

COMPANY NOTE | EQUITY RESEARCH | April 1, 2014

# Healthcare: BioPharmaceuticals

# Concert Pharmaceuticals, Inc. | CNCE - \$13.45 - NASDAQ | Buy

## **Analysis of Sales/Earnings**

Stock Data	
52-Week Low - High	\$11.42 - \$16.26
Shares Out. (mil)	17.90
Mkt. Cap.(mil)	\$240.8
3-Mo. Avg. Vol.	NA
12-Mo.Price Target	\$28.00
Cash (mil)	\$119.0
Tot. Debt (mil)	\$17.0
Cash is an estimate as of March 2	2014, post the company's IPO of

Cash is an estimate as of March 2014, post the company's IPO of February 2014.

EPS \$			
Yr Dec	<b>—2013</b> —	—2014E—	—2015E—
		Curr	Curr
1Q	-	(0.32)E	-
2Q	-	(0.34)E	-
3Q	-	(0.26)E	-
4Q	-	(0.29)E	-
YEAR	(4.99)A	(1.21)E	(0.16)E
P/E	NM	NM	NM

Specific quarterly estimates in prior years for both EPS and revenue have not been provided by Concert. 2014 EPS estimate is pro forma Concert's IPO

Revenue	(\$ millions)		
Yr Dec	<b>—2013</b> —	2014E	—2015E—
		Curr	Curr
1Q	-	2.5E	-
2Q	-	2.5E	-
3Q	-	4.5E	-
4Q	-	4.5E	-
YEAR	25.4A	14.0E	33.5E



### CNCE: 2013 Points Toward A Productive 2014

Concert creates therapeutics by selectively adding deuterium to molecules. Its clinical and partnered are all expected to progress materially during 2014. CTP-354, its proprietary GABA-A modulator for spasticity/anxiety should move into Phase 2, and CTP-499, for diabetic kidney disease has data and an end of Phase 2 meeting with FDA shortly. Partnered programs with Jazz (JZP-386, a long-acting Xyrem), Avanir (AVP-786, an improved Neudexta), and Celgene, should advance as well.

**Concert In Brief.** Concert creates new medicines by selectively adding deuterium to molecules which strengthens certain internal bonds, a change that can significantly alter biological activity. Concert has created a broad portfolio based on deuterium substitution, and along with several partners (Jazz, Avanir, and Celgene), is advancing a number of promising candidates. **We maintain our Buy rating and \$28 target for CNCE shares.** 

Concert's Proprietary Programs are Promising. CTP-354, a selective GABA-A modulator with familiar yet distinct GABA activity, possesses a oncedaily profile with minimal sedation, and should have utility not only in spasticity associated with multiple sclerosis and spinal cord injury, but also in anxiety and pain settings, which provide it with blockbuster potential. '354 moves into Phase 2 in spasticity in 2H14, and we believe into anxiety shortly as well. CTP-499, a PDE inhibitor for diabetic kidney disease, is finishing up Phase 2 work, with data to be presented on April 25, and could move into phase 3 with a partner later this year after meeting with FDA.

Concert's Partnered Programs to Progress. Concert's collaborations include Avanir's AVP-786's, a deuterated dextromethorphan that contains less quinine than Avanir's other programs. '786 is entering Phase 2 in 2H14 for treatment-resistant major depressive disorders, and can utilize data from other Avanir programs. Jazz's JZP-386 is a deuterated analog of the active ingredient in Xyrem, a brand which reached revenue of \$569mm (+50%) in 2013. JZP-386 has the potential to avoid intra-night dosing, and should move into Phase 1 for narcolepsy this year. Concert's deal with Celgene for multiple deuterated compounds includes CTP-730, which is moving into Phase 1 for inflammatory diseases. The Celgene agreement is potentially very lucrative, with \$35mm upfront, \$1.4B in milestones, and low double-digit royalties.

