

## Initiation of Coverage

### Akebia Therapeutics Inc

## Gaining Altitude in Anemia Correction: Initiate AKBA Shares at Buy

#### Initiating AKBA coverage with a Buy and \$28 Price Target

Akebia Therapeutics is a clinical-stage biotech company that we believe is well-positioned to produce a treatment for anemia that is potentially safer than current products, which have black box warnings for increased death and cardiovascular events but generated >\$6bn in sales in 2013. The company's wholly-owned once-daily oral HIF-PH inhibitor AKB-6548 is in Phase-2b for anemia of chronic kidney disease (CKD). Akebia's second candidate, AKB-6899, is in preclinical studies for oncology.

#### HIFs, if safer than ESAs, could become standard of care

Key tenets of our Buy thesis: [1] HIF activators could become the standard of care in the anemia market if they are approved without the same black box warnings as injectable erythropoiesis-stimulating agents (ESAs) and hence are perceived to be safer than ESAs. The safety of AKB-6548 is supported by clinical and pre-clinical data and the high-altitude literature, which shows no untoward effect of HIF activation. [2] We see blockbuster potential for '6548 if it is found to be safe and effective. It would be second to market but would be well-positioned among competitors due to attractive once-daily dosing and still be ahead of two additional competitors in a multi-billion dollar market. [3] Near term ph2b data (4Q14e) could drive a valuation step-up in AKBA shares. [4] Management has extensive knowledge and experience executing in the CKD segment.

#### Treating anemia without safety concerns could improve CKD clinical outcomes

All ESAs carry a black box warning on their drug label highlighting the safety risks of causing heart attacks and strokes. '6548 has been shown to be safe so far in its clinical studies, while reversing anemia by restoring a physiological diurnal EPO response. If HIF's can raise hemoglobin without increasing CV risks, then we see potential that clinical outcomes can be improved in CKD and lower direct costs to dialysis providers.

#### Valuation: \$28 Price Target by SOTP supported by DCF

We model annual sales of '6548 exceeding \$1bn in the US by 2023.

#### Equities

Americas  
Biotechnology

**12-month rating** **Buy**  
*Prior: Not Rated*
**12m price target** **US\$28.00**  
*Prior: -*
**Price** **US\$16.86**
**RIC:** AKBA.O **BBG:** AKBA US

#### Trading data and key metrics

<b>52-wk range</b>	US\$26.70-16.86
<b>Market cap.</b>	US\$0.31bn
<b>Shares o/s</b>	18.3m (COM)
<b>Free float</b>	32%
<b>Avg. daily volume ('000)</b>	267
<b>Avg. daily value (m)</b>	US\$6.2
<b>Common s/h equity (12/13E)</b>	US\$0.03bn
<b>P/BV (12/13E)</b>	5.6x
<b>Net debt / EBITDA (12/13E)</b>	1.4x

#### EPS (UBS, diluted) (US\$)

	12/13E			
	From	To	% ch	Cons.
<b>Q1</b>	-	-	-	-
<b>Q2</b>	-	-	-	-
<b>Q3</b>	-	-	-	-
<b>Q4E</b>	-	-	-	-
<b>12/13E</b>	-	(1.30)	-	-
<b>12/14E</b>	-	(1.02)	-	-
<b>12/15E</b>	-	0.84	-	-

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Highlights (US\$m)	-	-	-	12/13E	12/14E	12/15E	12/16E	12/17E
<b>Revenues</b>	-	-	-	0	0	84	82	87
<b>EBIT (UBS)</b>	-	-	-	(16)	(23)	18	(18)	(33)
<b>Net earnings (UBS)</b>	-	-	-	(13)	(20)	20	(15)	(30)
<b>EPS (UBS, diluted) (US\$)</b>	-	-	-	(1.30)	(1.02)	0.84	(0.61)	(1.25)
<b>DPS (US\$)</b>	-	-	-	0.00	0.00	0.00	0.00	0.00
<b>Net (debt) / cash</b>	-	-	-	21	101	121	226	197
Profitability/valuation	-	-	-	12/13E	12/14E	12/15E	12/16E	12/17E
<b>EBIT margin %</b>	-	-	-	-	-	20.8	-21.2	-38.1
<b>ROIC (EBIT) %</b>	-	-	-	-	(243.9)	319.7	>500	>500
<b>EV/EBITDA (core) x</b>	-	-	-	-18.9	-10.9	11.1	-7.8	-3.0
<b>P/E (UBS, diluted) x</b>	-	-	-	(13.0)	(16.5)	20.0	(27.5)	(13.5)
<b>Equity FCF (UBS) yield %</b>	-	-	-	(3.7)	(6.3)	6.8	(4.5)	(9.5)
<b>Net dividend yield %</b>	-	-	-	0.0	0.0	0.0	0.0	0.0

Source: Company accounts, Thomson Reuters, UBS estimates. Metrics marked as (UBS) have had analyst adjustments applied. Valuations: based on an average share price that year, (E): based on a share price of US\$16.86 on 11 Apr 2014 19:38 EDT

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# Investment Thesis

## Akebia Therapeutics

### Investment case

The key tenets of our Buy rating on AKBA are: [1] HIF activators could become the standard of care in the anemia market if they are approved without the same black box warnings as injectable erythropoiesis-stimulating agents (ESAs) and hence are perceived to be safer than ESAs. The safety of AKB-6548 is supported by clinical and pre-clinical data and the high-altitude literature, which shows no untoward effect of HIF activation. [2] We see blockbuster potential for '6548 if it is found to be safe and effective. It would be second to market but would be well-positioned among competitors due to attractive once-daily dosing and still be ahead of two additional competitors in a multi-billion dollar market. [3] Near term ph2b data (4Q14e) could drive a valuation step-up in AKBA shares. [4] Management has extensive knowledge and experience executing in the CKD segment.

### Upside scenario

Our \$49 upside scenario reflects a higher probability of success, 65%, in dialysis and non-dialysis patients.

### Downside scenario

Our \$15 downside scenario assumes that '6548 is approvable in anemia but with an uncertain commercial outlook due to some safety concerns. The downside scenario is likely to change in value as '6899 progresses into the clinic.

### Upcoming catalysts

[1] Phase-2b data for '6548 in 4Q14; [2] Feedback from end-of-ph2 meeting with FDA in 2015; [3] Initiate '6548 Phase-3 in mid-2015

12-month rating

**Buy**

12m price target

**US\$28.00**

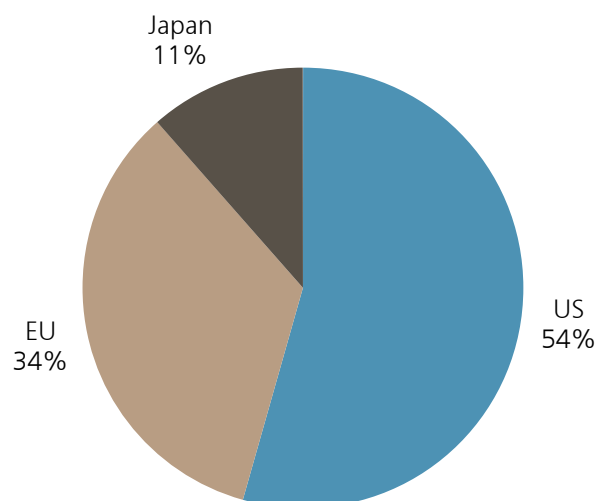
### Business description

Akebia Therapeutics is a clinical-stage company that focuses on the development of treatments for kidney disease based on hypoxia inducible factor biology. The company is developing AKB-6548 for anemia secondary to chronic kidney disease. This once-daily oral therapy has been shown in clinical studies to increase hemoglobin levels with a better safety profile than current erythropoiesis-stimulating agents used to treat anemia, while potentially restoring normal diurnal erythropoietin patterns. In addition, Akebia is studying AKB-6899 for oncology and ophthalmology.

### Industry outlook

While we expect large cap biotech to continue positive momentum on strong earnings growth, the smid cap universe will continue to be very data-driven and tightly correlated to market risk appetite. Many smid-cap names have got credit for pipeline optionality during the recent biotech rally, but we believe AKBA can be an outperformer of peers based on pipeline development and potential partnering.

