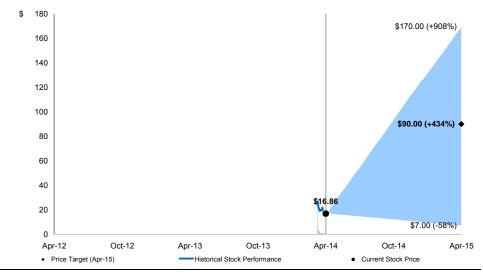
Anemia	A disease in which the body does not receive enough oxygen because the blood has insufficient red blood cell and hemoglobin mass to carry it.
Hemoglobin	Protein contained within red blood cells that carries oxygen.
Chronic Kidney	Condition in which the kidney gradually loses function.
Disease (CKD) / Non- Dialvsis	
Dialysis	progressed to end-stage renardisease.
Dialysis / End-Stage Renal Disease	Condition in which kidney function fails and an artificial kidney is required to remove waste from blood.
HIF Pathway	Body's natural response to being at elevated altitudes which results in increased red blood cell production.

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### Risk-Reward Snapshot: Akebia (AKBA, OW, PT \$90)

#### AKB-6548 in CKD and Dialysis Anemia Drives Risk-Reward



Source: Morgan Stanley Research estimates, Thomson Reuters

ource: Morgan Stanley Research estimates, Thomson Reuters						
Price Target \$90	We derive our PT from a discounted cash flow analysis that uses a WACC of 12.5% and a 0% terminal growth rate. The main revenue driver in our model is the launch of AKB-6548.					
Bull Case \$170	DCF	AKB-6548 makes it to market in CKD and dialysis. Our bull case has slightly higher (CKD) and significantly higher (dialysis) penetration of the HIF class than the base case and assumes that AKB-6548 splits the market with a single HIF competitor:  1) ~\$2.2bn US peak (2025) AKB-6548 sales for CKD revenue 2) ~\$275mn US peak (2025) AKB-6548 sales for dialysis revenue 3) AKB-6548 penetrates half of HIF drug usage in the CKD market and dialysis markets at peak, 4) HIF drugs capture ~55% of the CKD market and ~35% of the dialysis market at peak, 5) ~\$4.3bn WW peak (2025) AKB-6548 sales (\$2.9bn to AKBA), and 6) No value for AKB-6899.				
Base Case \$90	DCF	AKB-6548 makes it to market in CKD and dialysis and performs well commercially, but splits the HIF market with ~2 other HIF drugs. We assume:  1) ~\$1.2bn US peak (2025) AKB-6548 sales for CKD revenue 2) ~\$70mn US peak (2025) AKB-6548 sales for dialysis revenue 3) AKB-6548 penetrates ~1/3rd of HIF drug usage in the CKD market and dialysis markets at peak, 4) HIF drugs capture <50% of the CKD market and <15% of the dialysis market at peak, 5) ~\$2.2bn WW peak (2025) AKB-6548 sales (\$1.5bn to AKBA), and 6) No value for AKB-6899.				
Bear Case \$7	Cash Based Value	AKB-6548 does not make it to market.  We expect the stock would trade at or modestly below cash in this scenario as the remaining pipeline, while interesting, is much earlier and hard to place concrete values on.				

#### **Investment Thesis**

- We are OW Akebia as we believe AKB-6548, a novel, oral drug for the treatment of anemia, has a solid,
   \$2+bn opportunity for anemia in dialysis and CKD patients.
- AKB-6548 impacts the HIF pathway, which is part of the body's normal approach to being at higher altitude and better oxygen utilization, and may be a more physiologic approach to anemia treatment than current therapy.
- Ph 2a efficacy data has shown that AKB-6548 was able to significantly increase hemoglobin levels in CKD patients by ~1 gm/dL while avoiding overshooting hemoglobin.
- AKB-6548's safety profile is mostly clean, with the most common side effects being gastrointestinal.
- The CKD and dialysis anemia markets are large with high unmet need. We see additional upside opportunities in other anemia indications as well.
- Current standard of care for anemia management, erythropoiesis stimulating agents (ESAs) is suboptimal given serious mortality and CV safety risks and IV or subcu dosing.
- Though interesting, AKB-6899 is early and is not part of our valuation.

#### Risks to our price target

1) AKB-6548 efficacy data may be worse than expected, 2) AKB-6548 may encounter a safety issue, 3) AKB-6548 commercial opportunity may be smaller than we expect.

#### **Investment Case**

#### **Summary & Conclusions**

## We are initiating coverage of Akebia (AKBA) with an Overweight rating and a \$90 price target.

Akebia is a biotechnology company focused on drugs impacting the hypoxia-inducible factor (HIF) pathway. The lead drug, AKB-6548, is a once daily pill currently in Ph 2b for the treatment of anemia in the setting on chronic kidney disease (CKD), with plans to broaden the target market in Ph 3 (dialysis) and beyond (idiopathic age related anemia, etc.). We expect AKB-6548 to be partnered ex-US in 2017, be on the market by 2018, and have peak (2025) WW sales of \$2.2bn. A second drug, AKB-6899, is preclinical and may be developed for indications including oncology and ophthalmology.

## Below, and in further detail inside, we discuss the key focus points for AKB-6548:

- 1) the solid Ph 1/2 efficacy to date,
- 2) the evolving, currently clean, safety profile,
- 3) the potential path to market, and
- 4) the sizeable commercial opportunity.

In addition, we briefly discuss the earlier stage AKB-6899.

#### 1) Efficacy so far is solid

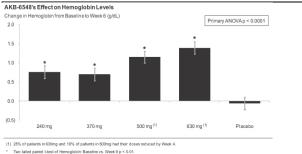
AKB-6548 targets the HIF pathway. This pathway is typically relatively quiescent, with increased activity in response to low oxygen environment at altitude and, more severely, with hypoxia. At altitude, the body makes a few key adaptations including a) increased erythropoietin (Epo) secretion, b) increased reticulocyte (immature RBC) and RBC production as a result of the Epo secretion, and c) improvements in iron absorption and utilization. The responses to hypoxia can include these but also others. The company notes that AKB-6548 is more selective for HIF-2 $\alpha$  subtype, which is more responsible for altitude changes, vs. HIF-1 $\alpha$ , which is more broadly expressed and more relevant for hypoxia.

We believe a drug that causes these changes will be a potentially useful drug for patients with anemia, a disease of insufficient red blood cell/hemoglobin mass in the body.

The primary AKB-6548 data set generated so far is the 6 week, placebo controlled Ph 2a trial in anemic chronic kidney disease patients (n=~70 patients on drug across 4 doses, Ex. 1). These data showed a) a clear dose response, b) a rise in hemoglobin (hgb) of ~1 gm/dL at the 500mg dose closest to the Ph 2b dose (450mg), and c) compensatory changes in

reticulocyte, Epo, and iron protein as expected with the mechanism. Importantly, the drug proved to be easily titrated, with no patients significantly overshooting the hemoglobin level of 13 gm/dL (a sensitive level for the FDA).

Exhibit 1
Ph 2a - AKB-6548's Effect on Hemoglobin



Source: Company Data, Morgan Stanley Research

The company has Ph 2b CKD patient data (n=~135 patients on drug for 20 weeks) reading out by YE14, serving as a key efficacy de-risking step. Importantly, this trial includes patients naïve to erythropoietin stimulating agents (ESAs - Epogen, Procrit, and Aranesp), patients remotely on ESAs, and patients recently on ESAs. This population mix is both broad and reflective of the patient mix commercially (and likely in Ph 3).

#### 2) Safety is early but clean so far

The safety has been evaluated in multiple single dose Ph 1 studies and two short (4 weeks, 6 weeks) Ph 2a trials. The most predominant signal has been mild/moderate gastrointestinal side effects (e.g. diarrhea). This may be due to the formulation, which has changed from a capsule to a tablet for the Ph 2b.

In any CKD patient trial, given the nature of the patient population, there are often severe adverse events and even deaths recorded in Ph 2 and 3 trials. The AKB-6548 Ph 2a trials were no exception, but the lack of any predominant side effect trend or attribution to drug provide extra levels of comfort. In addition, given both the patient population and the HIF mechanism, it was good to see no dose related or significant impacts on kidney function, VEGF levels, or platelets. Finally, we note that given some safety signals seen with other HIF drugs, we will be keeping our eye on liver function tests, platelet levels, cholesterol levels, and blood pressure.

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#### 3) Ph 3 plans hopefully to be set in next 12 months

An outstanding question for Akebia is what the Ph 3 trial program will need to look like in order to gain approval for the treatment of anemia in CKD (and dialysis) patients – the initial target populations. This is a focus question for investors given the heightened regulatory uncertainty in the anemia space post-the label revisions for ESAs.

Exhibit 2

#### **ESA Trials Seemed to Favor Lower Hgb Targets**

Trial	Drug	Arm A Target (g/dL)	Arm B Target (g/dL)	Brief Comments
CREATE	Epoetin Beta	13-15	10.5-11.5	No overall CV event difference; Shorter time to dialysis in Arm A (higher target)
CHOIR	Epoetin Alfa	13.5	11.3	Overall CV event rate higher in Arm A (higher target)
TREAT	Darbepoetin Alfa	13	9	No overall CV event difference; higher stroke rate in Arm A (higher target)

Source: Company Data, Morgan Stanley Research

For context, the ESA class had a major label revision (black box) and commercial shift when it was noted that targeting higher hgb levels with higher drug doses was associated with no clear, consistent benefits on average and in some cases adverse outcomes (Ex. 2). While it was originally viewed as a hgb target issue, some now believe that it is more related to the higher (sometimes quite supraphysiologic) doses of ESAs required to hit normal hgb levels.

