

## CONCERT PHARMACEUTICALS INC.

### CNCE: Positive Discussions With FDA for CTP-499 in Diabetic Kidney Disease

CNCE (NASDAQ)

#### Company & Market Data

Closing Price (as of July 7, 2014):	\$9.34
Rating:	BUY
Price Target:	\$24.00
52 Week Range:	\$7.12 - \$16.26
Shares Outstanding (MM):	18
Market Capitalization (MM):	\$167
Cash (MM):	\$108.0
Debt (MM):	\$13.0
Fiscal Year End:	Dec

#### Estimates

EPS	2013A	2014E	2015E
1Q	—	\$(0.76)A	—
2Q	—	\$(0.37)	—
3Q	—	\$(0.38)	—
4Q	—	\$(0.28)	—
Full Year	\$(4.99)	\$(1.61)	\$(0.52)
Revenue (MM)	\$25.4	\$10.4	\$27.5

#### Ratios

P/E	NA	NA	NA
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Concert Pharmaceuticals, founded in 2006 by Richard Aldrich, Roger Tung, and Christoph Westphal, creates novel medicines by applying its DCE (Deuterated Chemical Entity) Platform technologies to molecules. The DCE approach involves the selective addition of deuterium, a stable isotope of hydrogen, to molecules, resulting in clinical therapeutic candidates with improved pharmacology. This approach has the potential to enable more efficient drug discovery and clinical development. Concert's proprietary programs include CTP-354, a novel GABA-A modulator for spasticity and anxiety, and CTP-499, a PDE inhibitor for diabetic kidney disease. Promising partnered programs include Jazz's JZP-386, a long-acting Xyrem, Avanir's AVP-786, an improved Neudexta, and multiple programs with Celgene. Concert has also developed a broad portfolio of deuterated molecules that are expected to migrate into and through the clinic over time.

**Material Event: Positive Discussions With FDA for CTP-499.** CTP-499, a deuterated-PDE inhibitor for diabetic kidney disease, recently finished up encouraging Phase 2 work, where it demonstrated activity in reducing the number of patients progressing toward more serious forms of that condition. Today Concert announced it concluded end-of-Phase 2 discussions with FDA which provide clarity toward Phase 3: Concert can conduct a single large trial or two Phase 3 studies utilizing a relatively new endpoint, the reduction of a composite endpoint of increases in serum creatinine (greater than or equal to 50%) or end stage renal disease.

In its Phase 2 work, CTP-499 demonstrated a statistically significant reduction in large serum creatinine increases in diabetic kidney disease patients, which bodes well for the molecule for this new endpoint. The company has stated it is seeing a Special Protocol Assessment (SPA) for CTP-499. The company also prefers to partner '499 for the indication; we estimate a partnership can occur during 2015, once an SPA is formally agreed upon between Concert and FDA.

**Concert's CTP-354 Should Also Progress.** CTP-354, is a subtype-selective GABA-A modulator with familiar yet distinct GABA agonist activity, and possesses a once-daily profile with minimal sedation compared to benzodiazepines. We believe '354 has the potential for utility not only in spasticity associated with both multiple sclerosis (MS) and spinal cord injury, but we believe there is significant potential for its development in anxiety and pain settings over time. '354 should move into Phase 2 for spasticity in MS in 2H14 and into other indications during 2015.

**Concert's Partnered Programs Are Moving Toward Prominence.** Concert's collaborations include Avanir's AVP-786, a deuterated dextromethorphan that contains less quinidine than Avanir's Neudexta; we believe it could have much more broad consideration than the approved Neudexta as a result. '786 is expected to enter Phase 2 in 2H14 for treatment-resistant depression, and can utilize data generated by Neudexta, a notable efficiency that could help it also move into Phase 3 in agitation associated with Alzheimer's disease in 2015.

Jazz Pharmaceutical's JZP-386 is a deuterated analog of sodium oxybate, the active ingredient in Xyrem, a brand which reached revenue of \$569mm (+50%) in 2013. JZP-386 has the potential to avoid Xyrem's inconvenient intra-night dosing, and is expected to move into Phase 1 for narcolepsy this year, triggering a milestone.

Concert also has a broad-ranging agreement with Celgene for multiple deuterated compounds in inflammation and oncology. These include CTP-730, which is moving into Phase 1 for inflammatory diseases. Though the specific molecules have not yet been disclosed, the Celgene agreement is potentially very lucrative, with \$35mm upfront, \$1.4B in milestones, and low double-digit royalties.

**CNCE Share Valuation: Attractive In Our View.** Concert has created a diverse portfolio of assets, and along with partners Jazz, Avanir, and Celgene, is advancing a number of candidates into and through the clinic. We continue to value CNCE shares at \$24, based on fully-taxed, risk-weighted NPV calculations that totals \$24.20. We assess Concert's major assets at the following NPV/CNCE share: CTP-354 at \$7.17, CTP-499 at \$5.16, and the Avanir, Jazz, and Celgene collaborations at \$3.87, \$2.37, and \$3.61, respectively, with cash and other assets comprising the difference.

Disclosures and Analyst Certifications can be found in Appendix A.

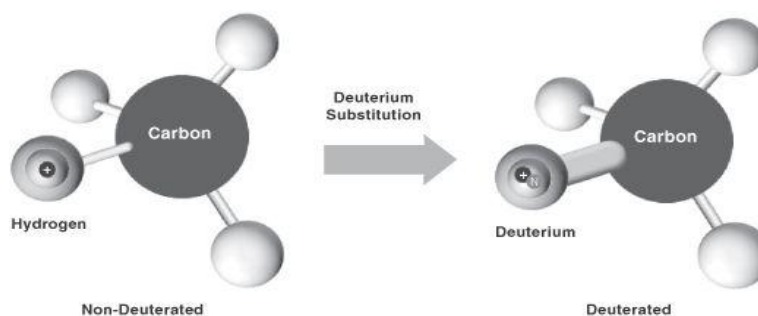
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## Concert Pharmaceuticals – Executive Summary

**Concert Pharmaceuticals: Developing Deuterium-Based Drugs.** Founded in 2006, Concert Pharmaceuticals focuses on creating and developing new medicines through its proprietary DCE (deuterated chemical entity) Platform. The DCE Platform selectively employs deuterium, a naturally-occurring relative of hydrogen. Deuterium modification of a molecule has the potential to improve its metabolic properties, with minimal change to its intrinsic pharmacology. Concert's business strategy initially involved establishing novel intellectual property for a number of deuterium-modified molecules across a wide range of therapeutic classes, and then advancing the most promising initial candidates, even as it continued to develop others. Five of these more mature deuterated assets are now currently in active development under the guidance of either Concert or its strategic partners, and all five should be advancing in the clinic by year-end 2014.

### Exhibit 1: Deuterium Substitution



Source: Concert Corporate Fact Sheet, May 2013.

The application of deuterium medicinal chemistry to compounds with well understood therapeutic utility can potentially provide an approach with modestly reduced risk with regard to creating new drugs. Concert believes (and we concur) that since its assets are generally materially related to a parent molecule, once Phase 1 is established for the deuterated molecule, especially in an indication that the parent shares, the program has been materially de-risked.

**Deuterium Medicinal Chemistry In Brief.** Deuterium is one of two naturally-occurring stable isotopes of hydrogen. Where hydrogen has one electron and one proton, deuterium also has a neutron in its nucleus, resulting in an atomic mass that is double that of hydrogen. Deuterium is not radioactive, and possesses physicochemical properties that are similar to those of hydrogen, but because of its increased mass, bonds involving deuterium are generally stronger than similar bonds with hydrogen. This strengthening can be enough to make significant changes in biological reactions with deuterium-based compounds compared to hydrogen-based ones. Many drugs are metabolized by pathways that involve the breakdown of carbon-hydrogen bonds, and the stronger deuterium-based bonds have the potential to alter or deflect the breakdown of the molecule or its metabolites. Deuterium modification therefore offers an approach to potentially creating significantly differentiated new medicines, and importantly, because the behavior of deuterium based bonds is not inherently predictable, novel intellectual property can be established.

**Concert's Drug Development Approach.** Concert's strategic development of deuterium-based molecules began with management initially broadly examining a host of both approved and novel molecules to selectively apply deuterium and establish intellectual property. Having now established a broad portfolio of deuterated molecules that span multiple therapeutic areas, it continues with that process. We note that

Concert's management team is well-seasoned in therapeutics development, having material experience at Vertex, Merck, Amgen, and other organizations; because of this, we believe Concert should have the ability to successfully navigate the development of its wide range of assets. With existing therapies, Concert is often utilizing significant information regarding the related non-deuterated (parent) compound, allowing it to efficiently identify lead compounds. In some cases, Concert or its partners can truncate the development timeline of a deuterated molecule compared to conventional drug development by sourcing the data from the related parent molecule.