### Revenues by region (%) (2019E)



Source: UBS estimates

### US Revenues by segment

(\$ millions)	2014e	2015e	2016e	2017e	2018e
Non-dialysis	-	-	-	-	6
Dialysis	-	-	-	-	13
<b>Total</b>	-	-	-	-	<b>19</b>

Source: UBS estimates

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# Overview

We are initiating coverage of Akebia Therapeutics (AKBA) with a Buy rating and a \$28 Price Target. Akebia is a clinical-stage biotech company that focuses on the development of treatments for kidney disease based on hypoxia inducible factor (HIF) biology. The company's lead product candidate, AKB-6548 ('6548), is a once daily oral therapy for anemia. In clinical studies, '6548 has been shown to improve production of hemoglobin (Hb) and red blood cells (RBCs) while maintaining normal levels of erythropoietin (EPO) that follow normal diurnal variation. We believe Akebia is well-positioned to enter a multi-billion dollar market that used to be significantly larger before safety concerns of increased death and adverse cardiovascular events were raised for erythropoiesis-stimulating agents (ESAs). With Akebia and other competitors potentially entering the market in the next few years, approvals without black box warnings would be a significant. We believe that comparable valuations suggest significant upside potential for Akebia, and on a risk-adjusted basis we believe the stock could reach \$28 over the next year.

**We are initiating AKBA with a Buy rating and a \$28 Price Target**

## Key Investment Points

### 1. HIF activators have the potential to be approved without the black box warning and become standard of care.

**'6548 has been shown to be safe so far in its ph2a study.** Akebia's '6548 is a once-daily pill that has positive ph2a data in reversing anemia. Dosing was well-tolerated, no drug-related SAEs were reported, and there was no evidence of undesirable vascular response. '6548 is currently in ph2b, again examining anemia correction and safety. We believe that meeting the efficacy endpoints of anemia correction will be relatively straightforward. Instead, the key question is whether it will be safe. Although '6548 has been shown to be safe thus far in clinical trials, we acknowledge that this includes the experience of only 191 patients dosed through ph2a, from one day through 6 weeks, at a range of dosing levels (80-1200mg). In addition to the 200 patients in the ongoing ph2b study, Akebia will be conducting larger ph3 trials beginning mid-2015 in 1,400-2,100 patients.

**'6548 has the potential to restore diurnal EPO response.** An attractive aspect of '6548 is that it was designed to mimic the normal body adjustments to high altitude, as opposed to pharmacologically driving a hormone level like EPO to saturation. Based on available data, it appears that the body reactions to the drug are gentle while achieving the correction result.

**High-altitude data is supportive.** HIF is constitutively activated at high altitude, and is nature's experiment showing that HIF activation does not lead to worse outcomes. Indeed, people living at altitudes that stimulate HIF do not have higher rates of cardiovascular events or cancer.

**'6548 may be safer than EPO, HIFs could become standard of care.** The implication is that this treatment approach may be safer than EPO, and the value proposition is that anemia can be more safely and better treated than with current therapies, leading HIFs to become the standard of care.

## 2. AKB-6548 has blockbuster potential.

**Anemia is a large segment.** Currently, the anemia market is served by Amgen's Epogen and its competitors. In total, the global branded ESA market is approximately \$6.2 billion. Although we expect the dollar size of the market will decline over time as ESA biogenerics are eventually launched, all ESAs carry safety risks. Specifically, they cause heart attacks and strokes, and their drug labels carry black box warnings. Due to the safety issues and related restrictions on reimbursement, utilization has declined since 2006. We believe that improved safety would enable broader penetration rates as better clinical outcomes are associated with high hemoglobin levels and lower ESA use.

**AKB-6548 is well-positioned in a large segment.** We expect that if successful, AKB-6548 would be second to market among the 4 HIF inhibitors in the clinic. FibroGen's FG-4592 is in the lead, but due to its higher potency, is utilizing longer dosing schedules (TIW during correction period followed by QW, BIW, or TIW during the maintenance period), whereas Akebia's once-daily dosing may be preferred. Further, AKB-6548 appears to restore the physiologic diurnal rhythm of endogenous erythropoietin, suggesting a more homeostatic Hb correction. Hence we think it may compete for a leading position in the HIF category given its early entrance and attractive profile.

**HIF activators could improve clinical outcomes and lower dialysis provider costs.** Better outcomes in CKD are associated with a lower anemia burden and lower ESA utilization. If Hb can be raised without increasing CV risks, then we think the bell curve of Hb in the dialysis population can be right-shifted, thereby lowering the number of patients below 9g/dL Hb who are getting transfused and are at high risk for hospitalization and increased morbidity and mortality. The dialysis providers strive for improved outcomes as it lowers costs and improves participation.

Further, we think providers may switch to oral medication for anemia to push the costs of injectable ESAs off their books. Recall the Centers for Medicare & Medicaid Services (CMS) has pushed out to 2024 the inclusion of oral medications in the composite payment bundle. We think this would enable pricing power (given it will not be sold into a capitated environment), and may entice dialysis providers to switch from ESAs to the oral alternatives (like '6548), which are a cost center to providers. As a reminder, dialysis providers like DaVita and Fresenius receive capitated (bundled) payments from CMS for dialysis treatment. Included in that is injectable drugs (such as ESAs), while oral agents (such as Amgen's calcium mimetic Sensipar) are excluded and are not considered a cost center for the providers. Under this environment, there is an incentive to limit ESA use, which has borne out over the last several years and is reflected by decreasing Epogen sales (\$2.5bn in 2006 to \$2.0bn in 2013).

The recent decision to push the oral exclusion from the dialysis bundle to 2024 could influence adoption at dialysis centers.

## 3. A catalyst path to value creation is well-defined

Over the next 9 months, data for '6548 should drive meaningful appreciation and valuation more in-line with comps. Data from the ph2b study is expected in 4Q14, and Akebia expects to begin ph3 mid-2015 with data in hand to submit an NDA in 2018.

#### 4. The management team has substantial renal and metabolic experience.

The Akebia team has deep expertise in drug development, having been involved in the development or commercialization of drugs for renal and metabolic disorders at companies like Genzyme, Amgen, Abbott, Ipsen, Reliant, Inspiration, and Ziopharm. CEO John Butler led Genzyme's renal division from 2002-2010. Prior to co-founding Akebia, CMO Dr. Bob Shalwitz was Medical Director at Abbott Labs for ten years and an academic pediatric endocrinologist for ten years.

#### 5. Both comps and fundamental valuation suggest significant upside potential in AKBA shares

By both DCF and sum-of-the-parts, we arrive at net present values that are higher than Akebia's market cap, despite significant risk-adjustments to AKB-6548 revenues (we assume a 40% probability of success). Looking at comps of companies with ph2 assets, the mean market cap is \$696m (see below for specific comps to AFFY and KERX).

### Upcoming Catalysts

Akebia's lead clinical product candidate, AKB-6548, is currently in Phase-2b for non-dialysis patients. The data for this study are expected in 4Q14. The company expects to begin Phase-3 studies in 2015 with the potential to submit an NDA by 2018. Specific catalysts are listed in Figure 1.

Figure 1: Upcoming catalysts – Akebia Therapeutics

Key Events	Timeline
AKB-6548: Initiate Phase 2 for dialysis patients with anemia	1H14
AKB-6548: Phase 2b data for anemia secondary to CKD	4Q14
AKB-6548: Feedback from end-of-Phase 2 meeting with FDA	2015
AKB-6548: Initiate Phase 3 for anemia secondary to CKD	mid-2015
AKB-6548: Submit NDA	2018
AKB-6548: Potential partnering for oUS?	2017-2018?
AKB-6548: Establish sales and marketing organization for commercialization in US	2017-2018

Source: Company reports and UBS research

### Valuation

**We reach our \$28 price target by SOTP supported by DCF.** Our revenue estimates include US sales from AKB-6548 and royalty / milestones from partners for Europe and Japan. Our model suggests '6548 will achieve about \$1.5bn US sales in 2028, which represents only 33% of the dialysis anemia market and 35% of the non-dialysis anemia market. The projected sales are further adjusted with a probability of success. Our DCF is driven off the risk-adjusted sales estimates, with a 12.5% discount rate applied to future cash flows. Our price target is DCF-based

but also supported by applying a multiple-based sum-of-the-parts analysis. Figure 2 summarizes the results of the two valuation methods.

**Figure 2: AKBA valuation by DCF and sum-of-the-parts**

Product	Risk-Adj. Revenue	Year	Discount Rate	NPV	NPV (Per Share)	% of Value
AKB-6548 sales - US (risk-adjusted)	344	2022	12.5%	403	\$20.44	69%
AKB-6548 royalties on risk-adj OUS sales	31	2022	12.5%	121	\$6.15	21%
<b>Total AKB-6548</b>	<b>375</b>			<b>524</b>	<b>\$26.59</b>	<b>90%</b>
Net cash				61	\$3.09	10%
<b>Total</b>				<b>585</b>	<b>\$29.68</b>	<b>100%</b>

	NPV	Per share
DCF	\$512m	\$25.98
Sum-of-the-parts	\$585m	\$29.68
Average	\$564m	\$27.83

Source: UBS research

**Our price target incorporates a 12.5% discount rate.** With shares trading at a market cap of about \$325 million, the current valuation implies a heavily risk-adjusted technology outlook on the Akebia program. We believe that a 12.5% discount rate is appropriate as it is in line with other companies with ph2 product candidates that are not yet commercialized.