Regardless, we do not expect Akebia to run a higher risk, paradigm changing Ph 3 program. Instead, we expect them to use a target of ~11 g/dL, as done in Ph 2b, avoiding massive overshoots towards 13 g/dL. In general, we see a CKD focused development plan similar to that outlined in Ex. 3, with a likely similar but smaller set of studies for dialysis patients.

Exhibit 3

#### Potential Ph 3 CKD Anemia Program for AKB-6548

Trial	Size	AKB-6548 Dose	Control Arm	Duration	Comments
1	>500 pts	450 mg with titration	Placebo/ESA rescue	52 wks + any extension	The control arm is the current US standard of care
2	>500 pts	450 mg with titration	Placebo/ESA rescue	52 wks + any extension	The control arm is the current US standard of care
3	<500 pts	450 mg with titration	Active/planned ESA dosing	52 wks + any extension	Primarily for EMEA
Pooled CV Analysis	All pts (likely >2000 pts)	450 mg with titration	Above	52 wks + any extension	The initial hurdle likely a HR of 1.5

Source: Company Data, Morgan Stanley Research

The cardiovascular (CV) analysis is another result of regulatory concern around ESAs. Akebia believes that attempting to rule out a hazard ratio (HR) of ~1.5 to start should be sufficient, which they believe can be done with ~2,000 patients. Over time, the "ruled out" threshold would go down to ~1.3. We believe that AKB-5648's approach to anemia correction could actually lead to improved cardiovascular outcomes with time, as we do not view being anemic as physiologically beneficial. However, as of now,

simply ruling out a problem is the first step and one we think can be met.

#### 4) Commercial Opportunity Potentially Large

We believe the CKD and dialysis anemia market is large. ESAs currently sell ~\$6bn WW, with a large portion of that coming from dialysis and late stage CKD (4/5). Before much of the above mentioned safety/regulatory issues and price declines in dialysis patients, the group was selling closer to \$12bn annually. Importantly, we believe the large number of anemic CKD and dialysis patients is only growing, and midstage (CKD 3/4) patients may not see ESA's or IV irons as an attractive option for a host of reasons (convenience, dosing route, safety, etc.).

Our US market model (Ex. 20) reflects an initial (2018) addressable, anemic CKD stage 3-5 population of ~2.4mn patients, with dialysis representing an additional ~400k anemic patients. Given the CKD patient growth trajectory in the US, this combined (CKD and dialysis) addressable patient population rises to ~3.2mn by 2025.

Exhibit 4

#### **Key Market Model Assumptions and Estimates**

	2018	2022	2025
US CKD Revenue (\$mn)	\$64	\$630	\$1,185
US CKD Addressable Market (millions of patients)	2.4	2.6	2.7
US AKB-6548 Penetration of Addressable CKD Patients	3%	10%	15%
US Dialysis Revenue (\$mn)	\$3	\$35	\$68
US Dialysis Addressable Market (thousands of patients)	423	476	521
US AKB-6548 Penetration of Addressable Dialysis Patients	1%	3%	4%
WW AKB-6548 Sales (\$mn)	\$67	\$1,030	\$2,217

Source: Company Data, Morgan Stanley Research

There is competition in the HIF space, which impacts our estimated AKB-6548 penetration into this market. The lead competitor is Fibrogen (Roxadustat / FG-4592), which is partnered with Astra Zeneca in the US and Astellas in the EU. The EU Ph 3 program has started, but the US program is inline with AKB-6548 timing wise. FG-4592 leads to more rapid and larger increases in hgb vs. AKB-6548, with broader impacts on cholesterol (decreased) and platelets (decreased). The dosing is still being worked out, with TIW, BIW, and QW in Ph 3. We currently assume this drug reaches the market and is used similarly to AKB-6548.

There are three other HIF drugs in development, including GSK in Ph 2, Bayer in Ph 2, and Japan Tobacco in Ph 1. As of now, we know little about these competitor drugs. Given Akebia seems to be ahead of these three, we assume they will as a group have less impact commercially than Fibrogen.

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There is a patent challenge ongoing with a granted Fibrogen patent that we think may dictate Akebia's freedom to operate in Europe. It is likely a couple of years before we hear any decision, and our legal experts are confident that Akebia has a range of arguments that any one of which, if successful, could provide them room to enter the EU market. In the end, while we do not view this as our base case, the US market is large enough to support a significant (\$1+bn) opportunity.

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data in any of these additional indications, we do not have any reason to believe the drug will not have activity in one or more of these other, large anemia opportunities. We expect the company to evaluate these options and start Ph 2 trial(s) in 2015/6 once the CKD and dialysis Ph 3 trials are running.

Exhibit 5

#### **Additional Anemia Markets Have Large Potential**

Anemia Market Segment	Number of Patients With Anemia
Chronic Kidney Disease Stage 3-5	~2.1+mn, growing to ~2.7+mn in 2025
End Stage Renal Disease	~350+k, growing to ~500+k in 2025
Idiopathic Age Related Anemia	~1.5mn
Congestive Heart Failure	~1mn
Iron Deficiency Anemia	~3.3mn women

Source: Company Data, Morgan Stanley Research

#### **AKB-6899**

AKB-6899, a HIFα stabilizing drug, is not part of our valuation given its early stage. The drug inhibits VEGF and phosphoglycerate kinase (PGK) mRNA, which are associated with tumor growth, and stimulates Epo. Potential indications include cancer (ovarian, breast, colon, and lung), chemotherapy induced anemia, and VEGF related eye diseases. Akebia plans to initiate a Ph 1 in oncology in 2015.

Finally, we note that the kidney related anemia markets may only be the first step (Ex. 4). While we have yet to see

Exhibit 6

#### **Catalyst Calendar**

<b>,</b>			
Drug	Туре	Event	Expected Timing
AKB-6548	Product Advancement	Initiate Ph 2 trial in dialysis patients	1H14
AKB-6548	Clinical Data	Ph 2b data in non-dialysis patients	4Q14
AKB-6548	Product Advancement	Initiate Ph 3 trial	2015
AKB-6899	Product Advancement	Initiate Ph 1 trial	2015

Source: Company Data, Morgan Stanley Research

#### **Valuation**

Exhibit 7

#### **DCF Drives Valuation**

(\$ in mn)	2012	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Free Cash Flow	(7)	(11)	(39)	(70)	(77)	80	(51)	63	190	215	338	483	646	792	882	932	958	972	97	97
YoY growth	-49.2%	57%	240.1%	81%	11%	-204%	-163%	-224.1%	202.3%	13.2%	56.8%	43.0%	33.7%	22.6%	11.3%	5.7%	2.8%	1.4%	-90.0%	0.0%
Net Cash Proxy for Dilution	\$0.0	\$0.0	-\$7.6	-\$8.0	-\$8.4	-\$8.6	-\$8.6	-\$8.5	-\$8.2	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0	-\$12.0
Free Cash Flow for DCF	-\$7.2	-\$11.4	-\$46.2	-\$77.8	-\$85.5	\$71.6	-\$59.4	\$54.4	\$182.1	\$203.5	\$325.9	\$471.1	\$634.1	\$780.3	\$870.0	\$919.9	\$946.3	\$959.8	\$85.2	\$85.2
PV of Free Cash Flow			-46.2	-71.3	-69.6	51.8	-38.2	31.1	92.5	91.9	130.8	168.1	201.1	220.0	218.0	204.9	187.4	168.9	13.3	11.8

Source: Company data, Morgan Stanley Research estimates

Exhibit 8

#### **DCF Valuation Suggests Significant Upside**

Valuation Date	2014.25
Discount Rate	12.5%
Terminal Growth Rate	0%
Terminal Value Year	2031
Sum of Discounted FCF (\$mn)	\$1,577.9
Discounted Terminal Value (\$mn)	\$94.8
Net Cash (\$mn), post-\$	\$139.5
Equity Value (\$mn), post-\$	\$1,812
Equity Value/Sh, post-\$	\$90
Shares Outstanding	20.2

Source: Company Data, Morgan Stanley Research estimates

#### \$90 PT includes AKB-6548 for CKD and dialysis.

We derive our PT from a discounted cash flow (DCF) analysis that uses a WACC of 12.5% and a terminal growth rate of 0% post 2031. We incorporate the cash cost of stock options.

Valuation Methodology: We use a DCF to value Akebia as well as most other companies under coverage. We believe a DCF best captures the longer term nature of drug development and commercialization. We do not feel that a multiples analysis accomplishes the same goal, as it only evaluates a company during a snapshot in time.

**Discount Rate**: We typically use a discount rate of 12.5% for development stage companies with proof-of-concept data in

a formal, company-run Ph 2 trial. We believe AKB-6548's Ph 2a trial fits these criteria.

**Terminal Growth Rate:** Our modeled cash flows extend to 2025. Beyond this, we grow cash flows at 50% of the prior year's rate. We decline cash flows by 90% in 2030 due to AKB-6548's patent expiry plus Hatch Waxman extension. Beyond 2031, we use a terminal growth rate of 0%.