**CNCE Valuation: Attractive In Our View.** We value CNCE shares at \$28, based on fully-taxed, risk-weighted NPV calculations, which assess CTP-354 at \$8.01 per CNCE share, CTP-499 at \$5.12, and the Avanir, Jazz, and Celgene collaborations at \$3.85, \$2.73, and \$4.59, respectively, with cash and other assets comprising the difference.

Intraday Price: \$13.40 at 10:38am ET

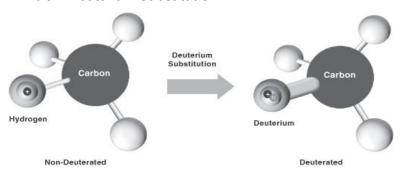
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#### Concert – Executive Summary

Concert: Description. Concert Pharmaceuticals was founded in 2006 with a strategy of creating and developing new medicines through its proprietary DCE Platform (deuterated chemical entity platform). The DCE Platform utilizes the naturally occurring element deuterium, which is a relative of hydrogen. Deuterium modification of a molecule/drug has the potential to improve its metabolic properties with minimal or no change in its intrinsic pharmacology. Concert has materially matured this deuterium modification approach by establishing novel intellectual property for a number of molecules. Five of these assets are currently advancing in clinical development under the guidance of either Concert or its strategic partners.

**Deuterium In Brief.** Deuterium is one of two naturally-occurring stable isotopes of hydrogen. It 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. Because of this increased mass, when compared to hydrogen, bonds involving deuterium are stronger than the corresponding bonds with hydrogen, and this strengthening can be enough to make significant changes in biological reactions. Many drugs are metabolized by pathways that involve the breakdown of carbon-hydrogen bonds, and the stronger bonds have the potential to alter or deflect the breakdown of the molecule. Therefore deuterium modification of a molecule offers an approach to potentially creating significantly differentiated new medicines, each with intellectual property protection.

**Exhibit 1: Deuterium Substitution** 



Source: Concert Corporate Fact Sheet, May 2013.

Concert's Drug Development Approach. Concert's efforts with deuteration began at the formation of the company with management broadly examining the drug development landscape, looking for obvious initial opportunities with both approved and novel molecules to apply the technology and establish intellectual property. The company has continued to aggressively mine the landscape for opportunities, establishing a broad patent estate of deuterated molecules that span multiple therapeutic areas (Appendix 1). With existing therapies, Concert is often building on significant information regarding the related non-deuterated compound, allowing it to efficiently identify lead compounds and in some cases, truncate the development timeline compared to conventional small molecule drug research and development. With a management team seasoned in therapeutics development, having experience at Vertex, Merck, Amgen, and other organizations, we believe Concert should have an ability to successfully navigate development of its wide range of assets.

Concert's Broad and Expanding Pipeline. Concert has a robust pipeline of deuterated compounds in or moving toward the clinic, as noted in Exhibit 2 below. CTP-354 is Concert's GABA-A selective modulator that is moving into Phase 2 for spasticity associated with multiple sclerosis and spinal cord injury, and potentially other indications such as anxiety and neuropathic pain. CTP-354 is trying to provide efficacy in these settings without the sedation seen with other therapies, and the larger opportunities such as anxiety and pain with limited sedation gives this compound considerable potential. CTP-499 is a PDE-inhibitor with anti-inflammatory and anti-fibrotic characteristics that is being developed in Phase 2 for diabetic kidney disease, and since pentoxifylline is its parent molecule, CTP-499 could have potential over the long-term for consideration in hepatic settings such as NASH and alcoholic liver disease. We expect CTP-499 to be partnered for additional development after an upcoming end of Phase 2 meeting with FDA. 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.