**We risk-adjusted revenues.** We risk-adjusted anemia revenues from '6548 with a 40% probability of success. In Europe and Japan, we assumed a double-digit royalty from an upcoming partner since management made their intentions clear for partnering this asset in markets outside the US.

**Comparable valuation suggests significant upside.** Figure 3 provides the comparable valuations for companies with significant market opportunities in Phase-2 candidates. The mean market cap of the companies is \$696m (range \$254m to 1,453m). At Akebia's current market cap, the comps suggest significant upside. Based on the revenue generation potential, the assumption at the range is that the probability of success is fairly low. We think the ph2b data would raise the probability of success and trigger a step-up in 4Q.

**Figure 3: Comparable valuations**

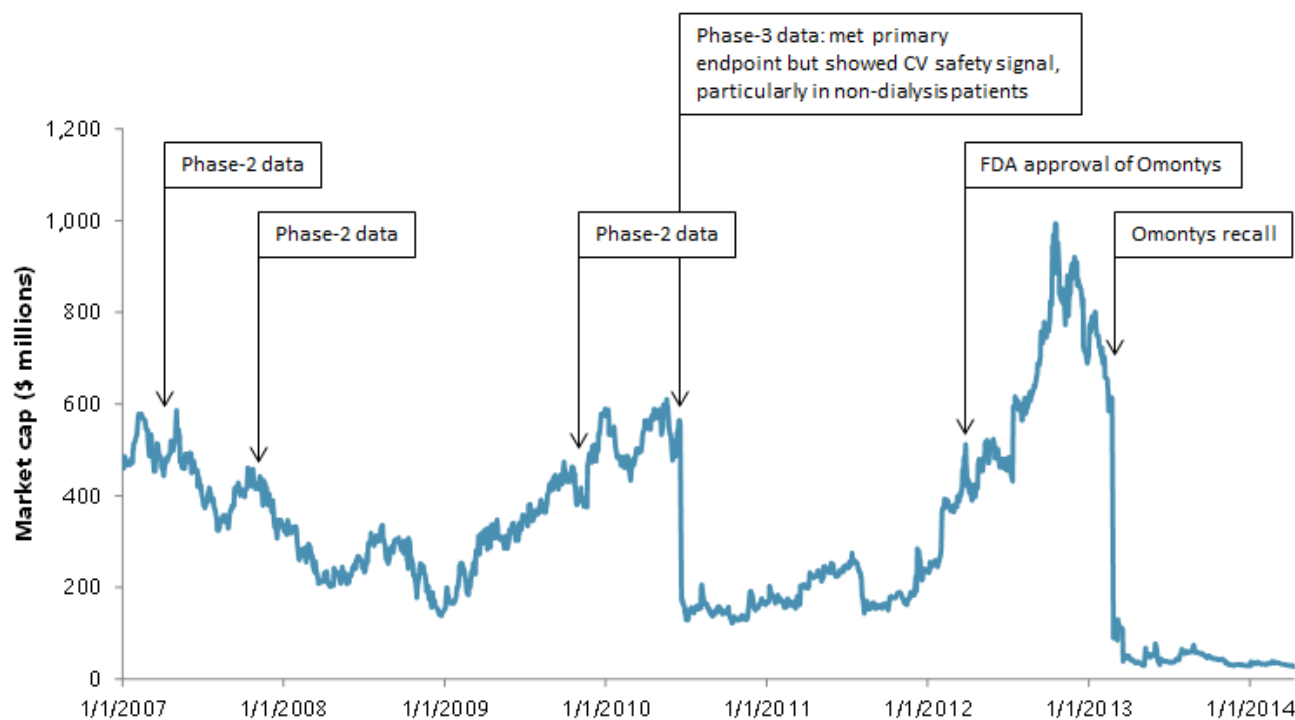
Company	Ticker	Last price (\$)	Market cap (\$M)	Enterprise value (\$M)	Cash & short term inv (\$M)	Last 12-mo NI (\$M)	Debt (\$M)	2014 consensus sales (\$M)
<b>Phase-2 Pipeline with Significant Market Opportunity</b>								
Accelaron Pharma Inc	XLRN	\$51.75	1,453	1,409	65	(22)	22	88
Keryx Biopharmaceuticals Inc	KERX	\$15.90	1,302	1,262	39	(36)	0	268
Portola Pharmaceuticals, Inc.	PTLA	\$25.23	996	865	131	(83)	0	233
Lexicon Pharmaceuticals, Inc.	LXRX	\$1.80	924	666	282	(104)	23	98
AMAG Pharmaceuticals, Inc	AMAG	\$21.88	476	249	227	(10)	0	184
Chemocentryx, Inc.	CCXI	\$7.25	311	222	89	(39)	1	1
Xenoport	XNPT	\$5.99	286	191	94	(86)	0	122
Alcobra Ltd.	ADHD	\$23.61	263	263	1	(11)	1	54
Esperion Therapeutics, Inc.	ESPR	\$16.48	254	272	2	(26)	20	0
<b>mean</b>			<b>696</b>	<b>600</b>				
<b>median</b>			<b>476</b>	<b>272</b>				

Source: UBS research, FactSet

**Affymax and Keryx also suggest significant upside potential.** As a reminder, Affymax (AFFY) and Takeda developed erythropoietic agent Omontys (peginesatide). It was approved by the FDA in March 2012 for treating anemia associated with CKD in adult patients on dialysis. In February 2013, Affymax and Takeda voluntarily recalled Omontys due to reports of anaphylaxis. While Omontys was in ph2, Affymax was traded between \$200-600m, with the lower end of that range during the financial crisis. Post approval, the company's market cap rose to over \$800m (see Figure 4). Keryx Biopharmaceuticals (KERX), whose kidney drug KRX-0502 has successfully completed ph3 trials for hyperphosphatemia in CKD patients on dialysis, trades at >\$1 billion market cap. At Akebia's current market cap, we believe Affymax and Keryx serve as examples of the significant upside potential if Akebia is successful in developing '6548.



Figure 4: Affymax stock chart during Omontys development and commercialization



Source: UBS research, FactSet

## Upside & Downside Scenarios

**Upside scenario: \$49.** Our upside scenario reflects a higher probability of success, 65%, in dialysis and non-dialysis patients.

**Downside scenario: \$15.** Our \$15 downside scenario assumes that '6548 is approvable in anemia but with an uncertain commercial outlook due to some safety concerns. The downside scenario is likely to change in value as '6899 progresses into the clinic.

## Key Risks

We see several risks to our Buy rating on AKBA shares.

- **Clinical risk:** The principle risk is clinical development. Failure of lead asset '6548 on safety and/or efficacy would represent a significant delay to commercialization, since AKBA would likely revert to '6889, which has not yet entered the clinic.
- **Regulatory risk:** If Akebia completes clinical trials and applies for marketing authorization in the US and EU, it would face risk that the regulatory agencies do not approve the drug candidate. In recent years, regulators have been particularly cautious on safety in kidney disease, so we believe Akebia will likely face a high bar from a regulatory perspective.

- **Competitive risk:** Akebia is not the only company developing treatments for anemia associated with CKD. FibroGen, partnered with Astellas, is about a year ahead of Akebia with FG-4592, which has a very strong activator (although it remains unclear whether that will be an advantage or disadvantage). GSK and Bayer are a year behind Akebia with GSK-1278863 and BAY-853934, respectively. Meanwhile, '6548 will compete with currently marketed ESAs like Epogen, Aranesp, and Procrit.
- **IP risk:** Akebia is currently involved in two opposition proceedings in Europe. In the first, FibroGen filed an opposition to Akebia's European Patent No. 2044005 ('005). This was decided in Akebia's favor, although both sides have appealed. The second is on FibroGen's European Patent No. 1463823 ('823), to which Akebia filed an opposition in December 2013. Both proceedings are fairly long and expected to take 2-3 years.
- **Commercial risk:** We believe the bar for coverage and reimbursement is higher than ever. Akebia plans to market '6548 in the US with a 125-person sales force to reach 7,000 nephrologists who treat anemia in patients with CKD. The sales force has yet to be hired, but will face the challenge of selling their first product together as a team. In addition, if the company brings its product to the market, generic competitors could challenge their patent estate.
- **Execution risk:** Biotech drug development and translation into commercialization is difficult.

## Environment, Social, and Governance Issues

The primary social issues we see affecting biotechnology are in relation to drug pricing and global access. While providing access to life-saving drugs is a priority for all of the companies, realities of the market are often balanced against perceived/intended social obligations. All of the companies we cover employ compassionate use programs that enable patients to benefit from therapies that are either too costly to afford or are still in clinical development but provide tremendous benefit to the patient, often life-saving.