**Revenue:** The revenue drivers in our model are sales of AKB-6548 in CKD and dialysis.

**Economics:** AKB-6548 is wholly owned by Akebia. We model Akebia partnering the drug ex-US with a \$200mn upfront and a mid-20s% royalty rate.

**COGS:** We model COGS of 10% at drug launches improving to 9% over time.

#### **Operating Expenses:**

**R&D:** We model R&D increasing through 2017 as Akebia runs Ph 3 trials. Post-2017, we expect R&D expenses to decrease as the company tries to better match expenses with revenue.

**SG&A:** We model SG&A increasing significantly in 2017+ as Akebia builds out a US sales force.

**Financings:** We model a ~\$100mn raise in 2015 post Ph 2b data.

**Key Risks To Our Price Target Include:** 1) AKB-6548 efficacy data may be worse than expected, 2) AKB-6548 may encounter a safety issue, 3) AKB-6548 commercial opportunity may be smaller than we expect.

### **Compelling Opportunity for AKB-6548 for Anemia**

We see significant commercial potential in AKB-6548 for the treatment of CKD and dialysis related anemia. For reference, anemia (Ex. 9) is a condition where the body does not receive enough oxygen due to low red blood cell/hemoglobin levels.

AKB-6548 is a once daily, oral tablet currently in a Ph 2b study in anemic CKD patients. We believe that AKB-6548 has the ability to increase hemoglobin levels through the HIF pathway, which may prove over time to be a safer, more convenient, and more physiologic way to treat anemia vs. the current standard of care of ESAs.

Our diligence suggests ~\$2.2bn peak (2025) WW sales for AKB-6548, which is primarily in the CKD market. We model a smaller contribution (~\$70mn peak US sales) from the dialysis market, although reimbursement (e.g. US bundling) dynamics could make this HIF class more attractive over time in dialysis patients. There is potential for AKB-6548 to target other anemia markets over time as well, but that is upside to our model.

Exhibit 9

Anemia Disease Summary

Anemia	
Disease	The body does not receive enough oxygen because the blood has insufficient red blood cell and hemoglobin mass to carry it
Causes	Chronic kidney disease, iron deficiency (iron is a component of hemoglobin), nutritional deficiency (patient does not consume enough iron), bone marrow disease (red blood cells are produced in the bone marrow), abnormal erythropoietin production, age, etc.
Symptoms	Fatigue, disease progression, cardiopulmonary complications, death
Current Treatments	Iron supplementation (oral or IV); ESAs (erythropoiesis stimulating agents); red blood cell transfusion

Source: Company Data, Morgan Stanley Research

#### Below, we address in more detail:

- 1)The HIF mechanism of action,
- 2) Solid efficacy data, primarily from a Ph 2a trial,
- 3) A relatively clean safety profile so far,
- 4) The **path forward** in the CKD and dialysis market, as well as potentially other indications, and
- 5) The \$2.2bn commercial opportunity.

#### 1) HIF Mechanism of Action

AKB-6548 works through HIF stabilization (Ex. 10), which is intended to mimic the body's natural response to being at elevated altitudes. More specifically, AKB-6548 and other drugs in this class block the action of HIF-prolyl hydroxylases (HIF-PH) which are a family of enzymes that typically break HIF down and keep it mostly inactive. Thus, the end result of HIF-PH inhibition is a rise in the proportion of stable HIF, leading to activation of the pathway downstream to HIF.

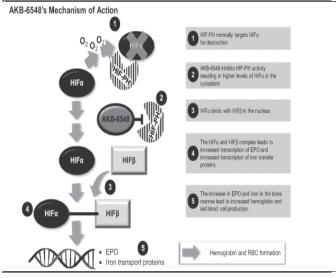
Normally, the key regulatory mechanism of HIF-PH is the body's oxygen concentration, with low oxygen causing less HIF-PH activity and thus higher HIF levels. Altitude is a key time when the body senses less oxygen. **Key changes in this pathway, when activated, include a) increased erythropoietin (Epo) level, b) increased red blood cell (RBC) and reticulocyte (immature RBC) production, and c) improvements in iron absorption and utilization.

These are steps the body takes to ultimately improve oxygen delivery to the body, which should similarly correct the problem in anemia where the body has low oxygen carrying** 

capacity. See P. 11-12 for additional details on anemia.

The above changes are thought primarily to be driven by HIF2 $\alpha$  which is less broadly expressed and may be the part of the pathway more specific to relative anemia correction at altitude. The HIF1 $\alpha$  part of the pathway is more broadly expressed and thought to be relevant in both altitude adjustment but also more severe hypoxia (extremely low oxygen levels). HIF1 $\alpha$  is more broadly expressed in the body and may influence cell life, vascular growth, and other factors. AKB-6548 tends to activate HIF2 $\alpha$ > HIF1 $\alpha$ .

AKB-6548 Mechanism of Action – HIF Stabilization



Source: Company Data, Morgan Stanley Research

### 2) Solid Ph 2 Efficacy So Far for AKB-6548

There have been a number of Ph 1a/b trials and two Ph 2a trials run so far. The Ph 2a trials suggest solid efficacy for AKB-6548 on the key metric for anemia – the rise in hemoglobin (primary endpoint). In addition, corresponding changes in reticulocyte (immature red blood cell) levels and iron utilization proteins were seen as well.

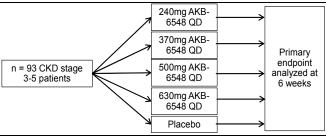
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6 Week Controlled Ph 2a Trial: Akebia's most advanced data set so far is from a 6 week Ph 2a trial in 93 CKD patients (Ex. 11) that looked at the mean absolute change in hemoglobin vs. baseline as the primary endpoint. The trial enrolled patients with hemoglobin levels ≤10.5 g/dL that were either ESA naïve or off ESAs for >11 weeks prior to screening.

Exhibit 11

AKB-6548 Ph 2a CKD Trial Design



Source: Company Data, Morgan Stanley Research

A key regulatory and commercial focus for anemia drugs is the ability to slow down or stop the rise in hemoglobin as you get towards a currently used goal of ~11 g/dL so as to avoid overshooting. This approach, as discussed briefly on P. 10 and in more detail below, is related to risks seen with the dosing of ESAs to target restoring hgb to normal levels.

In the Ph 2a (and ongoing Ph 2b trial), Akebia utilized a dose titration protocol that was based on absolute and/or relative hemoglobin changes. For example, if hemoglobin increased by 1.5 g/dL vs. baseline or reached 12.5 g/dL, patients had their dose cut in half. If hemoglobin levels increased above 13 g/dL (a current regulatory red flag), patients would stop drug.

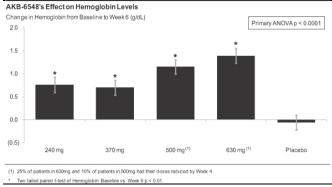
No patients had hemoglobin levels increase above 13 g/dL, and 26% of patients in the highest dose and 11% of patients in the next highest dose did decrease their dose. Importantly, we understand the dose titration was viewed as easy to do and is not an uncommon approach to drug dosing for nephrologists as many drugs for CKD and dialysis, including ESAs, involve active dose titration.

Hemoglobin and Reticulocytes: AKB-6548 increased hemoglobin levels vs. baseline (the primary endpoint) in a dose-dependent fashion (Ex. 12) and with a steady pattern over the 6 weeks of the study (Ex. 13). These results were statistically significant. The absolute changes in hemoglobin (~1 g/dL at 500mg) are clinically relevant, per our diligence, and avoided over-aggressive hemoglobin rises that may be more characteristic of a non-physiologic (and potentially

unsafe) change. In addition, no patient had a hemoglobin level above 13 g/dL, which is seen to be a "red flag" event. We expect that the slow, steady hemoglobin rise without overshooting, if replicated in future studies, is likely to meet the FDA's currently conservative stance on anemia drugs.

AKB-6548 increased reticulocytes initially, but reticulocytes did not remain significantly elevated (Ex. 13). The rationale may be due to a change in red blood cell life span with better iron utilization resulting in a new status quo that does not require a constant increase in RBC production rates. The company expects only small changes above baseline with longer dosing.

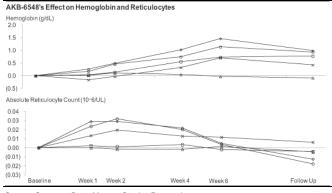
Exhibit 12
AKB-6548's Effect on Hemoglobin Levels (Primary Endpoint) in Ph 2a



Source: Company Data, Morgan Stanley Research

Exhibit 13

## AKB-6548's Effect on Hemoglobin and Reticulocytes in Ph 2a



Source: Company Data, Morgan Stanley Research

**Erythropoietin (EPO):** AKB-6548 slightly decreased EPO levels vs. baseline. This suggests to us that the drug is not overly stimulating EPO, as may be seen with ESAs. Ph 1 dosing with shorter time measurement intervals did show temporary rises in EPO with dosing of AKB-6548. This short

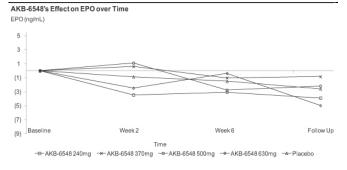
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rise pattern, without a maintained increase, may reflect a pattern that more closely mimics the body's normal variation. Regardless, the hgb rises were solid and the observed EPO changes were small, removing this as a safety concern as of now.