**Concert's Pipeline: Five In The Clinic During 2015.** Concert has a solid pipeline of deuterated compounds as noted in Exhibit 2. Concert's five most advanced programs are all expected to be materially progressing at various stages in the clinic by the end of 2014. Concert has two proprietary compounds and three partnered programs of significant importance. Given the urgency with which Concert has established its intellectual property, we expect continued advancement of new compounds in its proprietary pipeline into the clinic.

*Concert's Proprietary Pipeline: CTP-354 Has A Familiar Yet Distinctive GABA Profile.* CTP-354 is Concert's GABA-A selective modulator moving into Phase 2 for spasticity associated with both multiple sclerosis and spinal cord injury. It also could be considered for other much broader indications such as anxiety and neuropathic pain. CTP-354 is attempting to demonstrate efficacy in these settings without the sedation seen with other common GABA-focused therapies, and the larger opportunities such as anxiety and pain with limited sedation gives this compound considerable potential. Phase 2 should begin in 2H14 for the spasticity settings.

*Concert's Proprietary Pipeline: CTP-499--Finishing Phase 2 in Diabetic Kidney Disease.* CTP-499 is a PDE-inhibitor with anti-inflammatory and anti-fibrotic characteristics that has shown encouraging results in Phase 2 for diabetic kidney disease, and recent changes in trial endpoints have become helpful to the development of therapeutics for this indication. Also, since its parent molecule is pentoxifylline, CTP-499 could have potential for long-term consideration in hepatic settings such as alcoholic liver disease and NASH. '499 could be partnered after the recent positive end-of-Phase 2 meeting with FDA, and the upcoming issuance of a potential SPA for the program.

**Exhibit 2: Concert Pharmaceuticals - Pipeline**

Product Candidate	Lead Indication(s)	Preclinical	Phase 1	Phase 2	Anticipated Milestones	Potential Deal Value	Worldwide Rights
CTP-354	Spasticity associated with MS				<ul style="list-style-type: none"> <li>Ph1 MAD data expected 2H14</li> <li>Ph2 program expected to begin 2H14</li> </ul>		CoNCERT Pharmaceuticals Inc.
	Spasticity associated with SCI						
CTP-499	Diabetic Kidney Disease				<ul style="list-style-type: none"> <li>End of Ph2 FDA meeting expected mid-2014</li> </ul>		CoNCERT Pharmaceuticals Inc.
AVP-786 (Deuterated dextromethorphan)	Neurologic and Psychiatric Disorders				<ul style="list-style-type: none"> <li>Ph2 trial for treatment-resistant major depressive disorder expected to begin 2H14</li> </ul>	\$170 Million	AVANIR pharmaceuticals
CTP-730	Inflammatory Diseases				<ul style="list-style-type: none"> <li>Phase 1 expected to begin 2014</li> </ul>	\$1.4 Billion	Celgene
JZP-386 (Deuterated sodium oxybate)	Narcolepsy				<ul style="list-style-type: none"> <li>Phase 1 expected to begin 2014</li> </ul>	\$117 Million	Jazz Pharmaceuticals
C-10068	Pain and Seizures						CoNCERT Pharmaceuticals Inc.
Deuterated Ivacaftor	CF and COPD						CoNCERT Pharmaceuticals Inc.

Source: Concert Pharmaceuticals corporate presentation; June 2014.

**Partnered Programs With Avanir, Jazz, and Celgene, Are Advancing.** Concert initially implemented a partnering strategy for the development of its molecules in order to defer risk, and help establish and validate its DCE platform. It has three corporate agreements so far, and we believe there is the potential for additional collaborations over time. Concert has structured its partnerships with material developmental milestones, providing the company with potential for material cash and revenue generation from those programs even prior to the introduction of its own proprietary therapies.

*AVP-786 with Avanir for Neurologic/Psychiatric Disorders.* Avanir's (AVNR, \$5.40; Not Rated) AVP-786's is a deuterated version of Avanir's approved Neudexta, indicated for pseudobulbar affect (sudden, frequent episodes of laughing and/or crying). AVP-786 contains much less quinine than Neudexta, which could make its appeal much broader. '786 is being developed in treatment-resistant depression and neuropathic pain, and is entering Phase 2 for treatment resistant major depressive disorders in 2H14. Indications such as agitation in Alzheimer's disease and Parkinson's dyskinesia are also likely. Concert can earn up to \$166 million in additional regulatory, development, and sales milestones, and a royalty in the mid-single digits to low double digits on global sales.

*Jazz's JZP-386 – A Better Xyrem?* Jazz's (JAZZ, \$150.42; Not Rated) JZP-386 is a deuterated analog of sodium oxybate that is nearing Phase 1 development for narcolepsy; sodium oxybate is the active ingredient in Jazz's large and rapidly growing Xyrem franchise; Xyrem posted revenue of \$569 million in 2013, up +50% from the previous year. JZP-386 has the potential to materially expand the franchise by avoiding the cumbersome middle-of-the-night dosing. Concert can earn up to \$117 million in regulatory, development, and sales milestones, and a royalty in the mid-single digits to low double digits on worldwide sales.

*Celgene's Inflammation/Oncology Programs.* Celgene's (CELG, \$172.92; Not Rated) deuterated CTP-730 is in development for inflammatory diseases, and is expected to enter the clinic this year, with Phase 1 results expected in 2015. Though the specific target and parent molecule of CTP-730 has not been disclosed, milestones of up to \$1.4 billion point to the deal's significance (the deal also includes three other potential assets). In terms of inflammatory indications and franchises of importance to Celgene, we note that Thalomid has one inflammatory indication, and Celgene's pipeline contains Otezla/apremilast, pomalidomide, CC-220, CC-292, and others that are being examined for inflammatory indications. We expect greater visibility for this collaboration in 2015.

### Exhibit 3: Concert – Recent Events/Upcoming Catalysts

Date	Event	Comment	Significance
Feb-12	Avanir deal for deuterated dextromethorphan	Program gives solid PK profile with less quinidine	◆◆◆
Feb-13	Jazz deal for deuterated Xyrem (sodium oxybate)	Extension of significant Xyrem franchise	◆◆◆◆
Apr-13	Celgene collaboration - CTP-730, others	Large deal: \$35mm UF, \$1.4B MS, SD/low DD royalty	◆◆◆◆◆
Feb-14	Concert IPO	Capital to advance internal programs more rapidly	◆◆◆◆◆
Apr-14	P2 data for CTP-499 in diabetic kidney disease	Showed signal, leading to end of P2 FDA meeting	◆◆◆◆
2H14	Avanir AVP-786 into Phase 2 in treatment res't dep'n	Phase 2 start triggers \$2mm milestone to Concert	◆◆◆
2H14	Jazz JZP-386 moves into P1 in narcolepsy	Completion of P1 in 2015 to trigger milestone	◆◆◆
2H14	CTP-354 completes MAD study	Important for '854 in a range of indications	◆◆◆
2H14	CTP-354 FDA discussion about higher doses	Could lead to '854 in pain, other indications	◆◆◆◆
2H14	CTP-354 into Phase 2 in spasticity (spinal)	Data for this indication, should help establish PoC	◆◆◆
2H14	CTP-499 end P2 Meeting w/FDA	Should clarify Phase 3, lead to SPA, pot. partner	◆◆◆◆
2H14	Celgene's CTP-730 to start Phase 1 study	Program progress good visibility for Concert	◆◆◆◆◆
2015	CTP-354 moves into Phase 2 in spasticity (MS)	Data for this indication, should help establish PoC	◆◆◆
2015	Avanir to move '786 into P3 in Alzheimer's agitation	Phase 3 start triggers \$2mm milestone to Concert	◆◆◆◆
2015	Additional Concert proprietary assets progress	Concert's DCE platform should broaden during 2015	◆◆◆◆
2015	Jazz JZP-386 completes P1 in narcolepsy	Completion of P1 triggers \$4 milestone	◆◆◆
2015	Celgene's CTP-730 Phase 1 data	Results trigger \$8mm milestone, visibility for Concert	◆◆◆◆
2016	CTP-354 Phase 2 data in spasticity (MS, spinal)	Data in the indications could be a major catalyst	◆◆◆◆

(Significance: ◆ least important., ◆◆◆◆◆ most important.)

Source: Ladenburg Thalmann BioPharmaceuticals Research.

## Concert Pharmaceuticals – Upcoming Potential Catalyst for 2014, 2015

### *Concert's Proprietary Programs*

- **CTP-354** has recently completed additional preclinical toxicology work, and Concert will submit the data to FDA to permit repeated dosing with the molecule above 6mg. We expect clearance from the agency during mid-2014, providing some room for this drug to be dosed higher, if necessary in the pain indications. '354's top-line receptor occupancy data, important for licensing, should be released mid-year.
- **CTP-354** should also move into phase 2 during 2H14 for spasticity associated with spinal cord injury, and in early 2015 for spasticity associated with multiple sclerosis. Data from these Phase 2 studies should read out during 2016. Other larger opportunities such as anxiety and pain also have the potential to begin during 2015.
- **CTP-499** has shown encouraging results in Phase 2 for diabetic kidney disease, and recent changes in trial endpoints have become helpful to the drug development for this indication. Clarity on Phase 3 trial design (just received), an SPA, and a potential partnership could happen in that order over the next 12 months.