# The Need To Know

## HIF and HIF-PH inhibition

Akebia focuses on the development of treatments for kidney disease based on HIF biology. A potential novel mechanism of treating anemia, HIF is the main regulator in the production of red blood cells. It is a sensor in the body that the oxygen level is low and is stimulated in high altitude environments, stimulating production of RBCs.

HIF is the sensor for hypoxia and is upregulated at high altitude (hence our title "Gaining Altitude")

**HIF-PH inhibition acts to stimulate the body's response to anemia.** HIF-PH inhibitors block prolyl-hydroxylase enzymes, which typically promote breakdown of HIF $\alpha$  proteins, resulting in an increase of HIF $\alpha$  proteins. HIF1 $\alpha$  help cells survive in low oxygen conditions, while HIF2 $\alpha$  helps the body to adapt to changes in oxygen like going from sea level to higher altitudes. Stabilized HIF1 $\alpha$  bind to HIF $\beta$  in the nucleus of the cell, and the binding induces production of EPO and other proteins.

**HIF-PH inhibition may be safer than binding directly to EPO receptors.** The company believes that this differentiated mechanism of action could be safer than injectable ESAs by activating pathways for Hb and RBC production rather than binding directly to EPO receptors in the bone marrow, mimicking adjustments the body makes when exposed to reduced oxygen levels at higher altitudes. Stabilization of HIF $\alpha$  from either staying at higher altitudes or dosing with a HIF-PH inhibitor increases levels of Hb and RBCs, resulting in higher oxygen circulating in the blood. Akebia believes that this mechanism will allow AKB-6548 to restore normal levels of EPO in patients with anemia.

**What happens when a person is at higher altitudes?** Low oxygen levels in the blood results in reduced HIF-PH activity in the kidney and liver, which stabilizes and increases levels of HIF  $\alpha$  proteins (HIF1  $\alpha$  and HIF2 $\alpha$ ). This increases EPO secretion and RBC production.

## Anemia and chronic kidney disease

**Chronic kidney disease (CKD) is common among adults in the US.** CKD is a condition in which the kidneys are damaged and cannot filter blood as effectively, resulting in wastes from blood remaining in the body. The CDC estimates that over 20 million people (>10% of adults) in the US may have CKD. CKD is most common in those over 70 years old, while the risk for developing CKD increases after 50 years of age. Common risk factors include diabetes and high blood pressure, with 1 in 3 adults with diabetes and 1 in 5 with high blood pressure having CKD. One of the complications of CKD is that the hormone erythropoietin, which is responsible for generating new RBCs, is made in the kidney, and epo production gets shut down in kidneys that are failing, resulting in severe anemia.

Natural erythropoietin production is lost when kidney function fails

**Patients with anemia lack sufficient RBCs or Hb to deliver oxygen to tissues and cells.** Although some patients do not exhibit symptoms, common ones include fatigue, malaise, poor concentration, appearing pale, dyspnea (shortness of breath), or worsening of heart problems. The World Health Organization defines anemia by Hb thresholds of less than 13 g/dL in men and 12 g/dL in non-pregnant

women, and increased risk of mortality (the most dramatic effects of anemia) has been well documented.

#### **Anemia from CKD is treated with erythropoiesis-stimulating agents (ESAs).**

These are administered by subcutaneous injection and supplemented with iron, administered as a pill or directly into the vein, to ensure the body has sufficient iron to produce RBCs. The goal of treatment with ESAs is to prevent Hb levels from falling below 10 g/dL. Marketed ESAs include Amgen's Epogen and Aranesp, Janssen/JNJ's Procrit and Eprex, and Roche's Mircera, NeoRecormon, and Epogin (sold by Roche subsidiary Chugai in Japan).

**ESA side effects present an opportunity for safer alternatives.** Side effects from ESAs include thrombosis, stroke, myocardial infarction, and death. The prescribing labels for ESAs have black box warnings, and safety concerns led to a decline in use of this class since 2006. Specifically, decreasing average doses, duration of therapy, and number of patients treated with ESAs have been observed over the years. Global sales of branded ESAs were over \$6 billion in 2013, down from nearly \$12 billion in 2006 (see Figure 5). The decline in market revenue suggests that an opportunity may exist to replace injectable ESAs as the standard of care for anemia from CKD.

**Figure 5: Global branded ESA market in 2006 and 2013**

(\$ millions)	2006	2013
Epogen	2,511	1,953
Aranesp	4,121	1,911
Procrit / Eprex	3,180	1,364
Neorecormon / Epogin	1,777	561
Mircera	-	458
<b>TOTAL</b>	<b>11,589</b>	<b>6,247</b>

Source: Company data from respective companies, UBS research

## **Akebia's pipeline candidates**

Currently, Akebia has two wholly-owned product candidates in development for multiple indications. Each is being developed for oral administration. AKB-6548, the lead candidate, is currently in phase-2b development, while AKB-6899 has yet to enter the clinic.

**Figure 6: Akebia's product pipeline**

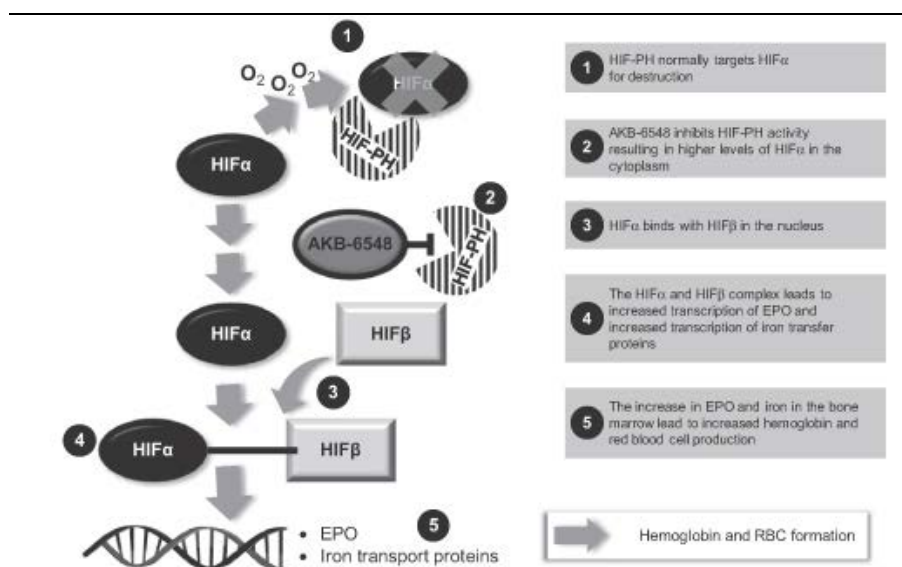
	Preclinical	Phase 1	Phase 2	Phase 3	NDA
AKB-6548	Anemia of CKD (Non-Dialysis)				
AKB-6548	Anemia of CKD (Dialysis)				
AKB-6548	Idiopathic Age-related Anemia				
AKB-6899	Oncology				
AKB-6899	Ophthalmology				

Source: Company reports

## AKB-6548

**Akebia's lead product candidate, AKB-6548, is a once-daily oral HIF-PH inhibitor.** HIF-PH inhibition results in increased levels of HIF $\alpha$  and improved production of Hb and RBCs, while maintaining normal levels of epo (see Figure 7). In addition, the company believes a more prominent HIF2 $\alpha$  response will be achieved, and epo will follow normal diurnal variation in patients.

**Figure 7: Mechanism of action for AKB-6548**



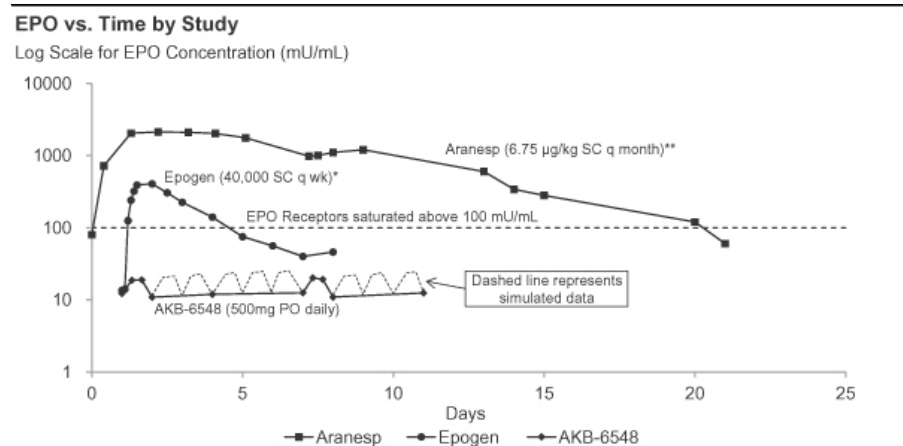
Source: Company reports

**AKB-6548 is wholly-owned.** Akebia currently owns worldwide rights to '6548, and plans to market it fully in the U.S. but may choose to partner markets outside the U.S. The company believes that with a 125-person sales force, they can reach the 7,000 nephrologists who treat anemia in patients with CKD.