Exhibit 14

#### AKB-6548's Effect on EPO in Ph 2a

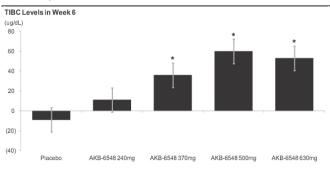


Source: Company Data, Morgan Stanley Research

Iron and Hepcidin: AKB-6548 significantly increased total iron binding capacity (TIBC) with a similar degree increase at the two top doses. Note that patients received small, 50mg oral doses of iron during the study. Hepcidin decreased over time and was statistically significant at week 6 for AKB-6548 500mg vs placebo. Hepcidin normally acts to control the amount of iron absorbed from the GI tract. A decrease in hepcidin allows the body to more efficiently take up more iron to feed the higher hgb levels, as iron is an integral part of hgb.

#### Exhibit 15

## AKB-6548's Effect on Total Iron Binding Capacity in Ph 2a



Source: Company Data, Morgan Stanley Research\

### 3) Safety Looks OK

AKB-6548 has a mostly clean safety profile. There were a few serious adverse events in the 6 week Ph 2a, as CKD patients tend to be on the more sick side with multiple

comorbidities. However, none of these were attributed to AKB-6548, and there did not seem to be any pattern within the events to suggest a potentially underappreciated correlation.

The main safety/tolerability issues that emerged were gastrointestinal (GI) in nature. GI events such as diarrhea, nausea, and constipation were the most common drug related events in Ph 1 and Ph 2. We view this as more of a tolerability issue, as no one discontinued dosing due to GI side effects and most were mild/moderate. The company believes that the GI events may partly be related to the capsule formulation, and think that the tablet formulation being used in the Ph 2b trial may result in fewer GI events.

Given our understanding of the HIF mechanism and safety data from other HIF drugs, some focus points for us going forward include changes in liver function, blood pressure, cholesterol, platelets, and VEGF. VEGF and platelets did not appear to change from baseline in AKB-6548's 93 patient 6 week Ph 2a trial. A 4 week, 10 patient Ph 2a study showed slight decreases in blood pressure and no effect on renal function. We will be closely monitoring these with longer term dosing to see if any other safety events emerge. Two healthy volunteers in one of the Ph 1 studies had temporarily elevated LFTs (<2xULN), but we do not see this as much of a signal for concern.

Given that Akebia likely intends to study AKB-6548 in other anemia populations such as IAA (idiopathic age related anemia) and anemia secondary to congestive heart failure (CHF), we see maintaining the currently good safety as key. These various populations (Ex. 19) are large and the patients are likely to have different comorbidities and urgencies to correct their anemia.

#### 4) Next Steps are Key

Akebia is currently conducting a  $\sim$ 200 patient Ph 2b trial of AKB-6548 with data expected 4Q14. Ph 3 plans in CKD patients are likely to be decided post Ph 2b data. There are several other studies Akebia may run as well, with the next up being a Ph 2 and 3 dialysis patient program. First we will discuss CKD, and then dialysis.

Ph 2b CKD Trial: The 4Q14 data read-out for this trial is the company's next key catalyst. This trial enrolled ~200 CKD patients and will analyze hemoglobin levels, among other endpoints, out to 20 weeks of dosing (Ex. 16). The primary endpoint is the percentage of patients who either 1) achieve or maintain a mean hgb of 11 g/dL or 2) increase their hgb by 1.2 g/dL over their pre-dose hgb. The pre-dose hgb in this

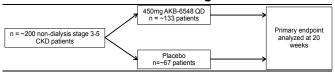
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trial is the average of the hgb levels at screening and at baseline. Patients who need to receive rescue ESAs or rescue transfusion are considered failures.

Exhibit 16

#### AKB-6548 Ph 2b CKD Trial Design



Source: Company Data, Morgan Stanley Research

Patients will be stratified into three groups at baseline including patients who are either a) naïve to ESAs, b) previously treated with ESAs and off ESAs for 11 weeks, or c) actively being treated with ESAs with the ESA discontinued prior to randomization but with no prolonged washout period. We see this as an important aspect of the trial, as it tests the drug's efficacy in a "real world" patient mix.

While the Ph 2a data was positive and we expect a positive Ph 2b result as well, there are a few trial design changes worth reviewing. The Ph 2b study is testing AKB-6548 at 450mg, a dose that was not used in the Ph 2a trial but is close to the 500mg dose (second highest dose in that trial). Given the Ph 2a dose response and longer dosing in this Ph 2b, we see a high likelihood of good efficacy in Ph 2b with the potential to possibly require less dose titration. Another change for the Ph 2b trial is that the dose titration protocol uses an algorithm based on both absolute and relative hgb levels in the Ph 2b vs. a simpler protocol in Ph 2a. We do not expect this to be a major hurdle for physicians, and could potentially help control any tendency to overshoot.

**Ph 3 CKD Program:** The design of the Ph 3 program and the specific regulatory requirements the trials will need to meet are key focus points and sources of identified risk on the Street. The AKB-6548 CKD Ph 3 program design will be determined after an end of Ph 2 meeting with the FDA and EMEA.

For context, we will briefly review the source of the regulatory scrutiny for anemia related drugs. When ESAs were used pre-2007, the approach was to try and push hgb levels into the normal range (13-15 g/dL). While some patients were able to get to those levels easily, some patients required significant, escalating doses of ESAs. A series of trials were run evaluating the merits of the goal of normal hgb restoration, which produced concerning, paradoxic results (Ex. 17).

Exhibit 17

#### **ESA Trials Revealed Safety Concerns**

Trial	Drug	Arm A Target (g/dL)	Arm B Target (g/dL)	Brief Comments
CREATE	Epoetin Beta	13-15	10.5-11.5	No overall CV event difference; Shorter time to dialysis in Arm A (higher target)
CHOIR	Epoetin Alfa	13.5	11.3	Overall CV event rate higher in Arm A (higher target)
TREAT	Darbepoetin Alfa	13	9	No overall CV event difference; higher stroke rate in Arm A (higher target)

Source: Company Data, Morgan Stanley Research

As a result of the above outcomes, the FDA revised the labeling of ESAs to steer physicians to use lower doses of ESAs and target lower hgb levels. This, and price competition in the dialysis setting as a result of bundled reimbursement, has led to the WW ESA market shrinking by 50% over the past 5+ years.

One interesting development over time has been a view held by some physicians that the problem with ESAs was not the restoration of normal hgb levels but the supraphysiologic doses that were required to approach normal hgb levels in hypo-responding patients. While we intuitively don't see a great rationale for assuming mild anemia (the current target) is better than a normal hgb, we do not expect this view to change without a significant body of evidence. We do believe, though, that an approach such as HIF stabilization, which approaches anemia correction from a different angle than ESAs, could over time potentially build that evidence.

Regardless, targeting hemoglobin levels above ~11 g/dL remains a sensitive subject for the FDA. So far, Akebia has fit within the FDA's risk averse stance by 1) implementing dose titration protocols in the Ph 2 trials that avoids hgb overshooting, 2) using doses of AKB-6548 that result in slow, steady rises in hemoglobin, and 3) targeting hemoglobin levels of ~11 g/dL for their Ph 2b trial and likely for their Ph 3 program. We believe this approach, if adhered to, should facilitate a reasonable Ph 3 program. The EMEA may be less restrictive on hemoglobin levels than the FDA, but we expect the Ph 3 program will target the most restrictive authority so it can be one global program.

Exhibit 18

#### Potential Ph 3 CKD Anemia Program for AKB-6548

Trial	Size	AKB-6548 Dose	Control Arm	Duration	Comments
1	>500 pts	450 mg with titration	Placebo/ESA rescue	52 wks + any extension	The control arm is the current US standard of care
2	>500 pts	450 mg with titration	Placebo/ESA rescue	52 wks + any extension	The control arm is the current US standard of care
3	<500 pts	450 mg with titration	Active/planned ESA dosing	52 wks + any extension	Primarily for EMEA
Pooled CV Analysis	All pts (likely >2000 pts)	450 mg with titration	Above	52 wks + any extension	The initial hurdle likely a HR of 1.5

Source: Company Data, Morgan Stanley Research

We expect that Akebia will initiate three trials in 2015 (Ex. 18) with ~2k patients total to facilitate FDA/EMEA approval.

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The aggregate of the data likely needs to show at least non-inferiority vs. the standard of care. Two primary trials enrolling >500 patients each are likely to be placebo controlled with ESA rescue (i.e. the standard of care in the US). Patients are likely to be followed for 1 year of dosing with a focus on a safe rise in hemoglobin levels, likely similar to Ph 2b trial. One comparability study, which will primarily facilitate EU approval, in 250-500 patients is likely to enroll primarily in Europe and will need to show at least comparability to ESAs on efficacy, with a chance of showing better safety.

In terms of an integrated cardiovascular analysis (another FDA requirement), management expects that AKB-6548 approval will require a non-inferiority margin to start of ~1.5. The required non-inferiority limit may decrease over time (towards the 1.3 required of AFFY's Omontys (recently approved but not currently marketed) as Akebia adds new indications, such as dialysis patients, to the label.