### *Concert's Partnered Programs*

- **Avanir's AVP-786**, a deuterated Neudexta, could enter Phase 2 for treatment resistant major depressive disorders in 2H14, triggering a milestone. A related program from Avanir, AVP-923, is now fully enrolled in a Phase 2 study in patients who have material agitation associated with Alzheimer's disease. Avanir has stated repeatedly that it intends to move forward with AVP-786 for the indication, creating the potential for '786 to move into Phase 3 during 2015, with a favorable readout for the Phase 2 study.
- **Jazz's JZP-386**, a deuterated analog of Xyrem could move into Phase 1 for narcolepsy; When JZP-386 completes a P1 study with this molecule, a \$4 million milestone payment is due to Concert. Advancement of this next-gen version of Xyrem, a \$500+mm program, should be a catalyst for CNCE shares.
- **Celgene's deuterated CTP-730** is in development for inflammatory diseases, and is expected to enter the clinic this year, with Phase 1 completion expected in 2015, triggering an \$8mm milestone. Advancement of this program has the potential to be a material catalyst for CNCE shares, despite not knowing material program specifics at this point.

## Concert Pharmaceuticals - Valuation

**Concert and CNCE Shares Valuation.** Because Concert's operations have the potential for significant revenue and earnings variability over the coming quarters and years, we value the company and its assets using a fully-taxed, risk-weighted net present value methodology for each of its assets. We note that with its multiple partnerships and advancing clinical programs, Concert has a diverse portfolio of therapeutic assets, and we assess the total value of these programs at \$22.49 per CNCE share, which underpins our \$24 CNCE price target (see Exhibit 4).

**Valuing Concert's Proprietary Pipeline.** Concert's two most advanced proprietary assets, CTP-354 for spasticity, and CTP-499 for diabetic kidney disease, have material valuation potential, in our view. CTP-354 for spasticity as a result of multiple sclerosis and/or spinal cord injury and possibly other indications such as anxiety and neuropathic



pain, is moving into Phase 2. We believe that a GABA-A modulator with familiar GABA mechanism, yet a distinct profile, with once-daily dosing and less sedation, should have material potential for consideration in spasticity, anxiety, and even pain settings, and have the potential to exceed \$1 billion in peak revenue. We value its collective opportunities at \$7.17 per share. CTP-499, for diabetic kidney disease appears to have achieved material validation after a more full analysis of its Phase 2 trial data, which bodes well for Phase 3 consideration. We assume licensing is to occur after discussions with FDA now that Phase 2 is winding up. Despite risks to the Phase 3 endpoints that remain, we believe more reasonable guidance is emerging along those lines from FDA, and estimate CTP-499 at \$1 billion peak revenue, and value the program at \$5.16 per CNCE share. Other less mature proprietary products are much more modest opportunities at this point and valued at \$0.31 per CNCE share, though proof of concept comes at Phase 1 for many of these deuterated programs, and this part of the portfolio could appreciate quite quickly.

**Exhibit 4: Concert – CNCE Share NPV Summary** (\$000, except per share amts)

Concert Pharmaceuticals - Assets	NPValue	NPV/Share
CTP-354 - Spasticity, Anxiety, others	\$ 128,386	\$7.17
CTP-499 - Diabetic Kidney Disease	\$ 92,330	\$5.16
Other Proprietary Dueterated Assets	\$ 5,468	\$0.31
AVP-786 - CNS indications (Avanir)	\$ 69,267	\$3.87
JZP-386 - Sleep indications (Jazz)	\$ 42,464	\$2.37
CTP-730 - Inflammation (Celgene)	\$ 54,214	\$3.03
Other Celgene - Onc/Inflam (Celgene)	\$ 10,421	\$0.58
Other Corporate	\$ (74,354)	(\$4.15)
Net Cash	\$ 95,006	\$5.31
NOLs, Credits, etc.	\$ 10,052	\$0.56
<b>Concert - Company Valuation</b>	<b>\$ 433,253</b>	<b>\$24.20</b>

Source: Ladenburg Thalmann BioPharmaceuticals Research.

**Valuing Concert's Collaborations.** Regarding Concert's partnered portfolio, Avanir seems to be operating with a good urgency with AVP-786, and is exploring dextromethorphan's broad neurotransmitter receptor activity with the molecule, looking at the therapy in multiple additional indications in addition to depression, including agitation and dyskinesia. Because of these multiple indications, and its potential for its rapid advancement, the economics of this program are valued at \$3.87 per CNCE share. The Jazz program JZP-386 attempts to provide the Xyrem franchise with a product that doesn't have middle of the night dosing, and can help protect against potential loss of exclusivity. Xyrem is growing rapidly (+50% yr/yr) and is large at \$569 million in 2013, and making a more convenient dosing form with longer patent life appears to be a material opportunity, generating a \$2.37 NPV per CNCE share. Finally Celgene has not disclosed the mechanism of CTP-730 inflammation collaboration, though the very large regulatory milestones and peak revenue along the lines of Xyrem, give this collaboration a \$3.03 NPV, by our calculation. The remainder of the Celgene assets are estimated at \$0.58, and net cash, NOLs and the drag of general corporate expense totals \$1.72 per CNCE share, yielding the \$24.20 total, driving our \$24 CNCE shares price target.

## Deuterium Medicinal Chemistry - In Brief

**Deuterium – Fast Facts.** Deuterium is one of two naturally-occurring stable isotopes of hydrogen. The far more common hydrogen isotope, protium, has no neutron in its nucleus. Deuterium, however, has a nucleus that contains both one proton and one neutron. Deuterium's symbol is D or  $^2\text{H}$ . Deuterium possesses physicochemical properties that are similar to those of hydrogen, but its atomic mass is double that of

hydrogen due to the presence of the additional neutron. Deuterium has a presence in the ocean water of about 0.0156% per each hydrogen atom, and is generally produced by starting with water, which contains a small amount of heavy water, where deuterium replaces the hydrogen in the water molecules; this heavy water is then separated for the deuterium. According to Concert (and multiple other sources), the average human body contains about 2 grams of deuterium.

**Deuteration – General Effects on a Molecule.** Chemically, deuterium behaves comparably to ordinary hydrogen, but there are differences in bond energy and bond length for compounds that are deuterated isotopes; these differences are larger than the isotopic differences in any other element. Bonds involving deuterium (and another more rare hydrogen isotope, tritium) are somewhat stronger than the corresponding bonds in hydrogen, enough to occasionally create significant changes in biological reactions. This is because many drugs are metabolized by pathways that involve the breaking of carbon-hydrogen bonds, and having stronger deuterium-carbon bonds or bonds helps deflect or prevent the breakdown of the bonds. Incorporation of deuterium in place of hydrogen at selective points in the molecule therefore has the potential of retaining the biochemical potency and selectivity of a physiologically active compound, while potentially modifying its metabolic properties, and substantially altering its therapeutic profile.

**Deuteration in Drug Development: Material Advancements, Fresh IP.** Deuterated compounds have been used in the clinic for some time as probes for pharmacokinetic and metabolism studies of the related non-deuterated therapeutics, though only relatively recently has deuterium modification received attention as an approach to creating enhanced therapeutics—Concert Pharmaceuticals is a leader in this field of medicinal chemistry. Deuteration can enhance bioavailability and improve the half-life of a compound, and deuterium substitution at specific molecular positions can improve metabolic stability, reduce or eliminate the formation of toxic metabolites, or even increase the formation of desired active metabolites. However, when deuterium is incorporated at a known site of oxidative metabolism, because of the complexity of the process, deuterium's effects on the absorption, distribution, metabolism, and excretion of a molecule is inherently unpredictable. For example, complex enzymatic metabolism may often have other rate-limiting steps, and/or the presence of a stabilized carbon-deuterium bond may cause metabolism to shift to another site or sites on the molecule. Since the behavior of the deuteration of a molecule is largely unpredictable (non-obvious), deuterated compounds are therefore able to generate new intellectual property.

**Deuteration May Result In A Truncated Development Scheme.** The application of deuterium to a molecule has the potential, depending upon specifics of the program, to have some elements of its development program truncated/reduced. For instance, with the Avanir program, FDA has permitted Avanir to utilize data generated from its dextromethorphan-based program (in this case, a different asset called AVP-923) and apply it to the development package for the deuterated dextromethorphan analog AVP-786 that Avanir licensed from Concert. This should help '786 without duplicating the entire clinical program of '923, but it can instead be substituted when the POC in a particular indication has been established. It is uncertain if this type of consideration is possible for all programs, though when it is, it should be clearly beneficial in terms of development time, spending, and efficiencies.