**An Asian partnership post-ph2b data could be a source of significant non-dilutive funding**

**Overview of clinical studies of '6548 in CKD.** Akebia believes '6548 will improve Hb levels using a dosing regimen that restores the normal diurnal EPO pattern with lower peak EPO levels than injectable ESAs (see Figure 8). In their Phase-2a study, the company demonstrated that '6548 raised Hb levels in patients with anemia secondary to non-dialysis CKD. Data from the ongoing Phase-2b in non-dialysis CKD is expected in 4Q14. Assuming positive results, a Phase-3 study for non-dialysis would begin in 2015 after an end of Phase-2 meeting with the FDA, with the potential to submit an NDA by 2018.

**Figure 8: EPO levels obtained with Aranesp, Epogen, and AKB-6548**



Source: Company reports

**AKB-6548 has been studied in 4 Phase-1 and 4-Phase 2 trials.** In addition to healthy volunteers, the studies have been conducted in stages 3, 4, and 5 CKD patients. In healthy males, '6548 was able to be dosed daily while inducing diurnal EPO secretion from a single dose, increasing new RBC production by the day 5 of dosing and increasing Hb levels by day 10 of dosing. Similarly, induction of diurnal EPO response was successful in CKD patients. In these studies, '6548 was well-tolerated with no SAEs. A summary of the trial designs is shown in Figure 9.

**Figure 9: Summary of completed '6548 studies**

Study	Population	Design	Doses	Sample Size
<b>Phase 1</b>				
CI-0001	Healthy males	Double-blind, placebo-controlled, fasted	single dose 80, 160, 300, 600, 900, or 1200mg	36 '6548 (6/cohort), 12 placebo (2/cohort)
CI-0002	Healthy males	Double-blind, placebo-controlled, fasted	10 days 500, 700, or 900mg	25 '6548 (8 at 500mg, 9 at 700mg, 8 at 900mg), 9 placebo (3/cohort)
CI-0006	Healthy males	Randomized, cross-over bioavailability study, fasted	single dose capsule and tablet with 3 days in between doses at 315mg	8 '6548
<b>Phase 2</b>				
CI-0003	CKD Stages 3, 4	Open-label, fed	single dose 500mg	22 '6548
CI-0004	CKD Stages 3, 4	Open-label	28-day dosing, within subject dose escalation (200, 300, 400, 500, 600, and 700mg)	10 '6548
CI-0005	CKD Stages 3, 4, 5, not on dialysis	Double-blind, placebo-controlled	42-day dosing of 240, 370, 500, or 630mg	72 '6548 (18 at 240mg, 18 at 370mg, 17 at 500mg, 19 at 630mg), 19 placebo
CI-0008	Healthy volunteers	Mass Balance	single dose 650mg	6 '6548
CI-0009	End-stage renal disease	Pharmacokinetics	450mg four hours before starting dialysis session; 450mg dose two hours after completing different dialysis session	12 '6548

Source: Company reports

**Common potential drug-related AEs were gastrointestinal disorders.** In the eight clinical trials, common gastrointestinal disorders included diarrhea, nausea, and constipation. We list these events in Figure 10.

**Figure 10: Summary of potentially drug-related adverse events in '6548 studies**

Study	Drug-related adverse event	# Patients
CI-0001	Diarrhea	1
CI-0002	Gastroesophageal reflux	1
	Dyspepsia	1
CI-0006	Nausea, headache, dizziness	3
CI-0003	Nausea, tachycardia, vomiting, pyrexia, upper respiratory tract infection, hypomagnesemia, myalgia, headache, somnolence, tremor, oropharyngeal pain, cold sweat, hypotension	5
CI-0004	Nausea, chills, peripheral neuropathy, peripheral sensory neuropathy, muscle spasms	3
CI-0005	Abdominal discomfort	1
	Constipation	3
	Diarrhea	1
	Nausea	2

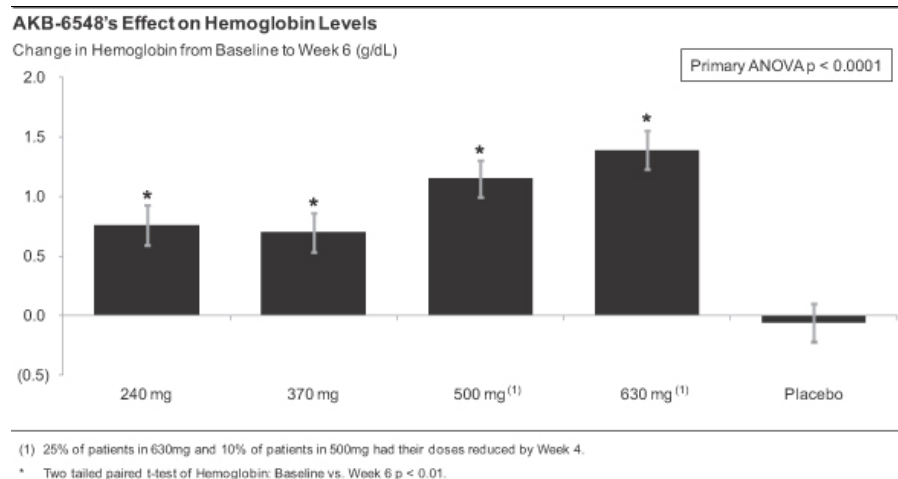
Source: Company reports, UBS research

## Phase-2a (CI-0005)

**Increased Hb levels were observed in dose-dependent manner.** In November 2012, Akebia presented results from the CI-0005 ph2a study in stage 3, 4, and 5

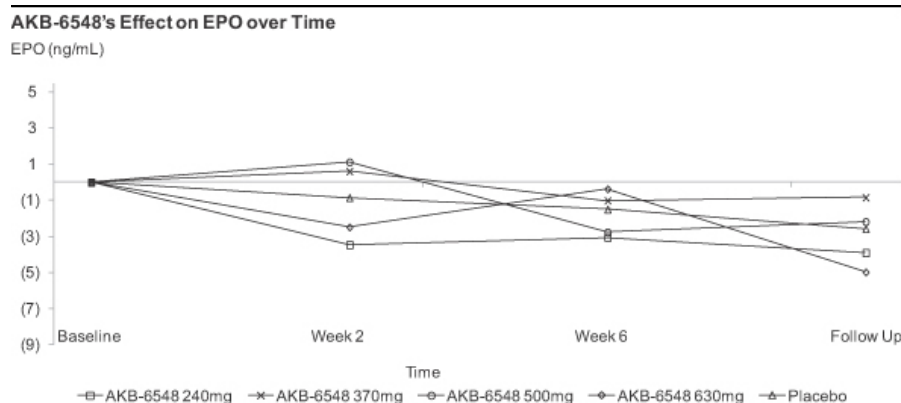
(not on dialysis) CKD patients. The 93 patients were treated once daily for 42 days with either placebo or AKB-6548 (240mg, 370mg, 500mg, or 630mg). In both the modified intent to treat (MITT) and per protocol populations, a statistically significant increase in mean absolute Hb from baseline to week 6 was observed compared to placebo ( $p < 0.0001$ , see Figure 11). A mean increase of 0.7 to 1.4 g/dL was seen by Day 42 with '6548, while a mean decrease of 0.1 g/dL was observed with placebo. Dose-dependent increases in Hb were observed despite 26% of patients on 630mg '6548 and 11% on 500mg decreased their dose (per protocol) due to an increase in Hb of more than 1.5g/dL by Day 28. In addition, Hb was increased without increasing EPO levels and no patient's measured Hb level exceeded 13 g/dL (see Figure 12 and Figure 13). The increase in Hb levels after an increase in reticulocytes indicates that the increase in Hb levels was a result of a physiologic increase in RBC production (see Figure 14).