**Ph 2 Dialysis Trial:** Akebia intends to initiate a Ph 2 trial in 60 dialysis patients in 1H14. The primary endpoint will be the change in hemoglobin for AKB-6548 - first at week 8 and then following dosing adjustments starting at week 8. Akebia is testing two different doses of AKB-6548 for this study, 450mg and 300mg, as there has been little dose ranging work for this population but we expect a longer T1/2 in dialysis patients. Given that other HIF drugs have shown activity in the dialysis population, we expect success in this trial. A Ph 3 program would likely quickly follow the completion of this Ph 2, pending success.

**Other Indications:** There are no disclosed plans as to when a trial in other indications such as Idiopathic Age-Related Anemia or Anemia Secondary to Congestive Heart Failure may start. Akebia may use a fixed, low dose of drug, and we expect that the company would need to run additional dosing work to determine a safe and effective dose. See p. 12-13 for more detail about these other large anemia opportunities.

#### 5) Commercial Opportunity is Large

The CKD and dialysis anemia markets are large, multi-billion dollar opportunities. We currently model most of AKB-6548's value from the larger CKD portion.

#### Below, we focus on:

- a) anemia,
- b) standard of care for anemia in dialysis and CKD patients,
- c) the ESA commercial landscape,
- d) AKB-6548's role in CKD and dialysis,
- e) other potential anemia markets,

- f) HIF competitors, and
- g) the IP landscape.

#### a) Anemia

Anemia occurs when the body does not receive enough oxygen because the blood has insufficient red blood cell and hemoglobin mass to carry it. The World Health Organization defines anemia as hemoglobin levels of <13 g/dL in men and <12 g/dL in women.

Erythropoeisis is the process of red blood cell formation, which occurs primarily in the bone marrow of large bones. In this process, immature red blood cells, known as reticulocytes, are released from the bone marrow into the circulatory system, where they soon become mature red blood cells, known as erythrocytes. Erythrocytes contain hemoglobin (hgb) which is the actual oxygen carrier within the cell. Erythropoiesis is stimulated by erythropoietin (EPO), which in turn can be stimulated by low oxygen levels.

Iron balance is another important aspect of anemia. Iron is essential to forming hemoglobin, and is a key part of the oxygen transfer from the lungs to hemoglobin and from hemoglobin to cells. Iron homeostasis is controlled by the hormone hepcidin, which regulates the uptake of iron from the GI tract.

Anemia has many causes, including chronic kidney disease (discussed below), iron deficiency (iron is a component of hemoglobin), nutritional deficiency (patient does not consume enough iron), bone marrow disease (red blood cells are produced in the bone marrow), abnormal erythropoietin production, age, etc. Untreated, anemia may lead to fatigue, disease progression, cardiopulmonary complications, and even death.

Anemia and Kidney Disease: Anemia is a common issue for kidney disease patients, and becomes worse as kidney disease progresses. There are three main drivers: 1) EPO production decline. EPO is produced by a type of cell in the kidney, peritubular fibroblast, which are fewer in number with progressive kidney damage. 2) Patients with CKD have faster red blood cell destruction (~70 days) vs. healthy people (~90-120 days). 3) There is reduced iron availability as hepcidin (the hormone that controls iron homeostasis) is regulated by both EPO levels and iron concentrations.

b) Standard of Care in Dialysis and CKD Market Current treatments for anemic patients with CKD or on dialysis may include oral or IV iron supplementation,

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erythropoiesis stimulating agents (ESAs), and red blood cell transfusions.

Standard of care front-line treatment for anemia in CKD and dialysis is iron, which is taken either orally or intravenously. As some patients absorb oral iron poorly, intravenous iron is an option. Iron supplementation is often required with ESA therapy as well.

However, oral (and IV) iron is often insufficient to treat severe anemia on its own, and other therapies are required. Erythropoiesis stimulating agents (ESAs) such as Epogen and Aranesp (sold by Amgen, covered by Matthew Harrison) are intravenous or subcutaneous drugs commonly used to manage anemia in these patients. These agents are the next line of therapy after iron supplementation. ESAs work by binding to EPO receptors on red blood cell precursors to stimulate these cells to become mature red blood cells.

ESAs work well in increasing hemoglobin levels, but optimal dosing and target hemoglobin levels are controversial given safety concerns. ESAs labels include black box warnings for serious cardiovascular events, stroke, increased mortality thromboembolic events, and increased risk of tumor progression or recurrence.

Despite iron supplementation and ESA use, red blood cell transfusions are sometimes necessary as well. Ideally, physicians would like to avoid using transfusions to minimize any potential for antibody sensitization for future kidney transplants, infections, adverse reactions, cost, etc. As a result, RBC transfusions are typically utilized only when patients are at very low hemoglobin levels.

#### c) Commercial ESA Market:

Safety concerns and reimbursement pressures in the dialysis markets have led to physicians using ESAs in fewer patients and using lower volumes of ESAs. At peak, in 2006, ESAs sold ~\$12bn WW. Sales have declined to \$6.3bn WW in 2012 (\$3.4bn in the US) due to concerns around safety and subsequent reimbursement pressures.

Biosimilar ESAs are currently available in the EU, but use varies significantly by country from <10% to 60+%. In the US, we expect that the launch of biosimilars will result in broad pricing declines.

Two notable biosimilar programs in development in the US are Hospira (covered by David Lewis) and Sandoz/Novartis (covered by Amy Walker). Hospira's drug is currently in Ph 3, and the company expects to submit an application in the late

2014/early 2015 timeframe. Sandoz/Novartis's drug is currently in Ph 3 with trials likely to complete in 2014 per clinicaltrials.gov. In addition, Roche (covered by Vincent Meunier) is planning to launch Mircera, a long acting ESA, in the US in mid-14.

#### d) Where AKB-6548 Fits In

We see a need for a therapy that can chronically increase hemoglobin levels (i.e. fit into a similar treatment role as ESAs) in anemic patients, but is safer and more convenient than ESAs. In our opinion, AKB-6548 can fit this role.

The CKD market is not subject to pricing pressures from the dialysis bundle. In the dialysis market, facilities have one payment for all the routine costs of dialysis treatment instead of paying separately for each item included in dialysis treatment. Though oral drugs were expected to be brought into the dialysis bundled payment system in 2016, this has now likely been delayed until 2024. We view this as a potential advantage for AKB-6548 as an effective anemia drug outside the bundled payment system may be cheaper/more profitable for dialysis facilities. However, it remains to be seen if facilities will be willing to change their standard practices, as long term contracts have tended to make this smaller market segment (vs. CKD) tough to penetrate.

Additionally, CKD patients often do not have the ready IV access or planned dialysis visits, which help make ESAs more convenient in the dialysis market. As a patient is transitioning from CKD to dialysis, there is often an effort to conserve venous access to allow easier dialysis fistula placement. The ability to avoid regular IV insertions could be an additional benefit of an effective oral option.

#### e) Other Potential Markets

Akebia may over time target other anemia markets, such as IAA (idiopathic age related anemia) and anemia secondary to congestive heart failure (CHF), which represent upside to our model. Anemia secondary to CHF may be caused by use of ACE inhibitors and angiotensin receptor blockers (angiotensin stimulates EPO), hemodilution (fewer cells in blood due to increased fluid retention), etc. Iron deficiency anemia, which may be due to cancer, GI disorders, abnormal uterine and post-partum bleeding, is another big potential market that is currently mostly treated with oral iron.

The markets highlighted above are large, with 1+mn anemic patients each (Ex. 19), and are currently not routinely addressed by ESAs due to safety concerns and sub-optimal convenience. As these markets are very large, we see a

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clean safety profile as a gating factor to penetrate these additional markets.

Exhibit 19

#### **Sizes of Various Anemia Markets**

Anemia Market Segment	Number of Patients With Anemia
Chronic Kidney Disease Stage 3-5	~2.1+mn, growing to ~2.7+mn in 2025
End Stage Renal Disease	~350+k, growing to ~500+k in 2025
Idiopathic Age Related Anemia	~1.5mn
Congestive Heart Failure	~1mn
Iron Deficiency Anemia	~3.3mn women

Source: Company Data, Morgan Stanley Research

#### f) Competition

There are a number of HIF drugs in development. We model at least two other similarly profiled HIF drugs coming to market, with AKB-6548 taking their pro-rata ~1/3<sup>rd</sup> share of the HIF market at peak. However, we note that many of the competitor drugs are early with several outstanding questions. Fibrogen's drug is the most advanced competitor.

Roxadustat / FG-4592 (Fibrogen, AstraZeneca, and Astellas): Fibrogen developed this drug and has licensed it to AstraZeneca (covered by Amy Walker) in the US and Astellas (covered by Shinichiro Muraoka) in the EU for Ph 3 development and commercialization. In the EU, Ph 3 has been initiated. In the US, AstraZeneca stated that Ph 3 is to begin in 2014 with an NDA filing in 2018.

In general, FG-4592 appears to be a more potent drug than AKB-6548. In a Ph 2 CKD trial with weight adjusted and fixed doses of TIW or BIW FG-4592, hemoglobin was raised ~2 g/dL by 8 weeks in some dosing cohorts, which is higher than AKB-6548's hemoglobin increases. ~8% of subjects had hemoglobin >14 g/dL during the study, which we view as a "red flag" event for the risk-averse FDA. No patients in the Ph 2a AKB-6548 trial had hemoglobin > 13 g/dL. Thus, while the rises tend to be quicker, it is not clear that this is advantageous. Furthermore, the seemingly long half life, that would allow <QD dosing, could impact the ability to titrate the drug as needed.