Partnered Programs are Rapidly Advancing. Concert's partnered clinical program consists of Avanir's AVP-786's, a deuterated dextromethorphan which is entering Phase 2 for treatment resistant major depressive disorders in 2H14. AVP-786 is a deuterated version of Avanir's Neudexta, which is approved for pseudobolar affect (sudden, frequent episodes of laughing and/or crying). AVP-786 contains much less quinine than Nuedexta, which could make its appeal much broader; 786 is being developed in treatment-resistant depression and neuropathic pain, and - 'indications such as agitation in Alzheimer's disease and Parkinson's dyskinesia are also likely. Jazz Pharmaceutical's JZP-386, is a deuterated analog of sodium oxybate that is in preclinical development for narcolepsy; sodium oxybate is the active ingredient in Jazz's large and rapidly growing Xyrem (Xyrem posted revenue of \$569 million in 2013, +50% from the year prior). In our view, JZP-386 has the potential to extend the franchise and avoid middle-of-the-night dosing.

Worldwide Phase 2 Candidate Indication(s) Ph1 MAD data CTP-354 Spasticity associated with MS expected 2H14 CoNCERT Ph2 program expected to begin Spasticity associated with SCI 2H14 Expect to request CONCERT **CTP-499 Diabetic Kidney Disease** end of Ph2 FDA meeting mid-2014 Ph2 trial for \$170 Million AVP-786 treatment-resistant **Neurologic and Psychiatric Disorders** major depressive disorder expected to begin 2H14 Clinical trials \$1.4 Billion CTP-730 **Inflammatory Diseases** expected to begin 2014 JZP-386 First-in-human trial \$117 Million Narcolepsy expected to (Deuterated sodium oxybate) begin 2014 CONCERT C-10068 Pain and Seizures Deuterated CONCERT **CF and COPD** ivacaftor Completed/Ongoing Planned in 2014

**Exhibit 2: Concert Pharmaceuticals - Pipeline** 

Source: Concert Pharmaceuticals corporate presentation March 2014.

Last but certainly not least, is Celgene's deuterated CTP-730 which is in preclinical development for inflammatory diseases; though the specific target and parent molecule of CTP-730 has not been disclosed, milestones associated with the deal of up to \$1.4 billion (the Celgene deal also includes three other potential assets) point to its significance. (In terms of inflammatory indications, 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.) CPT-730 is expected to enter the clinic this year, and Phase 1 results are expected by year end.

All together, Concert's five most advanced programs are all expected to be materially progressing at various stages in the clinic by the end of 2014. We note that Concert has structured its partnerships so there will be material developmental milestones as they progress, providing Concert with the potential for significant revenue generation even prior to the introduction of its own proprietary therapies.

#### **Concert 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 \$25.27 per CNCE share, representing the lion's share of our \$28 CNCE shares target (Exhibit 3).

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. 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. 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, we value the program at \$5.12 per CNCE share. Other less mature proprietary products are much more modest opportunities at this point and valued at \$0.97 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 3: Concert - CNCE Shares NPV Summary** 

Assets	^	<b>IP</b> Value	NPV/Share
CTP-354 - Spasticity, Anxiety, others	\$	138,160	\$8.01
CTP-499 - Diabetic Kidney Disease	\$	88,386	\$5.12
Other Proprietary	\$	16,773	\$0.97
AVP-786 - CNS indications (Avanir)	\$	66,369	\$3.85
JZP-386 - Sleep indications (Jazz)	\$	47,165	\$2.73
CTP-730 - Inflammation (Celgene)	\$	69,818	\$4.05
Other Celgene - Onc/Inflam (Celgene)	\$	9,295	\$0.54
Other Corporate	\$	(63,325)	(\$3.67)
Net Cash	\$	100,858	\$5.85
NOLs, Credits, etc.	\$	9,010	\$0.52
Valuation	\$	482,509	\$27.97

Source: ROTH Capital Partners Pharmaceuticals Research.

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 \$3.85 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 materially opportunity, generating a \$2.73 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 \$4.05 NPV, by our calculation. The remainder of the Celgene assets are estimated at \$0.54, and net cash, NOLs and the drag of general corporate expense totals \$2.70 per CNCE share, yielding the \$27.97 total, driving our \$28 CNCE shares target.