## CTP-499: Concert's PDE Inhibitor for Diabetic Kidney Disease

**Diabetic Kidney Disease Background.** Diabetic kidney disease (diabetic nephropathy) is a condition where the ability of a person's kidney to filter blood is materially impaired, which ultimately can result in the need for dialysis and renal transplantation. Type 2 diabetes is the leading cause of chronic kidney disease, and many patients with this

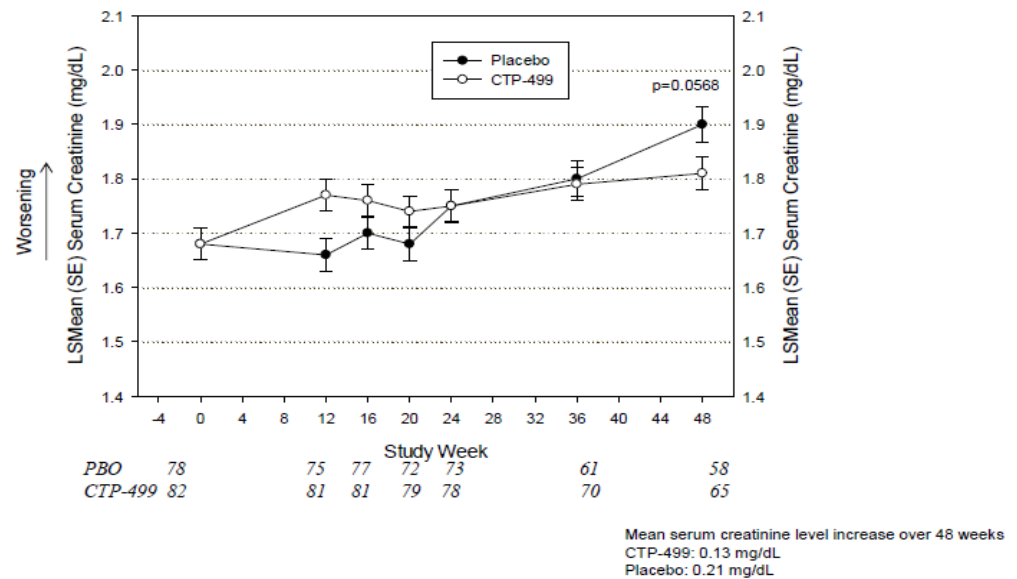
disease continue to experience a decline in renal function despite treatment with standard of care therapies, such as angiotensin modulators (ACEs or ARBs). There are between 900k and 1.8 million type 2 diabetics with macroalbuminuria in the US, according to Concert. Concert is developing CTP-499 as an add-on to the standard-of-care designed to slow progression of patients with the condition toward kidney failure.

**CTP-499 Development Rationale.** Type 2 diabetic kidney disease is a multifactorial disease involving inflammatory, oxidative and fibrotic processes. Phosphodiesterases (PDEs) are a family of enzymes that regulate the pathways involved in these processes. CTP-499 is a deuterated analog of 1-(S)-5-hydroxyhexyl-3,7-dimethylxanthine (or HDX), which is an active metabolite of pentoxifylline (Trental) that been deuterated to improve the compound's metabolic stability and allow greater exposure to pharmacologically active metabolites. Pentoxifylline is a broad spectrum inhibitor of phosphodiesterase (PDEs), that was approved more than 30 years ago for the treatment of intermittent claudication (lower limb pain resulting from obstructed arteries). Through multiple complex mechanisms pentoxifylline has been characterized as having a role in reducing inflammatory and fibrotic processes and has specifically been shown to reduce  $\text{TNF}\alpha$  production. PDEs are enzymes that are thought to play an important role in the progression and worsening of diabetic kidney disease, and as a result pentoxifylline has been reported in several clinical studies--by Lin, et al. in *American Journal of Kidney Disease* in 2008, by Perkins in *American Journal of Kidney Disease* in 2009, and by Navarro, et al. in *Journal of the American Society of Nephrology* in 2005, among others--to have beneficial effects on proteinuria and renal function decline, important measures in the progression of kidney disease.

**CTP-499's Mechanism: A Role in Renal Disease and Possibly Beyond.** CTP-499, a deuterated active metabolite of pentoxifylline, is also a novel, oral multi-subtype selective inhibitor of phosphodiesterases (PDEs). In preclinical studies, CTP-499 inhibits PDE 2, 3, 4, and 5. In addition to multiple preclinical studies, CTP-499 has been examined in an extensive Phase 2 study in diabetic kidney disease (described in detail below), where it has demonstrated encouraging results. We note that the anti-inflammatory and antifibrotic effects of the parent drug pentoxifylline have suggested a role for that molecule in reducing the consequences of hepatic fibrosis and even cirrhosis in various settings. For instance, pentoxifylline has been studied in settings such as alcoholic cirrhosis, fibrosis due to radiation, and is being evaluated in the more severe types of non-alcoholic fatty liver disease, such non-alcoholic steatohepatitis (NASH). Given a similar PDE inhibition mechanism, CTP-499 could also have consideration in these additional hepatic settings, and in particular NASH, in addition to diabetic kidney disease, which create an interesting long term course of development for the molecule.

**CTP-499 in Diabetic Kidney Disease: Phase 2 Trial Specifics.** The Phase 2 trial was recently completed for CTP-499. Part 1 was a double-blind, parallel, two-arm study evaluating the safety and efficacy of 600 mg of CTP-499 bid vs. placebo for 24 weeks which enrolled 182 patients. Part 2 was a blinded 24-week extension in which all who completed Part 1 were eligible to continue on CTP-499 or placebo; 143 patients enrolled in this part and 124 completed. Concert has analyzed the combined 48 weeks of data from Parts 1 and 2 of the clinical trial for 123 of the 124 patients that completed Part 2. Top line results for the first 48 weeks are discussed below. (There is also a 48 week open-label extension study which has enrolled 102 patients.) The primary endpoint was the change in urine albumin to creatinine ratio (UACR) at 24 weeks. Key secondary endpoints included changes in serum creatinine and eGFR. Enrollment criteria included UACR of  $\geq 200$  mg/g for men, and 300 mg/g for women, and eGFR of 23 to 89 mL/min/1.73 m<sup>2</sup>, indicating mild to moderately severe type 2 diabetes.



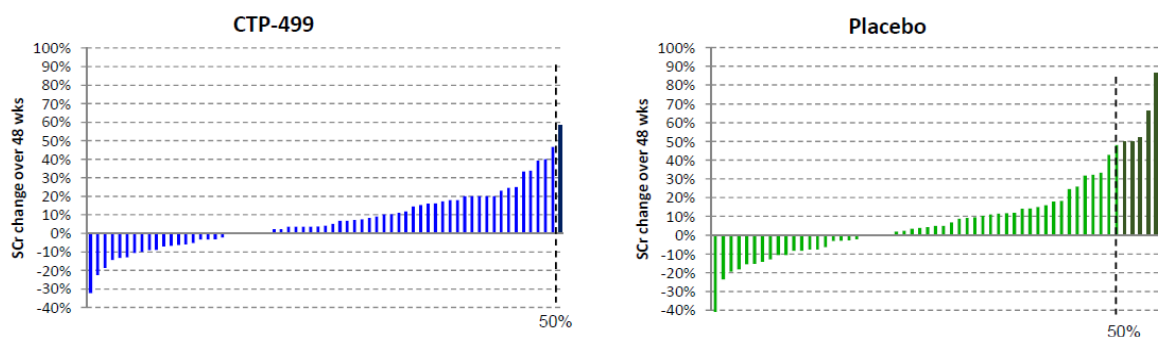
**Exhibit 5: CTP-499 - Shows Trend Against Serum Creatinine Increases**

Source: Concert corporate presentation May 2014.

**CTP-499 Trial Results Encourage.** In this trial, CTP-499 did not demonstrate a statistically significant difference at the primary endpoint of UACR at 24 weeks. At 48 weeks, the mean level in those taking CTP-499 increased by 0.13 mg/dL versus an increase of 0.21 mg/dL for placebo (Exhibit 5). We note that while UACR is used as an indicator of activity in diabetic kidney disease trials, it is not an accepted Phase 3 endpoint by FDA for US approval in these patients. Importantly, 499 did show additional encouraging results in the study. These include:

- Even though the trial was not powered for statistical significance with respect to serum creatinine or eGFR, and 499s results at 48 weeks were nearly significant on serum creatinine levels (Exhibit 12) and there was a positive trend in eGFR levels;
- The reduction in the number of patients with large declines in eGFR (a worsening marker) was nearly significant, and a reduction in patients with large increases in serum creatinine (another worsening marker) was significant (Exhibit 13), though this was examined in a post-hoc analysis;
- Almost all of those with the greatest decline in eGFR (>30%) occurred in those patients with UACR above the median of approximately 850 m/g, providing the potential for an enriched trial group to be enrolled in a subsequent clinical trial, which would mean fewer patients would be required for such a trial.