At this point, it appears that AstraZeneca and Astellas are trying to determine an appropriate dosing scheme. Trials listed on clinicaltrials.gov include dosing TIW, BIW, or QW during a maintenance period. Exploring various dosing regimens may be motivated by FG-4592's rapid and large increase in hemoglobin in past trials, which the FDA may not be entirely comfortable with. As AKB-6548 has a smaller and more gradual impact on hemoglobin and QD dosing, we see a potential competitive advantage for Akebia if AZN cannot determine a more flexible, cautious dosing regimen.

However, our base case now is that both drugs look similar when on the market.

FG-4592 showed decreased cholesterol and platelet levels, though platelets remained within the normal range. We look forward to seeing if these effects are present with an optimized dosing regimen.

**GSK-1278863 (GSK):** This drug is in Ph 2 in dialysis and CKD, with a primary completion in 2015 per clinicaltrials.gov. A 4 week Ph 2a trial showed ~1 g/dL increase in hemoglobin at the highest dose (5mg) over 4 weeks, while lower doses (0.5mg and 2mg) showed a small, dose dependent treatment effect. VEGF levels did not change, apparently.

Molidustat / BAY85-3934 (Bayer): Ph 2 in dialysis and CKD is likely to complete in 2015, with Ph 3 to begin potentially in 2015 as well. Bayer recently outlined their DIALOGUE Ph 2 program at ASN, which consists of three large, randomized trials and 2 safety extension trials vs. placebo and darbepoetin alpha and epoetin alpha. Ph 1 single dose data showed a dose dependent response for EPO levels.

**JTZ-951 (Japan Tobacco):** Little is available on this drug, which is currently in Ph 2 in Japan and Ph 1 overseas.

#### g) Intellectual Property

Our diligence supports that Akebia will have freedom to operate in the US and in the EU, though this is an outstanding issue for the company and a key risk. Most of the debate has been centered in the EU, not the US. In the US, AKB-6548 has issued patents and pending applications that cover AKB-6548 composition of matter (2027 expiry), method of treating anemia, and pharmaceutical compositions.

In the EU, composition of matter has been granted (2027 expiry) for AKB-6548, and there are other pending applications. A third party initiated a patent opposition against Akebia's patent '005, and the EU Patent Office maintained claims directed to 8 compounds including AKB-6548 and claims to compositions and methods for treating various diseases including anemia. While both parties have appealed, the final opposition proceeding timeline is lengthy, and we are comfortable in how the patent currently stands.

Akebia also filed an opposition vs. Fibrogen's '823 patent in 2013 requesting that the patent be revoked in entirety. This case, which may be important for freedom to operate, may also take years to resolve. Our work

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suggests Akebia has a solid position that gives us comfort in them ultimately achieving freedom to operate.

#### h) We see ~\$2.2bn WW market potential for AKB-6548.

We model peak (2025) WW AKB-6548sales of ~\$2.2bn with ~\$1.5bn to Akebia. Our assumptions include:

- 1) AKB-6548 launches in 2018 in the US,
- 2) Peak US penetration of all HIF drugs into CKD population

- is <50%.
- 3) Peak US penetration of all HIF drugs into ESRD population is <15%,
- 4) Peak US AKB-6548 share of CKD and ESRD patients on HIF drugs is 33%, and  $\,$
- 5) Akebia partners the ex-US market with a 22-25% royalty rate.

Exhibit 20

#### **Market Model for AKB-6548**

US AKB-6548	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
JS Population		320,209,390	323,411,484					339,908,720	343,307,807	346,740,885			357,247,481
YoY Growth	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
JS Population >18	240.949.640	243,359,136	245.792.728	248.250.655	250.733.162	253.240.493	255.772.898	258.330.627	260.913.933	263.523.073	266.158.303	268.819.886	271.508.085
% >18	76%	76%	76%	76%	76%	76%	76%	76%	76%	76%	76%	76%	76%
CKD MARKET													
CKD Stages 3-5	15,331,626	15,639,791	15,954,151	16,274,830	16,601,954	16,935,653	17,276,059	17,623,308	17,977,537	18,338,885	18,707,497	19,083,518	19,467,096
% of Pop'n >18	6.4%	6.4%	6.5%	6.6%	6.6%	6.7%	6.8%	6.8%	6.9%	7.0%	7.0%	7.1%	7.2%
Addressable CKD Patients	2,146,428	2,189,571	2,233,581	2,278,476	2,324,274	2,370,991	2,418,648	2,467,263	2,516,855	2,567,444	2,619,050	2,671,692	2,725,393
% Anemic	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%
HEMODIALYSIS MARKET													
HD Patients	456,477	470,171	484,276	498,804	513,768	529,182	545,057	561,409	578,251	595,598	613,466	631,870	650,827
YoY Growth	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
Addressable Dialysis Patients	365,181	376,137	387,421	399,043	411,015	423,345	436,046	449,127	462,601	476,479	490,773	505,496	520,661
% with Hg <11 g/dL	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
HIF PATIENTS													
HIF Penetration - CKD Pts						118,550	302,331	493,453	629,214	770,233	916,667	1,068,677	1,226,427
HIF Penetration - % of Addressable CKD Pts						5%	13%	20%	25%	30%	35%	40%	45%
HIF Penetration - HD Pts						5,292	13,626	22.456	28.913	42,883	51,531	60,660	70,289
HIF Penetration - % of Addressable HD Pts						1%	3%	5%	6%	9%	11%	12%	14%
AKB-6548 PATIENTS													
CKD Patients on AKB-6548						59,275	151,166	222,054	220,225	254,177	302,500	352,663	404,721
% of HIF Use in CKD						50%	50%	45%	35%	33%	33%	33%	33%
% of Addressable CKD Stages 3-5						3%	6%	9%	9%	10%	12%	13%	15%
ESRD Patients on AKB-6548						2,646	6,813	10,105	10,119	14,151	17,005	20,018	23,195
% of HIF Use in Hemodialysis						50%	50%	45%	35%	33%	33%	33%	33%
% of Addressable Dialysis Patients						1%	2%	2%	2%	3%	3%	4%	4%
DURATION AND PRICE													
Duration (months)						3	4	5	6	7	7.5	8	8
Gross Price/Month						\$425	\$434	\$442	\$451	\$460	\$469	\$479	\$488
Price Increase							2%	2%	2%	2%	2%	2%	2%
Gross to Net Discount						15%	20%	21%	22%	23%	24%	25%	25%
Net Price/Month						\$361	\$347	\$349	\$352	\$354	\$357	\$359	\$366
REVENUE													
CKD Revenue						\$64	\$210	\$388	\$465	\$630	\$809	\$1,013	\$1,185
Dialysis Revenue						\$3	\$9	\$18	\$21	\$35	\$45	\$57	\$68
AKB-6548 US Sales						\$67	\$219	\$405	\$486	\$665	\$855	\$1,070	\$1,253
AKB-6548 ex-US Sales							\$13	\$77	\$223	\$365	\$566	\$769	\$963
% of US Revenue							20%	35%	55%	75%	85%	90%	90%
AKB-6548 ex-US Revenue to Akebia							\$3	\$17	\$49	\$83	\$132	\$185	\$235
Royalty							22.0%	22.0%	22.0%	22.6%	23.3%	24.0%	24.4%
AKB-6548 WW Sales						\$67	\$233	\$482	\$709	\$1,030	\$1,420	\$1,839	\$2,217

Source: Company Data, Morgan Stanley Research

Morgan Stanley Bank AG ("Morgan Stanley") is acting as financial advisor to Bayer AG ("Bayer") in relation to the proposed acquisition of Dihon Pharmaceutical Group Co., Ltd. as announced on 27 February 2014. Bayer has agreed to pay fees to Morgan Stanley for its financial services. Please refer to the notes at the end of the report.