**Revenue**. Concert has generated revenue in 2011 and 2012 of \$19.5 million and \$12.8 million, respectively, due to work on compounds as part of collaborations with existing and previous partners. That revenue total grew materially in 2013 to \$25.4 million, due to the signing of the material Celgene collaboration and Concert booking as revenue a part of that deal's \$35 million upfront payment. Revenue is estimated to return to \$14 million in 2014, however. With material variability in the timing of deal-related milestones, Concert's revenue is estimated to rise to \$33.5 million in 2015 as a portion of the anticipated licensing milestones for CTP-354 and CTP-499 are recorded, before dropping down to \$21.5 million during 2016. A pick up in revenue to \$49 million is expected in 2017, then moving to \$358 million in 2019 with the beginning of CTP-354 revenue in the US, and increasing to \$537 million in 2020 with the

beginning of CTP-449 revenue as well; this growth is expected largely due to progress across all of its collaborations in those years, with the Celgene collaborations and their expected regulatory milestones having by far the most impact.

**Earnings.** Concert's revenue of \$19.5 million and \$12.8 million in 2011 and 2012, respectively, was not enough to generate a profit as expenses of approximately \$31 million annually influenced earnings those years. The \$35 million upfront from the Celgene collaboration nearly turned a profit for Concert in 2013, though modest increases in company expenses beginning in 2014 due to Concert becoming a public company, and a reduction in revenue due to the lack of a Celgene-like upfront that year, increased the expected loss materially to \$20.3 million. Variability in the total milestones from 2015 through 2017 results in a loss in the first two of those year, and a \$5.6 million profit in 2017. From 2018 onward through 2020 (and beyond) the expected material milestones for Concert have its operations to material profits, even despite expected increases in R&D and SG&A.

**Cash Flow.** In general, Concert's cash flow has largely tracked, and should flow in the same magnitude and direction of earnings for the company. However, in Feb 2014, Concert raised approximately \$87million from its initial public offering (IPO). In terms of additional one-time items, we model an additional \$40 million upfront cash payment for the international rights for CTP-354 in 2015, and we also model an additional \$25 million upfront payment for worldwide rights to CTP-499 for diabetic kidney disease and potentially other indications. \$17 million in debt remains outstanding, and at this point, given the expected operations of the company, which include material milestones from existing collaborations, we do not foresee any new cash raises.

Exhibit 4: Concert – Recent Material Events/ Upcoming Catalysts

DATE	EVENT	OUTCOME/COMMENT	IMPACT
Feb-12	Avanir deal signed for deuterated dextromethorphan	Deal gives solid PK profile with less quinidine than other versions	****
Feb-13	Jazz deal signed for deuterated sodium oxybate (Xyrem)	Provides potential extension of large, rapidly growing Xyrem franchise	****
Apr-13	Celgene deal signed for multiple compounds, CTP-730	Large deal: \$35mm upfront, \$1.4B milestones, SD/low DD royalty	****
Feb-14	Concert IPO	Raised money to advance internal programs more rapidly	****
1H14	Concert - ROTH Conference Presentation	Helped build awareness of Concert in the public markets	***
Apr-14	Final CTP-499 Phase 2 diabetic kidney disease data	Should solidify longer term data, lead to end of P2 FDA meeting	****
2H14	AVP-786 into Phase 2 in treatment resistant depression	Phase 2 start triggers \$2mm milestone to Concert	***
2H14	Jazz JZP-386 moves into P1 in narcolepsy	Completion of Phase 1 expected by YE 2014; triggers milestone	****
2H14	CTP-354 completes MAD study	Important for '854 in a range of indications	****
2H14	CTP-354 moves into Phase 2 in spasticity	Data for this indicaiton, should help establish proof of concept	***
2H14	End of Phase 2 FDA Meeting for CTP-499	Should clarify Phase 3 design; lead to a potential partnership	****
2H14	Celgene's CTP-730 to start Phase 1 study	Important as the results trigger a milestone, visibility for Concert	****

Source: ROTH Capital Partners BioPharmaceuticals Research.