**Phase 2 Results Encouraging For A Phase 3 Trial.** Importantly, the endpoints for diabetic kidney disease are evolving favorably for the industry and for Concert. This is due to the multiple recent trial failures with a number of therapies, so the migration to less onerous endpoints appears to be underway. Specifically, the reduction in the number of patients with large declines in eGFR, or a reduction in those with large increases in serum creatinine specifically defined as time to >50% increase in serum creatinine compared to placebo, may be acceptable endpoints in Phase 3 trials in type 2 diabetes patients with kidney disease.

**Exhibit 6: CPT-499 in Phase 2: Protects Against Large Increases in Serum Creatinine****CTP-499**

- 1/65 (1.5%)  $\geq 50\%$  increase

**p = 0.026****Placebo**

- 6/58 (10.3%)  $\geq 50\%$  increase

*Except for one placebo patient all instances of a  $\geq 50\%$  increase in serum creatinine after 48 weeks occurred in patients with a baseline UACR greater than the median value of 850 mg/g*

Source: Concert corporate presentation June 2014.

**FDA Recently Granted An SPA Utilizing A New, More Achievable Endpoint.** This new Phase 3 endpoint has recently been granted by FDA in a Special Protocol Assessment (SPA) for Nephrogenex. This endpoint migration comes through discussions sponsored by the National Kidney Foundation and FDA in December 2012, which concluded as a result of an extensive analysis of kidney disease studies that there is a highly significant correlation with  $>50\%$  increase in serum creatinine and time to end stage renal disease. We believe that solidifying a Phase 3 trial with those endpoints could be within reach of CTP-499. Solidification of these endpoints with FDA has the potential to result in licensing of CTP-499. The company is now beginning its dialog with FDA regarding its end of Phase 2 meeting and potential Phase 3 trials for CTP-499, and we believe Concert is likely to pursue an SPA for the indication. We believe this solidification of a development pathway could lead to a licensing deal for '499, and we model that being achieved in 2015 as we consider our estimates for the drug.

**CTP-499 Economics to Concert.** As significant Phase 3 trials are contemplated with CTP-499, we expect the molecule to ultimately be developed in a partnership. We assume international licensing could occur in 2H14 after Concert's discussions with FDA at their end of Phase 2 meeting, and that could be a validating event for the CTP-499 program; we model a licensing deal occurring in 2015. For revenue modeling purposes, since CTP-499 is being partnered at a later stage than the other Concert molecules, but does not have an existing brand it is extending, we expect deal terms slightly north of the Jazz and Avanir deals, somewhat in line with that of Celgene, though with a higher royalty and more modest milestones due to regulatory success.

The potential for an effective compound in the setting is quite material, as there are more than one million diabetics in the US with macroalbuminuria ( $>300\text{mg/g}$ ). If successful in Phase 3, we believe pricing of a therapy in the range of \$10,000 to \$20,000 per year might be considered for such a treatment, with 50,000 potential candidates for the therapy at peak, providing an estimated US peak revenue potential exceeding \$1 billion in the US, with similar potential internationally. Though we do have some higher risk weightings for this program, given the questions about pivotal trial endpoints, with its considerable revenue potential, we assess the fully taxed, risk-weighted CTP-499 NPV at \$5.16 per CNCE share (Exhibit 7).

**Exhibit 7: CTP-499 – NPV Calculation to Concert**

	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
CTP-499 - Diab. Kidney Dis. + more	-	-	-	-	-	-	105,000	325,000	600,000	825,000	1,025,000	1,200,000	1,375,000	1,525,000	1,675,000	1,825,000	1,975,000
US Sales	-	-	-	-	-	-	70,000	250,000	425,000	550,000	650,000	725,000	800,000	850,000	900,000	950,000	1,000,000
Int'l Sales	-	-	-	-	-	-	35,000	75,000	175,000	275,000	375,000	475,000	575,000	675,000	775,000	875,000	975,000
US Upfront/Milestones	-	25,000	-	-	10,000	20,000	50,000	-	-	-	50,000	-	-	-	-	-	100,000
US Royalty Rate	-	0%	0%	0%	0%	0%	15%	15%	15%	20%	20%	20%	20%	20%	20%	20%	25%
US Royalty	-	-	-	-	-	-	10,500	37,500	63,750	110,000	130,000	145,000	160,000	170,000	180,000	190,000	250,000
Total US Rev to Concert	-	25,000	-	-	10,000	20,000	60,500	37,500	63,750	110,000	180,000	145,000	160,000	170,000	180,000	190,000	350,000
Int'l Upfront/Milestones	-	-	15,000	-	5,000	15,000	25,000	-	-	25,000	-	-	-	-	-	-	-
Int'l Royalty Rate	-	0%	0%	0%	0%	0%	15%	15%	15%	20%	20%	20%	25%	25%	25%	25%	25%
Int'l Royalty	-	-	-	-	-	-	5,250	11,250	26,250	55,000	75,000	95,000	143,750	168,750	193,750	218,750	243,750
Total Int'l Rev to Concert	-	-	15,000	-	5,000	15,000	30,250	11,250	26,250	80,000	75,000	95,000	143,750	168,750	193,750	218,750	243,750
Total Revenue to Concert	-	25,000	15,000	-	5,000	15,000	105,500	287,500	488,750	685,000	780,000	870,000	960,000	1,020,000	1,080,000	1,140,000	1,250,000
Concert Expenses	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
COGS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
COGS pct	-	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na	na
SG&A	-	250	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
R&D	-	5,000	1,000	500	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Concert Expenses	-	5,250	6,000	1,000	500	-	-	-	-	-	-	-	-	-	-	-	-
Net to Concert	(5,250)	19,000	14,000	(500)	5,000	15,000	105,500	287,500	488,750	685,000	780,000	870,000	960,000	1,020,000	1,080,000	1,140,000	1,250,000
Days to End	25.0	390.0	756.0	1121.0	1486.0	1851.0	2217.0	2582.0	2947.0	3312.0	3678.0	4043.0	4408.0	4773.0	5139.0	5504.0	5869.0
Years to end	0.1	1.1	2.1	3.1	4.1	5.1	6.1	7.1	8.1	9.1	10.1	11.1	12.1	13.1	14.1	15.1	16.1
NPV/year	-5209.4	13787.7	7519.3	-252.0	1270.7	2279.1	8988.3	16329.5	18506.8	17291.9	13112.1	9750.1	7172.5	5080.5	3582.2	2520.8	1842.7
Discount Rate	12%	35%	35%	25%	40%	45%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Tax rate used	0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
NPV Taxed (effective rate)	\$ (5,209)	\$ 13,788	\$ 7,519	\$ (252)	\$ 1,271	\$ 2,279	\$ 8,988	\$ 10,614	\$ 12,029	\$ 11,240	\$ 8,523	\$ 6,338	\$ 4,662	\$ 3,302	\$ 2,328	\$ 1,639	\$ 1,198
Total Value		\$126,762															
NPV Per Share		\$7.08															
Total Value taxed		\$92,330															
NPV/share taxed		\$5.16															

Source: Ladenburg Thalmann BioPharmaceuticals Research.

**Diabetic Kidney Disease Statistics.** Approximately 26 million in the US in 2010 had diabetes and 90% to 95% were type 2 diabetes. There are between 900k and 1.8 million type 2 diabetics with macroalbuminuria in the US, and diabetic kidney disease is now the nation's leading cause of dialysis, kidney transplant, and death from kidney failure. According to Concert, the transition of a patient to dialysis increases patient cost by ~\$60,000 per year. Patients with both type 2 diabetes and chronic kidney disease have a 270% increase in mortality compared to type 2 diabetics without chronic kidney disease (NHANES Survey in 2011).

**Concert Pharmaceuticals - Risks**

The following Risks to purchasing CNCE shares include, but are not limited to:

**Regulatory/FDA.** As with any company whose main business focuses on the development of pharmaceuticals, Concert is subject to the strenuous regulatory requirements of the US Food and Drug Administration (FDA) and other international regulatory agencies such as the EMEA to have its new drugs approved. Promotion of its approved drug products is also highly regulated by FDA and related agencies throughout the globe. Also, in general, though the company's specific focus on ethical (prescription) pharmaceuticals places significant risk on its operations due to the scrutiny of FDA and other governmental regulatory bodies, we believe this specific risk over time should be no greater than that for any other research-based drug development company.

**Material Dependence Upon CTP-499, CTP-354 Progress.** CTP-354 and CTP-499 are two of Concert's most advanced proprietary clinical candidates in development. These novel molecules may take material time and resources to finish clinical development, if they are able to complete at all, and there is certainly no guarantee that the company will be successful in doing so. In addition, Concert may seek one or more collaborators for future development of CTP-499. There is a risk that the company may not be able to enter into a collaboration for the therapy, or is able to enter into one with terms that are beneficial to CNCE shareholders. These development programs have garnered major investor interest within Concert's operations; if they do not progress, there is material risk that CNCE shares could trade downward.