#### MORGAN STANLEY RESEARCH

April 14, 2014 Akebia Therapeutics Inc

(\$ in millions except per-share data)	2011A	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Sales															
US Sales								67	219	405	486	665	855	1.070	1,253
EU Sales								0	13	77	223	365	566	769	963
WW Sales								67	233	482	709	1,030	1,420	1,839	2,217
Revenue to Akebia															
US Sales								67	219	405	486	665	855	1,070	1,253
EU Royalty								0	3	17	49	83	132	185	235
WW Revenue to Akebia								67	222	422	535	748	987	1,255	1,489
Other		0	0	0	0	0	200	0	0	0	0	0	0	0	0
Total Revenues	0.0	0.0	0.0	0.0	0.0	0.0	200.0	67.1	222.1	422.4	535.3	747.9	986.6	1,255.2	1,488.9
YoY Revenue Growth							-	-66%	231%	90%	27%	40%	32%	27%	19%
COGS			0	0	0	0	0	0	11	41	49	67	77	96	113
YoY Growth			-	-	-	-	-		-	270.1%	19.9%	36.8%	15.6%	25.2%	17.1%
% of US Revenue									5%	10%	10%	10%	9%	9%	9%
R&D	13	6	11	27	55	55	60	35	35	35	35	35	35	35	35
YoY Growth		-56.4%	91.3%	153.0%	103.7%	0.0%	9.1%	-41.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
% of Revenue					-	-	30.0%	52.2%	15.8%	8.3%	6.5%	4.7%	3.5%	2.8%	2.4%
SG&A	2	3	4	15	18	23	46	95	103	111	118	120	122	124	127
YoY Growth		15.9%	31.1%	292.0%	25.0%	25.0%	102.8%	106.6%	8.3%	7.7%	6.4%	1.8%	1.8%	1.9%	1.9%
% of Revenue					-	-	23.0%	141.4%	46.3%	26.2%	22.0%	16.0%	12.4%	9.9%	8.5%
Total Operating Expenses	15.2	8.4	14.4	41.5	73.1	77.7	105.9	129.9	148.7	186.3	201.4	221.5	234.1	255.7	274.6
Operating Income (Loss)	(15.2)	(8.4)	(14)	(42)	(73)	(78)	94	(63)	73	236	334	526	753	999	1,214
Operating Margin Other Income and Interest Income	0.2	2.0	3.5	0.8	1.2	1.0	<i>47.0%</i> 1.1	(93.6%)	33.0% 1.4	55.9% 2.7	62.4% 4.9	70.4% 7.7	76.3% 11.9	79.6% 17.7	81.6% 25.0
Interest Expense	0.2	(1.6)	(0.7)	0.0	0.00	0.00	0.00	1.3 0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pretax Income (Loss)	(\$15)	(\$8)	(\$12)	(\$41)	(\$72)	(\$77)	\$95	(\$62)	\$75	\$239	\$339	\$534	\$764	\$1.017	\$1,239
Provision For Income Taxes	0	0	0	0	0	0	0	0	0	37	119	187	268	356	434
Effective Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	15.6%	35.0%	35.0%	35.0%	35.0%	35.0%
Non-GAAP Net Income (Loss)	(\$15)	(\$8)	(\$12)	(\$41)	(\$72)	(\$77)	\$95	(\$62)	\$75	\$202	\$220	\$347	\$497	\$661	\$806
Stock Compensation Expense	\$0	\$0	\$2	\$3	\$5	\$7	\$9	\$11	\$13	\$15	\$17	\$19	\$21	\$23	\$25
% of Operating Expenses	2.0%	1.5%	10.9%	7.2%	6.8%	9.0%	8.5%	8.5%	8.7%	8.1%	8.4%	8.6%	9.0%	9.0%	9.1%
Non-GAAP Net Income (incl. ESO)	(\$15)	(\$8)	(\$13)	(\$44)	(\$77)	(\$84)	\$86	(\$73)	\$62	\$187	\$203	\$328	\$476	\$638	\$781
GAAP Net Income (Loss)	(\$18)	(\$12)	(\$69)	(\$43.7)	(\$77)	(\$84)	\$86	(\$73)	\$62	\$187	\$203	\$328	\$476	\$638	\$781
EPS, Basic (Non-GAAP, Pre-ESO)	(\$89.74)	(\$19.50)	(\$21.33)	(\$2.19)	(\$3.11)	(\$2.92)	\$3.55	(\$2.25)	\$2.68	\$7.08	\$7.60	\$11.79	\$16.64	\$21.85	\$26.31
EPS, Diluted (Non-GAAP, Pre-ESO)	(\$89.74)	(\$19.50)	(\$21.33)	(\$2.19)	(\$3.11)	(\$2.92)	\$3.29	(\$2.25)	\$2.50	\$6.65	\$7.17	\$11.18	\$15.84	\$20.91	\$25.29
EPS - Diluted (GAAP, Post- ESO)	(\$109.36)	(\$27.82)	(\$126.94)	(\$2.36)	(\$3.33)	(\$3.19)	\$2.98	(\$2.65)	\$2.07	\$6.15	\$6.61	\$10.56	\$15.17	\$20.18	\$24.51
Shares Outstanding - Basic Shares Outstanding - Diluted	0.17	0.41	0.54 0.54	18.55	23.13 23.13	26.23 26.23	26.81 28.92	27.39 27.39	27.94 29.90	28.47 30.33	28.97 30.72	29.44 31.06	29.87 31.36	30.26 31.63	30.62 31.85
	0.17	0.41		18.55											

Source: Company Data, Morgan Stanley Research

#### MORGAN STANLEY RESEARCH

April 14, 2014 Akebia Therapeutics Inc

Exhibit 22

#### **Balance Sheet**

(\$ in millions)	2011A	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Assets															
Cash and Cash Equivalents	5.0	1.6	21.2	92.7	125.7	53.2	138.7	94.2	164.3	362.8	587.6	935.8	1,430.3	2,088.8	2,894.6
Investments	1.4		11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3
Accounts Receivables	0.1	0.1	0.1	-	-	-	-	-	-	-	-	-	-	-	-
Prepaid Expenses and Other Current Assets	0.8	0.5	0.7	1.7	2.9	3.1	4.2	5.2	5.9	7.5	8.1	8.9	9.4	10.2	11.0
Inventory	-				-	-	16.0	5.4	16.7	29.6	34.8	44.9	59.2	75.3	89.3
Total current assets	7.2	2.2	33.4	105.7	140.0	67.6	170.3	116.1	198.3	411.2	641.7	1,000.9	1,510.2	2,185.7	3,006.2
Property and Equipment, Net	-		0.0	0.3	0.7	0.8	1.0	1.2	1.5	1.8	2.0	2.2	2.3	2.4	2.6
Deferred offering costs	-		1.1	-	-	-		-		-	-	-	-		-
Other assets	-		0.1	0.4	0.6	0.7	0.9	1.1	1.3	1.6	1.8	1.9	2.0	2.2	2.4
Total assets	7.2	2.2	34.7	106.4	141.3	69.1	172.2	118.5	201.0	414.6	645.5	1,005.0	1,514.5	2,190.3	3,011.2
Liabilities															
Accounts Payable	1.4	0.4	0.7	2.1	3.6	3.9	5.3	6.5	7.4	9.3	10.0	11.0	11.6	12.7	13.6
Accrued Expenses	0.4	0.4	3.2	4.2	6.6	6.2	7.4	7.8	7.4	9.3	10.1	11.1	11.7	12.8	13.7
Current portion of capital lease obligation	_		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2012 Series X preferred stock subject to mandatory															
redemption	-	4.2	-	-	-	-	-	-	-	-	-	-	-	-	-
Total current liabilities	1.8	4.9	3.9	6.2	10.2	10.1	12.7	14.3	14.8	18.6	20.1	22.1	23.3	25.5	27.4
Capital lease obligation, net of current portion	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Liabilities	1.8	4.9	3.9	6.2	10.2	10.1	12.7	14.3	14.8	18.6	20.1	22.1	23.3	25.5	27.4
Shareholder's Equity															
Redeemable Convertible Preferred Stock	53.6	56.9	157.8	157.8	157.8	157.8	157.8	157.8	157.8	157.8	157.8	157.8	157.8	157.8	157.8
Common Stock (Plus APIC)	0.0	0.0	0.0	113.1	220.9	232.5	246.9	264.1	284.3	307.5	333.7	363.0	395.4	430.9	469.3
Accumulated Other Comprehensive Income	_				_					_	_				
Accumulated Deficit	(48.2)	(59.6)	(127.1)	(170.8)	(247.7)	(331.3)	(245.2)	(317.7)	(255.9)	(69.3)	133.8	462.0	937.9	1,576.1	2,356.6
Total Shareholder's Equity	5.4	(2.7)	30.8	100.2	131.1	59.0	159.5	104.2	186.2	396.0	625.4	982.9	1,491.2	2,164.8	2,983.8
	•	•	•			•		•		•	•		•	•	
Total Liabilities and Shareholder's Equity	7.2	2.2	34.7	106.4	141.3	69.1	172.2	118.5	201.0	414.6	645.5	1,005.0	1,514.5	2,190.3	3,011.2