**Figure 11: Mean absolute change in hemoglobin from baseline in CI-0005**



Source: Company reports

**Figure 12: RBC production improved without elevating EPO levels in CI-0005**

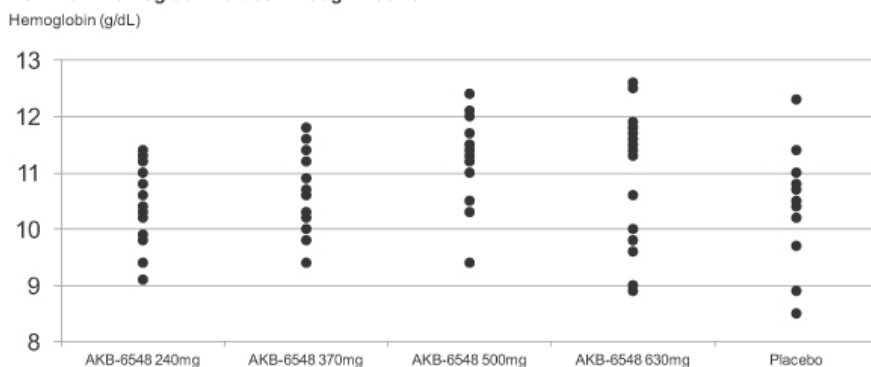


Source: Company reports



**Figure 13: Hemoglobin levels did not exceed 13 g/dL in CI-0005**

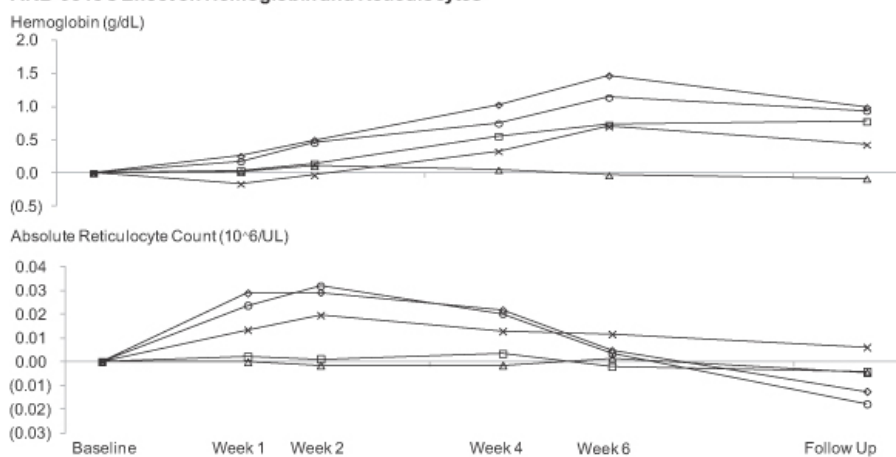
**Maximum Hemoglobin Values Through Week 6**



Source: Company reports

**Figure 14: Physiologic increase in RBC production led to increase in Hb levels**

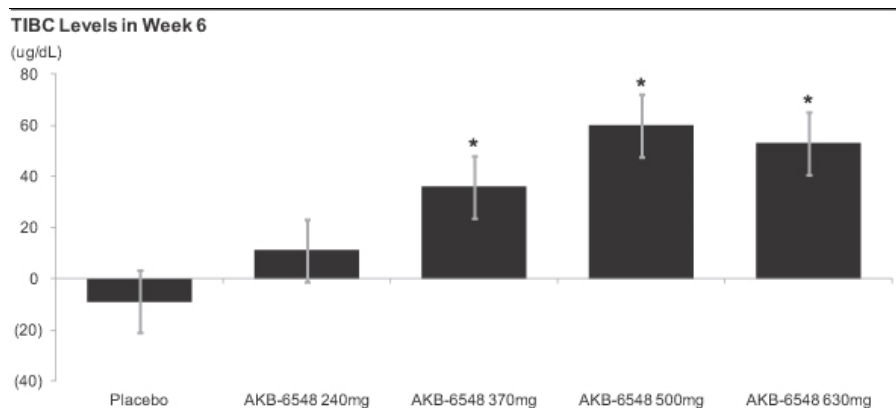
**AKB-6548's Effect on Hemoglobin and Reticulocytes**



Source: Company reports

**'6548 may reduce the need for iron supplementation in CKD patients.** In the ph2a study, a dose-related increase in total iron binding capacity (TIBC) levels was observed (see Figure 15). This indicates the potential to stabilize iron supply to bone marrow while increasing production of Hb, which may result in a reduced need for iron supplementation in CKD patients. Of note, the ability to stabilize iron supply would be an advantage over ESAs, as high levels of iron in the blood are associated with higher risk of infections.

**Figure 15: Total iron binding capacity levels from '6548 ph2a study**



Source: Company reports

**'6548 well-tolerated, with no indication SAEs were drug-related.** '6548 was generally well-tolerated, with adverse events seen in 47% of patients on '6548 and 58% on placebo. No apparent dose effect was seen with the AEs, which were evenly distributed across dosing groups. 13.9% of those on '6548 (n=10) and 5.3% on placebo (n=1) had AEs that were deemed study drug related. Eight SAEs were observed (7 on '6548, 1 on placebo) but all were considered unrelated to study drug by the investigators, and all but one recovered. The '6548 patient who did not recover died following sustained ventricular tachycardia and cardiac arrest after being hospitalized for several days for uremia following an in-hospital procedure. Akebia believes the patient only received 3-4 doses of '6548. No statistically significant change in VEGF levels were observed from baseline for any '6548 groups, and no significant changes were observed in inflammation (C-reactive protein), renal function (Cystatin-C), heart rate, blood pressure, and EKG values (including QT assessments).

## Phase-2b (CI-0007)

**Phase-2b to implement adaptive dosing scheme.** Akebia is currently enrolling a ph2b study in 200 patients with anemia secondary to CKD not requiring dialysis. Patients will be randomized 2:1 to once daily 450mg of '6548 (adjusted with patient's Hb response) or placebo for 20 weeks. The ph2b study will use adaptive dosing with '6548 to help patients raise Hb from baseline without exceeding 13.0 g/dL. All patients will receive oral iron therapy to maintain ferritin between 50-300 ng/mL. The primary endpoint will be percent of patients who achieve or maintain mean Hb  $\geq$  11.0 g/dL or increase Hb by  $\geq$  1.2 g/dL over pre-dose average Hb between screening and baseline. Patients receiving ESA or transfusion rescue will be considered failures and those receiving transfusion for a non-rescue reason will be removed from the primary analysis. Enrollment is expected to complete in 2Q14, with top-line results in 4Q14.

## Additional CKD Studies

**Dialysis ph2 efficacy study to begin in 1H14.** Akebia expects to begin an open label ph2 in 60 patients on dialysis to examine change in Hb from baseline for

once daily 450mg and 300mg '6548 given after hemodialysis. At Week 8, the initial analysis will be conducted on change in Hb. A subsequent analysis will be conducted to determine change in Hb starting at Week 8.

**Phase-3 development to include three studies.** Akebia is currently planning to conduct three studies for registration, with two identical studies enrolling 700-900 patients each with mean dosing duration of 1.25 year. The third study will be a comparability study of 300 patients primarily in Europe. The goal for the ph3 studies will be raise Hb levels to >10.5 g/dL, and the trials will be based on the Omontys approval studies.

**Thorough QT (TQT) study in healthy volunteers began in January 2014.** The 50 patient TQT study began early this year. To date, '6548 has not shown any impact on the QT interval in humans or animals.

**Carcinogenicity study planned in two rodent species.** The two-year study in rats and mice will be conducted to test '6548 in a chronic setting. So far, '6548 has not been shown to cause mutations that could lead to cancer.

**Drug interaction study expected for registration package.** Since CKD patients often take multiple medications, Akebia is exploring the need to study drug interactions with '6548. The company is expecting to complete at least one of these studies.

## Other Indications

**Two potential indications are IAA and CFH.** Akebia is planning to study anemia associated with aging (IAA) and congestive heart failure (CHF) in future trials. Anemia affects 10% of individuals over 65 years old and 20% of those over 85 years old. Of these, a third are considered to be IAA. Current ESAs are not used in either IAA or CHF because they have been associated with increased cardiovascular events. Additional Phase-2 studies would be required to determine '6548 dose levels and to evaluate cardiac performance and other critical outcomes. Akebia expects to file an IND after the ph2b CI-0007 study is completed.

If HIFs are safe, then wider anemia indications may become approachable

## AKB-6899

In preclinical studies of cells at low oxygen levels, AKB-6899 has been shown to inhibit VEGF expression and phosphoglycerate kinase (PGK) mRNA, as well as stimulate production of soluble vascular endothelial growth factor receptor 1 (sVEGFr1). VEGF expression and PGK mRNA are associated with growth of cancerous tumors, and sVEGFr1 is known to be an inhibitor of VEGF signalling by inhibiting interactions with transmembrane receptors. Akebia believes that '6899 will increase EPO levels while reducing VEGF levels. The company plans to file an IND and conduct Phase-1 studies in oncology and ophthalmology.

## Management

**John Butler, President and Chief Executive Officer.** Mr. John Butler joined Akebia as a director in July 2013 and became President and CEO of Akebia in August 2013. Previously, he served as CEO of Inspiration Biopharmaceuticals and held various positions at Genzyme, Amgen, and Hoffmann-La Roche. Mr. Butler received his BA in Chemistry from Manhattan College and MBA from Baruch College, City University of New York. We've known John since 2005 and have a lot of confidence in his deep understanding of the kidney disease segment, and that he will execute if the trials of '6548 are successful.