**Risks With Partnered Programs.** Concert has a number of partnered programs, including material efforts with Celgene, Jazz Pharmaceuticals, and Avanir Pharmaceuticals. These partnered development programs have garnered major investor interest within Concert's operations. Because these programs are ultimately under the direction of other companies, there is no guarantee those programs will progress at all, or in a way that is beneficial to Concert or CNCE shareholders. If any or all of these programs do not progress in a way that is beneficial to Concert, it is possible that CNCE shares may come under material negative pressure.

**Deuteration: Approval, Manufacturing Risks.** To the best of our knowledge, no deuterated drug has ever been successfully approved or commercialized. There may be specific risks to gaining licensure for these types of agents from regulatory authorities, though these do not appear to have not emerged at this point. In addition, the company may also incur unforeseen manufacturing challenges with deuterated compounds, or manufacturing costs that are required for the production of any product candidate that receives marketing approval may turn out to be substantial, though excessive cost have not specifically manifested at this point.

**Other Risks.** Concert has incurred significant losses since inception, expects to incur losses for at least the next several years, and may never sustain profitability. Concert also has a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for future viability. Concert is an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may make its common stock less attractive to investors.

**Concert Pharmaceuticals, Inc.**

	2011A	2012A	2013A	1Q14A	2Q14E	3Q14E	4Q14E	2014e	2015E	2016E	2017E	2018E
<b>Income Statement (\$000, except per share amts.)</b>												
Product Revenue												
CTP-354 Total (Int'l to partner)	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
CTP-499 Total (top line to partner)	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Other/Collab revenue	0	0	0	0	0	0	0	0	0	0	0	0
<b>Total Proprietary Sales Revenue</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
Milestone & Royalty Revenue												
<b>Total Royalties from Partners</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>0</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>
<b>Upfront, Milestones from Partners</b>	<b>\$ 5,500</b>	<b>\$ 1,500</b>	<b>\$ 2,000</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 2,000</b>	<b>\$ 2,000</b>	<b>\$ 19,000</b>	<b>\$ 13,750</b>	<b>\$ 40,750</b>	<b>\$ 152,750</b>
<b>License and Development Revenue</b>	<b>13,967</b>	<b>11,349</b>	<b>23,408</b>	<b>1,613</b>	<b>2,000</b>	<b>2,250</b>	<b>2,500</b>	<b>\$ 8,363</b>	<b>8,500</b>	<b>8,500</b>	<b>9,000</b>	<b>9,000</b>
<b>Total Concert Revenue</b>	<b>\$19,467</b>	<b>\$12,849</b>	<b>\$25,408</b>	<b>\$1,613</b>	<b>\$2,000</b>	<b>\$2,250</b>	<b>\$4,500</b>	<b>\$10,363</b>	<b>\$27,500</b>	<b>\$22,250</b>	<b>\$49,750</b>	<b>\$161,750</b>
<b>Expenses:</b>												
COGS	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
R & D	23,436	24,193	21,790	5,594	6,000	6,500	6,750	\$ 24,844	26,500	30,000	30,000	35,000
S G & A	7,377	7,266	8,028	2,538	2,400	2,500	2,600	\$ 10,038	10,000	10,200	13,000	20,000
<b>Total Expenses</b>	<b>\$30,813</b>	<b>31,459</b>	<b>29,818</b>	<b>\$8,132</b>	<b>\$8,400</b>	<b>\$9,000</b>	<b>\$9,350</b>	<b>\$ 34,882</b>	<b>\$36,500</b>	<b>\$40,200</b>	<b>\$43,000</b>	<b>\$55,000</b>
Operating Income	(11,346)	(18,610)	(4,410)	(6,519)	(6,400)	(6,750)	(4,850)	\$ (24,519)	(9,000)	(17,950)	6,750	106,750
Operating Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Interest Income	44	22	20	4	60	65	60	\$ 189	150	175	200	800
Interest Expense	(18)	(1,856)	(1,666)	0	0	0	0	\$ -	0	(200)	(200)	(200)
Other Income (Expense)	0	0	0	0	0	0	0	\$ -	0	0	0	0
Other financing income (expense)	0	0	0	(435)	(100)	(100)	(100)	\$ (735)	(500)	(400)	(350)	0
Total Other Income, net	26	(1,834)	(1,646)	(431)	(40)	(35)	(40)	\$ (546)	(350)	(425)	(350)	600
<b>Pretax Income</b>	<b>(11,320)</b>	<b>(20,444)</b>	<b>(6,056)</b>	<b>(6,950)</b>	<b>(6,440)</b>	<b>(6,785)</b>	<b>(4,890)</b>	<b>\$ (25,065)</b>	<b>(9,350)</b>	<b>(18,375)</b>	<b>6,400</b>	<b>107,350</b>
Pretax Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
<b>Effective Taxes</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>448</b>	<b>9,125</b>
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	7.0%	8.5%
<b>Fully Taxed rate</b>	<b>(4,302)</b>	<b>(7,769)</b>	<b>(2,301)</b>	<b>(2,641)</b>	<b>(2,447)</b>	<b>(2,578)</b>	<b>(1,858)</b>	<b>\$ (9,525)</b>	<b>(3,553)</b>	<b>(6,983)</b>	<b>2,432</b>	<b>40,793</b>
Tax Rate	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%	38.0%
Other Convertible Preferred, other securities transactions	(1,069)	(388)	(396)	(55)	(50)	(45)	(40)	(190)	-	-	-	-
<b>Net Income (Loss) - Effective taxed</b>	<b>(12,389)</b>	<b>(20,832)</b>	<b>(6,452)</b>	<b>(7,005)</b>	<b>(6,490)</b>	<b>(6,830)</b>	<b>(4,930)</b>	<b>\$ (25,255)</b>	<b>(9,350)</b>	<b>(18,375)</b>	<b>5,952</b>	<b>98,225</b>
<b>Income - Fully taxed</b>	<b>(7,018)</b>	<b>(12,675)</b>	<b>(3,755)</b>	<b>(4,309)</b>	<b>(4,043)</b>	<b>(4,207)</b>	<b>(3,032)</b>	<b>\$ (15,590)</b>	<b>(5,797)</b>	<b>(11,393)</b>	<b>3,968</b>	<b>66,557</b>
Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Other Comprehensive Income (Loss)	16	(5)	(1)	(8)	-	-	-	(8)	-	-	-	-
<b>Comprehensive Income (Loss)</b>	<b>(11,304)</b>	<b>(20,449)</b>	<b>(6,057)</b>	<b>(6,958)</b>	<b>(6,440)</b>	<b>(6,785)</b>	<b>(4,890)</b>	<b>\$ (25,073)</b>	<b>(9,350)</b>	<b>(18,375)</b>	<b>6,400</b>	<b>107,350</b>
<b>EPS (ex-charges; eff. taxed)</b>	<b>(\$9.66)</b>	<b>(\$16.15)</b>	<b>(\$4.99)</b>	<b>(\$0.76)</b>	<b>(\$0.37)</b>	<b>(\$0.38)</b>	<b>(\$0.28)</b>	<b>(\$1.61)</b>	<b>(\$0.52)</b>	<b>(\$1.02)</b>	<b>\$0.31</b>	<b>\$5.15</b>
<b>EPS (ex-charges; fully-taxed)</b>	<b>(\$5.47)</b>	<b>(\$9.83)</b>	<b>(\$2.91)</b>	<b>(\$0.47)</b>	<b>(\$0.23)</b>	<b>(\$0.24)</b>	<b>(\$0.17)</b>	<b>(\$1.00)</b>	<b>(\$0.32)</b>	<b>(\$0.63)</b>	<b>\$0.21</b>	<b>\$3.44</b>
EPS - comprehensive Income (eff taxes)	(\$8.81)	(\$15.85)	(\$4.69)	(\$0.76)	(\$0.36)	(\$0.38)	(\$0.27)	(\$1.60)	(\$0.52)	(\$1.02)	\$0.33	\$5.54
Shares O/S (000), Basic	1,283	1,290	1,292	9,188	17,750	17,800	17,850	15,647	17,875	17,975	18,975	19,075
Shares O/S (000), Diluted	1,283	1,290	1,292	9,188	17,750	17,800	17,850	15,647	17,875	17,975	19,275	19,375
<b>-- Expenses (% of sales) --</b>												
Cost of Sales (product sales)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	NM	NM	NM
Gross	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
R & D	NM	NM	NM	NM	NM	NM	NM	NM	96.4%	134.8%	60.3%	21.6%
S G & A	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%	31.0%
Total	158.3%	244.8%	117.4%	504.2%	420.0%	400.0%	207.8%	336.6%	132.7%	180.7%	86.4%	34.0%
<b>-- Year / Year Growth --</b>												
Revenue	NM	NM	NM	NM	NM	NM	NM	NM	96.4%	-19.1%	123.6%	225.1%
Operating Income	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Pretax Income	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Income	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
EPS (ex-charges)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
EPS (ex-charges; fully-taxed)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM

Source: Concert Pharmaceuticals Inc. SEC documents and Ladenburg Thalmann BioPharmaceuticals estimates.