Source: Company Data, Morgan Stanley Research

Exhibit 23

#### **Cash Flow Statement**

(\$ in millions)	2011A	2012A	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
CASH FLOWS FROM OPERATING ACTIVITIES															
Net Income (Loss)	(15.3)	(8.2)	(13.2)	(43.7)	(76.9)	(83.6)	86.1	(72.5)	61.8	186.6	203.2	328.2	475.9	638.2	780.6
Gain on extinguishment of debt and other liabilities	0.0	0.0	(2.4)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Depreciation and Amortization	0.0	0.0	0.0	0.1	0.4	0.641	0.856	1.045	1.3	1.5	1.8	2.0	2.2	2.5	2.5
Loss on sale of investments	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Amortization of debt issue costs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Amortization of debt discount and interest expense	0.0	1.7	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Gain on cancellation of preferred stock future trancherights	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Issuance of 2007 Series X preferred stock forLicensing Agra	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Compensation recognized under stock option plan	0.3	0.1	1.6	3.0	5.0	7.0	9.0	11.0	13.0	15.0	17.0	19.0	21.0	23.0	25.0
Change in assets and liabilities:															
Accounts Receivables	(0.0)	(0.0)	(0.0)	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Prepaid Expenses and Other Current Assets	(0.6)	0.2	(0.2)	0.2	(1.3)	(0.2)	(1.1)	(1.0)	(0.8)	(1.5)	(0.6)	(0.8)	(0.5)	(0.9)	(0.8)
Other Assets	0.0	0.0	(0.1)	(0.2)	(0.3)	(0.0)	(0.2)	(0.2)	(0.2)	(0.3)	(0.1)	(0.2)	(0.1)	(0.2)	(0.2)
Accounts Payable and Other Accrued Expenses	1.5	(1.0)	2.3	2.3	4.0	(0.1)	2.6	1.6	0.6	3.7	1.5	2.0	1.3	2.2	1.9
Inventories	0.0	0.0	0.0	0.0	0.0	0.0	(16.0)	10.6	(11.3)	(12.9)	(5.2)	(10.1)	(14.3)	(16.1)	(14.0)
Net cash provided by (used in) operating activities	(14.1)	(7.2)	(11.3)	(38.2)	(69.1)	(76.4)	81.2	(49.4)	64.4	192.2	217.5	340.1	485.5	648.6	795.1
Proceeds from maturities of short-term investments  Proceeds from Sale of Short-Term Investments  Purchases of Short-Term Investments	1.7 0.1 (2.4)	1 0.0 0.0	2 0 (13)	0 0 0											
Net cash used in investing activities	(0.7)	1.4	(11.4)	(0.4)	(0.7)	(0.8)	(1.1)	(1.3)	(1.5)	(1.9)	(2.0)	(2.2)	(2.3)	(2.6)	(2.7)
	(0)		()	(0)	(0)	(0.0)	(,	(1.0)	(1.0)	(1.0)	(2.0)	(2.2)	(2.0)	(2.0)	(2)
CASH FLOWS FROM FINANCING ACTIVITIES															
Proceeds from Issuance of Preferred Stock	18.0	0	41	0	0	0	0	0	0	0	0	0	0	0	0
Preferred Stock Issuance Costs	0.0	0	(1)	0	0	0	0	0	0	0	0	0	0	0	0
Debt Issue Costs	0.0	(0)	0	0	0	0	0	0	0	0	0	0	0	0	0
Initial public offering issuance costs	0.0	0	(0)	0	0	0	0	0	0	0	0	0	0	0	0
Proceeds from Issuance of Common Stock	0.0	0.0	0.0	106.9	99.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from Options	0.0	0.0	0.0	3.2	3.8	4.6	5.4	6.2	7.2	8.2	9.2	10.3	11.4	12.4	13.4
Stock Issue Costs	(0.3)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Proceeds from issuance of 2012 Series X preferredstock	0.0	2.5	2.50	0	0	0	0	0	0	0	0	0	0	0	0
Net cash provided by financing activities	17.7	2.5	42.3	110.1	102.8	4.6	5.4	6.2	7.2	8.2	9.2	10.3	11.4	12.4	13.4
Change in Cook and Cook Equivalents	0.000	(0.070)	40.0	74.5	22.0	(70.0)	05.5	(44.5)	70.0	400.5	004.7	240.0	101.5	050.5	005 =
Change in Cash and Cash Equivalents	2.869	(3.370)	19.6	71.5	33.0	(72.6)	85.5	(44.5)	70.2	198.5	224.7	348.2	494.5	658.5	805.7
Cash and Cash Equivalents at Beginning of Year	2.1	5.011	1.6	21.2	92.7	125.7	53.2	138.7	94.2	164.3	362.8	587.6	935.8	1,430.3	2,088.8
Cash and Cash Equivalents at End of Year	5.0	1.6	21.2	92.7	125.7	53.2	138.7	94.2	164.3	362.8	587.6	935.8	1,430.3	2,088.8	2,894.6
Marketable Securities	1.37	0.0	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3

Source: Company Data, Morgan Stanley Research

#### **Company Description**

Akebia is a pharmaceutical company focused on the development of drugs targeting the HIF (hypoxia inducible factor) pathway. Their lead drug, AKB-6548, is in development for anemia secondary to CKD chronic kidney disease and dialysis.

**Biotechnology/United States of America** 

**Industry View: In-Line** 

**GICS Sector: Health Care** 

Strategist's Recommended Weight: 17.6%

S&P 500 Weight: 13.1%



Morgan Stanley ModelWare is a proprietary analytic framework that helps clients uncover value, adjusting for distortions and ambiguities created by local accounting regulations. For example, ModelWare EPS adjusts for one-time events, capitalizes operating leases (where their use is significant), and converts inventory from LIFO costing to a FIFO basis. ModelWare also emphasizes the separation of operating performance of a company from its financing for a more complete view of how a company generates earnings.

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The following analysts hereby certify that their views about the companies and their securities discussed in this report are accurately expressed and that they have not received and will not receive direct or indirect compensation in exchange for expressing specific recommendations or views in this report: David Friedman

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Biopharma Corp, Ultragenyx Pharmaceutical Inc.
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Biogen Idea Inc., Ceigene Corp, Chilmerx Inc., Cubist Pharmaceuticals Inc., Neurocrine Biosciences Inc., NPS Pharmaceuticals, Ophthotech Corp, Pharmaceuticals, Inc., Regeneron Pharmaceuticals Inc., Relypsa, Inc., Synageva Biopharma Corp, Tesaro Inc., Theravance Inc., Ultragenyx Pharmaceutical Inc, Vertex Pharmaceuticals, XenoPort Inc.

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#### MORGAN STANLEY RESEARCH

April 14, 2014 **Akebia Therapeutics Inc** 

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(as of March 31, 2014)

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	Coverage U	niverse	Investment Banking Clients (IBC					
_		% of		% of 9	% of Rating			
Stock Rating Category	Count	Total	Count	Total IBC	Category			
Overweight/Buy	1035	35%	354	38%	34%			
Equal-weight/Hold	1286	43%	446	48%	35%			
Not-Rated/Hold	99	3%	24	3%	24%			
Underweight/Sell	539	18%	105	11%	19%			
Total	2,959		929					

Data include common stock and ADRs currently assigned ratings. Investment Banking Clients are companies from whom Morgan Stanley received investment banking compensation in the last 12 months.

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Overweight (O). The stock's total return is expected to exceed the average total return of the analyst's industry (or industry team's) coverage

Overweight (O). The stock's total return is expected to exceed the average total return of the analyst's industry (or industry team's) coverage universe, on a risk-adjusted basis, over the next 12-18 months.

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Unless otherwise specified, the time frame for price targets included in Morgan Stanley Research is 12 to 18 months

#### **Analyst Industry Views**

Attractive (A): The analyst expects the performance of his or her industry coverage universe over the next 12-18 months to be attractive vs. the relevant broad market benchmark, as indicated below.

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April 14, 2014 Akebia Therapeutics Inc

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#### **Industry Coverage:Biotechnology**

Company (Ticker)	Rating (as of) Price	* (04/11/2014)
David Friedman, M.D.		
Akebia Therapeutics Inc (AKBA.O)	O (04/14/2014)	\$16.86
AMAG Pharmaceuticals, Inc.	E (11/21/2011)	\$17.28
(AMAG.O)		
Alexion Pharmaceuticals (ALXN.O)	O (09/07/2010)	\$139.61
Alnylam Pharmaceuticals (ALNY.O)	E (01/14/2014)	\$55.07
Auxilium Pharmaceuticals (AUXL.O)	U (03/06/2014)	\$24.32
Chimerix Inc (CMRX.O)	O (05/06/2013)	\$19.85
Cubist Pharmaceuticals Inc.	O (03/00/2013)	\$63.19
(CBST.O)	0 (11/13/2013)	Ψ05.13
Idenix Pharmaceuticals, Inc. (IDIX.O)	E (03/18/2011)	\$5.38
Incyte Corporation (INCY.O)	U (01/23/2013)	\$46.25
InterMune (ITMN.O)	E (09/07/2010)	\$28.16
Ironwood Pharmaceuticals, Inc.	E (04/24/2013)	\$9.85
(IRWD.O)	L (04/24/2013)	ψ9.00
Lexicon Pharmaceuticals, Inc.	U (06/11/2013)	\$1.59
(LXRX.O) NPS Pharmaceuticals (NPSP.O)	O (10/03/2012)	\$23.84
Neurocrine Biosciences Inc	E (01/08/2014)	\$23.0 <del>4</del> \$13.08
(NBIX.O)	L (01/00/2014)	ψ13.00
Ophthotech Corp (OPHT.O)	O- (10/21/2013)	\$31.06
Portola Pharmaceuticals Inc	O (06/17/2013)	\$20.78
(PTLA.O)	0 (00/11/2010)	<b>420</b>
Relypsa, Inc. (RLYP.O)	O (12/10/2013)	\$24.05
Synageva Biopharma Corp (GEVA.O)	O (04/20/2012)	\$78.7
Tesaro Inc. (TSRO.O)	E (02/04/2014)	\$24.39
Theravance Inc (THRX.O)	U (07/22/2013)	\$27.99
Ultragenyx Pharmaceutical Inc (RARE.O)	O (02/25/2014)	\$58.99
Vertex Pharmaceuticals (VRTX.O)	E (05/08/2012)	\$63.06
XenoPort Inc (XNPT.O)	U (06/11/2013)	\$4.26
Matthew Harrison	- (	•
Amgen Inc. (AMGN.O)	O (03/26/2014)	\$111.94
Biogen Idec Inc. (BIIB.O)	O (03/26/2014)	\$274
Celgene Corp (CELG.O)	E (03/26/2014)	\$136.9
Gilead Sciences Inc. (GILD.O)	E (03/26/2014)	\$66.03
Pharmacyclics Inc. (PCYC.O)	E (03/26/2014)	\$86.11
Regeneron Pharmaceuticals Inc. (REGN.O)	E (03/26/2014)	\$288.36

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<sup>\*</sup> Historical prices are not split adjusted.