**John was the President of Renal at Genzyme and oversaw the development and commercialization of several products for CKD**

**Robert Shalwitz, Chief Medical Officer.** Before cofounding Akebia in 2007, Dr. Robert Shalwitz served as Vice President of Clinical Development at Reliant Pharmaceuticals and Medical Director at Abbott Labs. Previously, he was an academic pediatric endocrinologist for 10 years and conducted research at Washington University in St. Louis and at Children's Hospital of Orange County (CA). Dr. Shalwitz received his BGS from the University of Michigan and MD from SUNY Buffalo. We are very impressed with Bob's command of the program and of anemia and CKD in general, and find him to be an outstanding communicator.

**Jason Amello, Senior Vice President and Chief Financial Officer.** Mr. Jason Amello joined Akebia as Chief Financial Officer and Treasurer in 2013. Previously, he served as Executive Vice President, Chief Financial Officer, and Treasurer of Ziopharm Oncology. Mr. Amello has held various positions at Genzyme and Deloitte. Mr. Amello received his BA from Boston College and is a Certified Public Accountant in the Commonwealth of Massachusetts. In our view, Jason is highly qualified and adds a significant backbone to the company.

**Nicole Hadas, Vice President and General Counsel.** Ms. Nicole Hadas joined Akebia as General Counsel and Secretary in 2013. Previously, she served as Senior Vice President and General Counsel at Inspiration Biopharmaceuticals. Ms. Hadas has held various positions at Genzyme and Foley Hoag. Ms. Hadas received her BA from the University of Michigan and JD from Boston College Law School. We spoke with Nikki regarding the ongoing legal proceedings and believe Akebia's intellectual property position is quite strong.

**Michel Dahan, Vice President, Commercial.** Mr. Michel Dahan joined Akebia in 2013, where he leads global marketing and commercialization for AKB-6548. Previously, he led global marketing and commercial development at Inspiration Biopharmaceuticals and global marketing and strategic planning for the hemophilia franchise at Ipsen. Mr. Dahan received his graduate degree in business administration from HEC Paris (France), maitrise from University Paris VI (France), and executive education program (PLD) at Harvard Business School. Michel can clearly articulate the value proposition for '6548 and is highly responsive and professional in working with the Street.

## Akebia Therapeutics Inc (AKBA.O)

			12/13E	% ch	12/14E	% ch	12/15E	12/16E	12/17E
<b>Income statement (US\$m)</b>									
Revenues	-	-	0	-	0	-	84	82	87
Gross profit	-	-	-	-	-	-	-	-	-
<b>EBITDA (UBS)</b>	-	-	(15)	-	(23)	-50.0	18	(17)	(33)
Depreciation & amortisation	-	-	(1)	-	0	-86.2	0	0	0
<b>EBIT (UBS)</b>	-	-	(16)	-	(23)	-43.5	18	(18)	(33)
Associates & investment income	-	-	0	-	0	-	0	0	0
Other non-operating income	-	-	0	-	0	-	0	0	0
Net interest	-	-	3	-	3	0.0	3	3	3
Exceptionals (incl goodwill)	-	-	0	-	0	-	0	0	0
<b>Profit before tax</b>	-	-	(13)	-	(20)	-52.7	20	(15)	(30)
Tax	-	-	0	-	0	-	0	0	0
<b>Profit after tax</b>	-	-	(13)	-	(20)	-52.7	20	(15)	(30)
Preference dividends	-	-	0	-	0	-	0	0	0
Minorities	-	-	0	-	0	-	0	0	0
Extraordinary items	-	-	0	-	0	-	0	0	0
<b>Net earnings (local GAAP)</b>	-	-	(13)	-	(20)	-52.7	20	(15)	(30)
<b>Net earnings (UBS)</b>	-	-	(13)	-	(20)	-52.7	20	(15)	(30)
Tax rate (%)	-	-	0.0	-	0.0	-	0.0	0.0	0.0
<b>Per share (US\$)</b>			12/13E	% ch	12/14E	% ch	12/15E	12/16E	12/17E
EPS (UBS, diluted)	-	-	(1.30)	-	(1.02)	21.5	0.84	(0.61)	(1.25)
EPS (local GAAP, diluted)	-	-	(1.30)	-	(1.02)	21.5	0.84	(0.61)	(1.25)
EPS (UBS, basic)	-	-	(1.30)	-	(1.02)	21.5	1.02	(0.61)	(1.25)
Net DPS (US\$)	-	-	0.00	-	0.00	-	0.00	0.00	0.00
Cash EPS (UBS, diluted) <sup>1</sup>	-	-	(1.22)	-	(1.02)	17.1	0.85	(0.60)	(1.22)
Book value per share	-	-	3.04	-	5.57	83.6	6.19	9.25	7.84
Average shares (diluted)	-	-	10.13	-	19.70	94.4	24.04	24.10	24.34
<b>Balance sheet (US\$m)</b>			12/13E	% ch	12/14E	% ch	12/15E	12/16E	12/17E
Cash and equivalents	-	-	21	-	101	374.1	121	226	197
Other current assets	-	-	12	-	13	2.7	15	16	17
<b>Total current assets</b>	-	-	33	-	113	238.4	136	243	214
Net tangible fixed assets	-	-	0	-	1	3358.1	2	4	5
Net intangible fixed assets	-	-	0	-	0	0.0	0	0	0
Investments / other assets	-	-	1	-	1	0.0	1	1	1
<b>Total assets</b>	-	-	35	-	115	232.9	140	247	220
Trade payables & other ST liabilities	-	-	4	-	6	43.5	16	24	29
Short term debt	-	-	0	-	0	0.00	0	0	0
<b>Total current liabilities</b>	-	-	4	-	6	43.5	16	24	29
Long term debt	-	-	0	-	0	0.0	0	0	0
Other long term liabilities	-	-	0	-	0	-	0	0	0
Preferred shares	-	-	0	-	0	-	0	0	0
<b>Total liabilities (incl pref shares)</b>	-	-	4	-	6	43.4	16	24	29
Common s/h equity	-	-	31	-	110	256.9	123	223	191
Minority interests	-	-	0	-	0	-	0	0	0
<b>Total liabilities &amp; equity</b>	-	-	35	-	115	232.9	140	247	220
<b>Cash flow (US\$m)</b>			12/13E	% ch	12/14E	% ch	12/15E	12/16E	12/17E
Net income (before pref divs)	-	-	(13)	-	(20)	-52.7	20	(15)	(30)
Depreciation & amortisation	-	-	1	-	0	-86.2	0	0	0
Net change in working capital	-	-	2	-	0	-	0	0	0
Other operating	-	-	(1)	-	2	-	2	2	2
<b>Operating cash flow</b>	-	-	(11)	-	(18)	-62.4	22	(13)	(28)
Tangible capital expenditure	-	-	0	-	(1)	-5067.9	(1)	(1)	(1)
Intangible capital expenditure	-	-	0	-	0	-	0	0	0
Net (acquisitions) / disposals	-	-	0	-	0	-	0	0	0
Other investing	-	-	(11)	-	0	-	0	0	0
<b>Investing cash flow</b>	-	-	(11)	-	(1)	91.1	(1)	(1)	(1)
Equity dividends paid	-	-	0	-	0	-	0	0	0
Share issues / (buybacks)	-	-	0	-	99	-	0	119	0
Other financing	-	-	0	-	0	-	0	0	0
Change in debt & pref shares	-	-	43	-	0	-	0	0	0
<b>Financing cash flow</b>	-	-	42	-	99	133.5	0	119	0
<b>Cash flow inc/(dec) in cash</b>	-	-	20	-	79	305.8	21	105	(29)
FX / non cash items	-	-	-	-	0	-	0	0	0
<b>Balance sheet inc/(dec) in cash</b>	-	-	-	-	79	-	21	105	(29)

Source: Company accounts, UBS estimates. (UBS) metrics use reported figures which have been adjusted by UBS analysts. <sup>1</sup>Cash EPS (UBS, diluted) is calculated using UBS net income adding back depreciation and amortization.