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**Concert Pharmaceuticals, Inc.****Balance Sheet & Statement of Cash Flow (\$mm)**

	12/31/2011A	12/31/2012A	12/31/2013A	12/31/2014E	12/31/2015E	12/31/2016E	12/31/2017E
<b>BALANCE SHEET</b>							
<b>ASSETS</b>							
Cash & equivalents	\$22.9	\$7.5	\$9.6	\$69.3	\$78.7	\$77.5	\$80.0
Investments/Mktb. Securities	\$19.7	\$20.1	\$23.0	\$23.0	\$23.0	\$23.0	\$23.0
Account receivable	\$0.6	\$0.1	\$0.3	\$2.1	\$4.1	\$3.3	\$7.5
Prepaid & other current assets	\$0.9	\$1.2	\$1.1	\$0.1	\$0.3	\$0.2	\$0.5
<b>Total Current Assets</b>	<b>\$44.1</b>	<b>\$28.9</b>	<b>\$34.0</b>	<b>\$94.6</b>	<b>\$106.1</b>	<b>\$104.1</b>	<b>\$111.0</b>
Property & Equipment, net, other	\$4.4	\$3.5	\$2.5	\$2.5	\$2.5	\$2.5	\$2.5
Long term investment/Restricted Cash	\$0.0	\$0.0	\$0.7	\$0.7	\$0.7	\$0.7	\$0.7
Other Assets	\$0.8	\$0.8	\$2.5	\$2.5	\$2.5	\$2.5	\$2.5
<b>Total Assets</b>	<b>\$49.4</b>	<b>\$33.1</b>	<b>\$39.8</b>	<b>\$100.3</b>	<b>\$111.9</b>	<b>\$109.8</b>	<b>\$116.7</b>
<b>LIABILITIES &amp; S.E.</b>							
Accounts payable	\$1.6	\$0.8	\$1.0	\$1.4	\$2.8	\$3.3	\$7.5
Accrued expenses	\$1.5	\$2.0	\$2.5	\$2.7	\$2.9	\$3.1	\$3.4
Deferred short-term revenue	\$6.9	\$0.0	\$4.3	\$1.0	\$0.0	\$0.0	\$0.0
Leasehold improvement loan	\$0.3	\$0.3	\$0.3	\$0.3	\$0.3	\$0.3	\$0.3
Loans payable, net of discount	\$0.0	\$4.8	\$7.8	\$5.6	\$8.3	\$3.3	\$10.0
<b>Total Current Liabilities</b>	<b>\$10.3</b>	<b>\$7.9</b>	<b>\$15.9</b>	<b>\$11.0</b>	<b>\$14.2</b>	<b>\$10.1</b>	<b>\$21.1</b>
Deferred revenue, net of current	\$4.1	\$2.8	\$15.3	\$9.0	\$3.0	\$0.0	\$0.0
Leasehold improvement loan, net of current	\$0.9	\$0.6	\$0.2	\$2.0	\$2.0	\$2.0	\$2.0
Deferred lease incentive	\$1.4	\$0.9	\$0.4	\$2.0	\$2.0	\$2.0	\$2.0
Deferred rent, net of current	\$0.6	\$0.5	\$0.2	\$2.0	\$2.0	\$2.0	\$2.0
Warrant to purchase redeemable securities	\$0.2	\$0.5	\$0.5	\$0.5	\$0.5	\$0.5	\$0.5
Note Payable/Long-term Liabilities	\$7.1	\$14.9	\$7.1	\$7.1	\$7.1	\$7.1	\$7.1
<b>Total Liabilities</b>	<b>\$24.7</b>	<b>\$28.0</b>	<b>\$39.6</b>	<b>\$33.6</b>	<b>\$30.8</b>	<b>\$23.7</b>	<b>\$34.7</b>
<b>Total Shareholders Equity</b>	<b>\$24.7</b>	<b>\$5.2</b>	<b>\$0.1</b>	<b>\$66.7</b>	<b>\$81.1</b>	<b>\$86.1</b>	<b>\$82.0</b>
<b>Total Liabilities and Shareholders Equity</b>	<b>\$49.4</b>	<b>\$33.1</b>	<b>\$39.8</b>	<b>\$100.3</b>	<b>\$111.9</b>	<b>\$109.8</b>	<b>\$116.7</b>
<b>CASH FLOW STATEMENT</b>							
<b>Cash Flow from Operating Activities</b>							
Net income (loss)	(11.3)	(\$20.4)	(6.1)	(20.3)	(9.4)	(18.4)	6.4
Other adjustments	0.0	\$0.0	0.0	0.0	20.0	20.0	(15.0)
Depreciation & Amortization	1.6	\$1.5	1.3	1.1	1.2	1.4	2.0
Noncash compensation expense	0.9	\$0.9	1.0	1.0	1.5	2.0	2.5
Other non-cash financing expense	0.8	\$0.4	0.3	0.0	0.0	0.0	0.0
Amortization of financing costs, warrants	(0.5)	(\$0.1)	(0.4)	0.0	0.0	0.0	0.0
Accounts receivable	1.0	\$0.5	(0.2)	(1.8)	(2.0)	0.8	(4.1)
Interest receivable	0.1	\$0.0	0.0	0.0	0.0	0.0	0.0
Prepaid expenses, and other current assets	(0.0)	(\$0.4)	0.0	1.0	(0.1)	0.1	(0.3)
Other assets	(0.1)	\$0.0	0.1	0.0	0.0	0.0	0.0
Accounts payable and accrued expenses	0.7	(\$0.3)	0.1	0.6	1.6	0.8	4.4
Other oper.activities (deferred rent, revenue)	(11.2)	(\$8.4)	16.7	(8.5)	(3.4)	(7.9)	6.6
<b>Cash Flow from Operating Activities</b>	<b>(18.1)</b>	<b>(26.4)</b>	<b>13.0</b>	<b>(26.9)</b>	<b>9.4</b>	<b>(1.2)</b>	<b>2.5</b>
<b>Cash Flow from Investing Activities</b>							
Maturities of Investments	64	\$37.7	27	0	0	0	0
Purchase of investments	(41)	(\$38.4)	(30)	0	0	0	0
Capital Expenditures, net	(0.3)	(\$0.5)	(0.4)	0.0	0.0	0.0	0.0
Other	-	\$0.0	-	-	-	-	-
	<b>22.9</b>	<b>(1.2)</b>	<b>(3.64)</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>
<b>Cash Flow from Financing Activities</b>							
Issuance of loan payable, net	7.3	\$12.5	0	0	0	0	0
Principle pmts of loan payable	0.0	\$0.0	(5)	0	0	0	0
Repayment of leasehold impt loan	(0.3)	(\$0.3)	(0)	0	0	0	0
Proceeds from iss. of common stock (net)	0.0	\$0.0	0	86.6	0.0	0.0	0.0
Proceeds/Retirement of Debt, Other	0.0	\$0.0	0	0.0	0.0	0.0	0.0
Payment of IPO/offering costs	0.0	\$0.0	(2)	0.0	0.0	0.0	0.0
<b>Cash Flow from Financing Activities</b>	<b>7.0</b>	<b>12.2</b>	<b>(7.2)</b>	<b>86.6</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>
<b>Beginning cash balance</b>	<b>11.1</b>	<b>\$22.9</b>	<b>7.5</b>	<b>9.6</b>	<b>69.3</b>	<b>78.7</b>	<b>77.5</b>
Net increase (decrease) in cash	11.8	(\$15.5)	2.1	59.7	9.4	(1.2)	2.5
<b>Ending cash balance</b>	<b>22.9</b>	<b>7.5</b>	<b>9.6</b>	<b>69.3</b>	<b>78.7</b>	<b>77.5</b>	<b>80.0</b>

Source: Concert Pharmaceuticals Inc. SEC documents and Ladenburg Thalmann BioPharmaceuticals estimates.

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# APPENDIX A: IMPORTANT RESEARCH DISCLOSURES

## ANALYST CERTIFICATION

I, Robert C. Hazlett, attest that the views expressed in this research report accurately reflect my personal views about the subject security and issuer. Furthermore, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report, provided, however, that:

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## COMPANY BACKGROUND

Concert Pharmaceuticals, founded in 2006 by Richard Aldrich, Roger Tung, and Christoph Westphal, creates novel medicines by applying its DCE (Deuterated Chemical Entity) Platform technologies to molecules. The DCE approach involves the selective addition of deuterium, a stable isotope of hydrogen, to molecules, resulting in clinical therapeutic candidates with improved pharmacology. This approach has the potential to enable more efficient drug discovery and clinical development. Concert's proprietary programs include CTP-354, a novel GABA-A modulator for spasticity and anxiety, and CTP-499, a PDE inhibitor for diabetic kidney disease. Promising partnered programs include Jazz's JZP-386, a long-acting Xyrem, Avanir's AVP-786, an improved Neudexta, and multiple programs with Celgene. Concert has also developed a broad portfolio of deuterated molecules that are expected to migrate into and through the clinic over time.