## Akebia Therapeutics Inc (AKBA.O)

Valuation (x)	-	-	-	12/13E	12/14E	12/15E	12/16E	12/17E
P/E (local GAAP, diluted)	-	-	-	NM	NM	20.0	NM	NM
P/E (UBS, diluted)	-	-	-	(13.0)	(16.5)	20.0	(27.5)	(13.5)
P/CEPS	-	-	-	NM	NM	16.4	NM	NM
Equity FCF (UBS) yield %	-	-	-	(3.7)	(6.3)	6.8	(4.5)	(9.5)
Net dividend yield (%)	-	-	-	0.0	0.0	0.0	0.0	0.0
P/BV x	-	-	-	5.6	3.0	2.7	1.8	2.1
EV/revenues (core)	-	-	-	-	-	2.3	1.6	1.1
EV/EBITDA (core)	-	-	-	-18.9	-10.9	11.1	-7.8	-3.0
EV/EBIT (core)	-	-	-	NM	NM	11.3	NM	NM
EV/OpFCF (core)	-	-	-	NM	NM	12.0	NM	NM
EV/op. invested capital	-	-	-	-	NM	NM	NM	NM
<b>Enterprise value (US\$m)</b>	-	-	-	<b>12/13E</b>	<b>12/14E</b>	<b>12/15E</b>	<b>12/16E</b>	<b>12/17E</b>
Market cap.	-	-	-	308	308	308	308	308
Net debt (cash)	-	-	-	(21)	(61)	(111)	(174)	(212)
Buy out of minorities	-	-	-	0	0	0	0	0
Pension provisions/other	-	-	-	0	0	0	0	0
<b>Total enterprise value</b>	-	-	-	<b>287</b>	<b>247</b>	<b>197</b>	<b>134</b>	<b>97</b>
Non core assets	-	-	-	0	0	0	0	0
<b>Core enterprise value</b>	-	-	-	<b>287</b>	<b>247</b>	<b>197</b>	<b>134</b>	<b>97</b>
<b>Growth (%)</b>	-	-	-	<b>12/13E</b>	<b>12/14E</b>	<b>12/15E</b>	<b>12/16E</b>	<b>12/17E</b>
Revenue	-	-	-	-	-	-	-2.0	5.1
EBITDA (UBS)	-	-	-	-	-50.0	-	-	-89.8
EBIT (UBS)	-	-	-	-	-43.5	-	-	-88.7
EPS (UBS, diluted)	-	-	-	-	21.5	-	-	-103.3
Net DPS	-	-	-	-	-	-	-	-
<b>Margins &amp; Profitability (%)</b>	-	-	-	<b>12/13E</b>	<b>12/14E</b>	<b>12/15E</b>	<b>12/16E</b>	<b>12/17E</b>
Gross profit margin	-	-	-	-	-	-	-	-
EBITDA margin	-	-	-	-	-	21.1	NM	NM
EBIT margin	-	-	-	-	-	20.8	-21.2	-38.1
Net earnings (UBS) margin	-	-	-	-	-	24.1	NM	NM
ROIC (EBIT)	-	-	-	-	(243.9)	319.7	>500	>500
ROIC post tax	-	-	-	-	NM	NM	NM	NM
ROE (UBS)	-	-	-	-	(28.6)	17.4	(8.5)	(14.6)
<b>Capital structure &amp; Coverage (x)</b>	-	-	-	<b>12/13E</b>	<b>12/14E</b>	<b>12/15E</b>	<b>12/16E</b>	<b>12/17E</b>
Net debt / EBITDA	-	-	-	1.4	4.4	(6.8)	13.2	6.0
Net debt / total equity %	-	-	-	(68.9)	(91.6)	(98.6)	(101.6)	(103.2)
Net debt / (net debt + total equity) %	-	-	-	NM	NM	NM	NM	NM
Net debt/EV	-	-	-	(7.4)	(40.6)	(61.5)	NM	NM
Capex / depreciation %	-	-	-	NM	NM	NM	NM	NM
Capex / revenue %	-	-	-	-	-	1.5	1.6	1.6
EBIT / net interest	-	-	-	5.8	8.3	NM	6.3	12.0
Dividend cover (UBS)	-	-	-	-	-	-	-	-
Div. payout ratio (UBS) %	-	-	-	-	-	-	-	-
<b>Revenues by division (US\$m)</b>	-	-	-	<b>12/13E</b>	<b>12/14E</b>	<b>12/15E</b>	<b>12/16E</b>	<b>12/17E</b>
Others	-	-	-	0	0	84	82	87
<b>Total</b>	-	-	-	<b>0</b>	<b>0</b>	<b>84</b>	<b>82</b>	<b>87</b>
<b>EBIT (UBS) by division (US\$m)</b>	-	-	-	<b>12/13E</b>	<b>12/14E</b>	<b>12/15E</b>	<b>12/16E</b>	<b>12/17E</b>
Others	-	-	-	(16)	(23)	18	(18)	(33)
<b>Total</b>	-	-	-	<b>(16)</b>	<b>(23)</b>	<b>18</b>	<b>(18)</b>	<b>(33)</b>

Source: Company accounts, UBS estimates. (UBS) metrics use reported figures which have been adjusted by UBS analysts.

### Forecast returns

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Forecast price appreciation	+66.1%
Forecast dividend yield	0.0%
Forecast stock return	+66.1%
Market return assumption	5.4%
Forecast excess return	+60.7%

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### Statement of Risk

We see several risks to AKBA shares, including clinical, regulatory, IP, competitive, and commercial. Clinical risks include if AKB-6548 results in unforeseen safety, tolerability, or toxicity signals, or fails to yield positive clinical results. Regulatory risks include the regulatory agencies not approving the drug candidate after completing clinical trials. Competitive risks include Akebia not being the only company developing treatments for anemia secondary to chronic kidney disease, and new treatments coming to market will all compete with currently available erythropoiesis-stimulating agents. Branded and generic competitors could challenge Akebia's patent estate.

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UBS 12-Month Rating	Definition	Coverage <sup>1</sup>	IB Services <sup>2</sup>
<b>Buy</b>	FSR is > 6% above the MRA.	47%	33%
<b>Neutral</b>	FSR is between -6% and 6% of the MRA.	42%	34%
<b>Sell</b>	FSR is > 6% below the MRA.	11%	23%
UBS Short-Term Rating	Definition	Coverage <sup>3</sup>	IB Services <sup>4</sup>
<b>Buy</b>	Stock price expected to rise within three months from the time the rating was assigned because of a specific catalyst or event.	less than 1%	less than 1%
<b>Sell</b>	Stock price expected to fall within three months from the time the rating was assigned because of a specific catalyst or event.	less than 1%	less than 1%

Source: UBS. Rating allocations are as of 31 March 2014.

1: Percentage of companies under coverage globally within the 12-month rating category. 2: Percentage of companies within the 12-month rating category for which investment banking (IB) services were provided within the past 12 months.

3: Percentage of companies under coverage globally within the Short-Term rating category. 4: Percentage of companies within the Short-Term rating category for which investment banking (IB) services were provided within the past 12 months.

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## Company Disclosures

Company Name	Reuters	12-month rating	Short-term rating	Price	Price date
<b>Akebia Therapeutics Inc</b> <sup>2, 4, 5, 16</sup>	AKBA.O	Not Rated	N/A	US\$16.86	11 Apr 2014

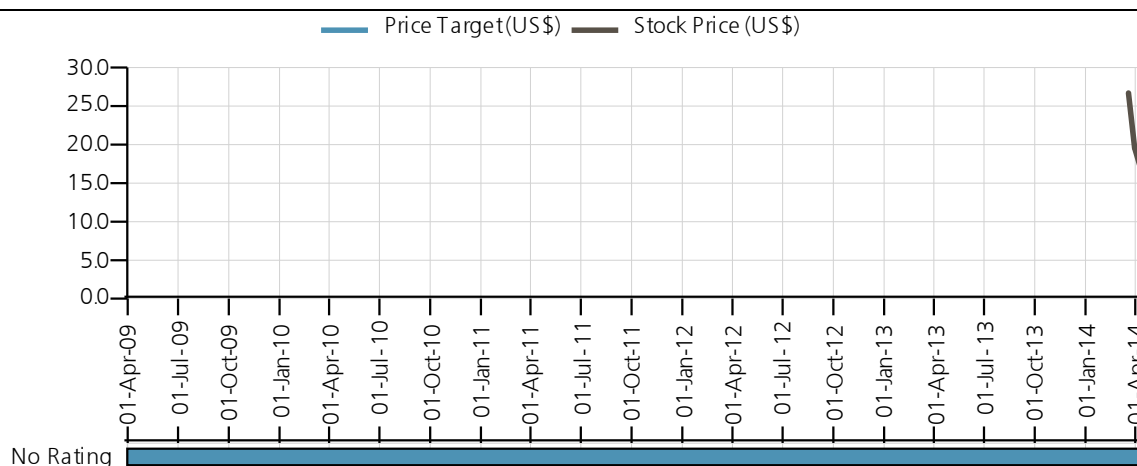
Source: UBS. All prices as of local market close.

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### Akebia Therapeutics Inc (US\$)



Source: UBS; as of 11 Apr 2014

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