## VALUATION METHODOLOGY

**Concert Pharmaceuticals Valuation.** Concert and CNCE Shares Valuation. Because Concert's operations have the potential for significant revenue and earnings variability over the coming quarters and years, we value the company and its assets using a fully-taxed, risk-weighted net present value methodology for each of its assets. We note that with its multiple partnerships and emerging clinical programs, Concert has a diverse portfolio that contributes to its valuation. Our total of the programs yield a value of \$24.20 per CNCE share, driving our \$24 CNCE shares price target.

**Concert's Proprietary Pipeline.** Concert's two most advanced proprietary assets, CTP-354 for spasticity, and CTP-499 for diabetic kidney disease, have material valuation. CTP-354 for spasticity as a result of multiple sclerosis and/or spinal cord injury and possibly other indications such as anxiety and neuropathic pain, is moving into Phase 2. We believe that a GABA-A modulator with familiar mechanism, yet a distinct profile, with once-daily dosing and less sedation, should have material potential for consideration in spasticity, anxiety, and even pain settings, and have the potential to exceed \$1 billion in peak revenue; we value its collective opportunities at \$7.17 per share. CTP-499, for diabetic kidney disease appears to have achieved material validation after a more full analysis of its Phase 2 trial data, which bodes well for Phase 3 consideration. We assume international licensing should be able to occur after discussions with FDA of their end of Phase 2 meetings in 2H14, and that could be a validating event for the CTP-499 program. We estimate CTP-499 at \$1 billion peak revenue in the US, despite risks to the endpoints that remain, value the program at \$5.16 per CNCE share. Other less mature proprietary products are much more modest opportunities at this point and valued at \$0.31 per CNCE share, though proof of concept comes at Phase 1 for many of these deuterated programs, and this part of the portfolio could appreciate quite quickly.

**Concert's Collaborations.** Regarding Concert's partnered portfolio, Avanir seems to be operating with a good urgency with AVP-786, and is exploring dextromethorphan's broad neurotransmitter receptor activity with the molecule, looking at the therapy in multiple additional indications in addition to depression, including agitation and dyskinesia. Because of these multiple indications, and its potential for its rapid advancement, the economics of this program are valued at \$3.87 per CNCE share. The Jazz program JZP-386 attempts to provide the Xyrem franchise with a product that doesn't have middle of the night dosing, and can help protect against potential loss of exclusivity. Xyrem is growing rapidly (+50% yr/yr) and is large at \$569 million annually, and making a more convenient dosing form with longer patent life appears to be a materially opportunity, generating a \$2.37 NPV per CNCE share. Finally, Celgene has not disclosed what the mechanism of CTP-730 inflammation collaboration, though the very large regulatory milestones and peak revenue along the lines of Xyrem, give this collaboration a \$3.61 NPV. The remainder of the Celgene assets are estimated at \$0.58, and net cash, NOLs and the drag of general corporate expense totals (\$4.15) per CNCE share, yielding the \$24.20 total, driving our \$24 CNCE shares price target.

Factors which could impede CNCE shares from reaching our price target include the lack of progress for Concert's proprietary therapeutics CTP-499 and CTP-354 in their respective indications. Progress by indirect competition in indications for chronic kidney failure or spasticity could also impede CNCE shares from reaching our target. Concert has a number of partnered programs, including efforts with Celgene, Jazz Pharmaceuticals, and Avanir, and there is no guarantee those programs will progress at all or in a way that is beneficial to Concert; a lack of progress with any or all of these partnered programs could be an impediment to CNCE shares reaching our target price. In addition, negative

equity market conditions overall, or in particular with regard to the biotechnology sector, or healthcare in general, could be an impediment to CNCE shares reaching our target. Also a change in the regulatory requirements for drugs in development could be an impediment to the advancement in CNCE shares. These risks listed are merely a sample of the types of issues that could impede CNCE shares from advancing, and are not meant to be all inclusive.

## RISKS

**Regulatory/FDA.** As with any company whose main business focuses on the development of pharmaceuticals, Concert is subject to the strenuous regulatory requirements of the US Food and Drug Administration (FDA) and other international regulatory agencies such as the EMEA to have its new drugs approved. Promotion of its approved drug products is also highly regulated by FDA and related agencies throughout the globe.

**Dependence on Proprietary Programs.** CTP-354 and CTP-499 are two of Concert's most advanced proprietary clinical candidates in development. These novel molecules may take material time and resources to finish clinical development, if they are able to complete is at all, and there is certainly no guarantee that the company will be successful in doing so. In addition, Concert may seek one or more collaborators for future development of CTP-499. There is a risk that the company may not be able to enter into a collaboration for the therapy, or is able to enter into one with terms that are beneficial to CNCE shareholders.

**Risks With Partnered Programs.** Concert has a number of partnered programs, including material efforts with Celgene, Jazz Pharmaceuticals, and Avanir Pharmaceuticals. Because these programs are ultimately under the direction of other companies, there is no guarantee those programs will progress at all, or in a way that is beneficial to Concert or CNCE shareholders.

**Deuteration: Approval, Manufacturing Risks.** To the best of our knowledge, no deuterated drug has ever been successfully approved or commercialized. There may be specific risks to gaining licensure for these types of agents from regulatory authorities, though these do not appear to have not emerged at this point.

## STOCK RATING DEFINITIONS

Buy: The stock's return is expected to exceed 12.5% over the next twelve months.

Neutral: The stock's return is expected to be plus or minus 12.5% over the next twelve months.

Sell: The stock's return is expected to be negative 12.5% or more over the next twelve months.

Investment Ratings are determined by the ranges described above at the time of initiation of coverage, a change in risk, or a change in target price. At other times, the expected returns may fall outside of these ranges because of price movement and/or volatility. Such interim deviations from specified ranges will be permitted but will become subject to review.

## RATINGS DISPERSION AND BANKING RELATIONSHIPS AS OF (July 8, 2014)

Rating	%	IB %
BUY	75.4	56.5
NEUTRAL	24.6	39.6
SELL	0.0	0.0

## COMPANIES UNDER ROBERT'S COVERAGE

Acadia Pharmaceuticals Inc. (ACAD)

CTI BioPharma Corp. (CTIC)

Prothena Corporation plc (PRTA)

Concert Pharmaceuticals Inc. (CNCE)

Nektar Therapeutics (NKTR)

## COMPANY SPECIFIC DISCLOSURES

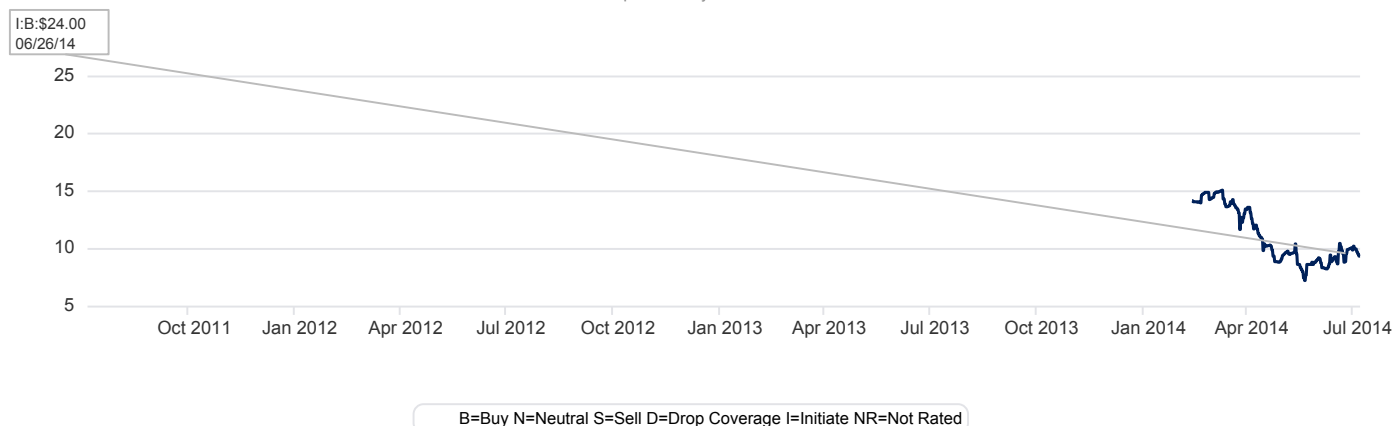
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Ladenburg Thalmann & Co. Inc. intends to seek compensation for investment banking and/or advisory services from Concert Pharmaceuticals Inc. within the next 3 months.

## OTHER COMPANIES MENTIONED

**INVESTMENT RATING AND PRICE TARGET HISTORY****Concert Pharmaceuticals Inc. Rating History as of 07/07/2014**

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