# **Concert – In Depth**

#### **Deuterium Background**

**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 the nucleus. The nucleus of deuterium, called a deuteron, contains one proton and one neutron. 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's symbol is D or  $^2$ H, although  $^2$ H is preferred. Deuterium has a natural abundance in the oceans of about one atom in 6,420 of hydrogen (or 0.0156%); it is produced for industrial, scientific and military purposes by starting with water, which contains a small amount of heavy water, where deuterium replaces the hydrogen in water molecules ( $D_2O$  or  $^2$ H<sub>2</sub>O); the heavy water is then separated for the deuterium. According to Concert, the average human body contains about 2 grams of deuterium.

**Deuteration – General Effects on a Molecule.** Chemically, deuterium behaves similarly to ordinary hydrogen, but there are differences in bond energy and length for compounds of deuterated isotopes which are larger than the isotopic differences in any other element. Bonds involving deuterium (and another hydrogen isotope tritium) are somewhat stronger than the corresponding bonds in hydrogen, and are enough to make significant changes in biological reactions. Many drugs are metabolized by pathways that involve the breaking of carbon-hydrogen bonds, and having the stronger deuterium-carbon bonds or bonds helps deflect the breakdown of the bonds. Selective incorporation of deuterium in place of hydrogen therefore has the potential to have the benefit of retaining the biochemical potency and selectivity of physiologically active compounds while potentially modifying their metabolic properties to substantially alter their overall therapeutic profile.

Deuteration in Drug Development. Deuterium substitution at specific molecular positions can improve metabolic stability, reduce formation of toxic metabolites, or increase the formation of desired active metabolites; deuteration can therefore enhance bioavailability and improve the half-life of a compound. However, when deuterium is oxidative metabolism, incorporated at а known site of the resulting deuterium absorption, distribution, metabolism, and excretion of a molecule remains inherently unpredictable. For example, complex enzymatic mechanisms often have other rate-limiting steps, and/or the presence of a stabilized carbondeuterium bond may cause metabolism to shift to another site or sites on the molecule. Because of the unpredictable (non-obvious) nature of the their effects, deuterated compounds are able to generate new intellectual property. Deuterated compounds have been in use in clinical settings for some time as probes for pharmacokinetic and metabolism studies of the corresponding non-deuterated therapeutics, though until recently deuterium modification has only received little attention as an approach to creating enhanced therapeutic agents.

**Deuteration Compounds Can Provide Expedited Development Potential.** Concert's DCE platform has the potential, depending upon specifics of the development program, to have some elements of its development program truncated, and therefore expedited. For instance, with the Avanir program, FDA has permitted Avanir to utilize data generated from its dextromethorphan- based program AVP-923 for the deuterated dextromethorphan analog AVP-786 that Avanir is advancing. This should help AVP-786 be considered more widely without duplicating the clinical effort for both programs, and could help AVP-786 have more rapid initial uptake. 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 time, spending and development efficiencies, and potentially helpful to the launch.

# **Concert's Proprietary Deuterated Opportunities**

#### CTP-354 – A Non-Sedating GABA-A Modulator for Spasticity, Anxiety, and Pain

**GABA-A Receptor Background.** GABA is the major inhibitory neurotransmitter in the nervous system, and the GABA-A receptor is a well-characterized, significant ionotropic receptor that is activated by GABA, and is the target of multiple therapeutics with indications in anxiety, insomnia, and spasticity, among others. The GABA-A receptor is a pentameric protein with subtypes composed of  $\alpha$ ,  $\beta$ , and  $\gamma$  subunits (Exhibit 5). The active site of the GABA-A receptor is the binding site for GABA and several therapeutics, and the receptor also contains a number of allosteric binding sites that modulate the activity of the receptor indirectly. Typical benzodiazepines (Valium, Xanax, etc.) activate the receptor in a non-selective manner, binding to an allosteric site at the interface of a  $\gamma$  subunit and either an  $\alpha$ 1,  $\alpha$ 2,  $\alpha$ 3, or  $\alpha$ 5 subunit. Benzodiazepines are well known for their efficacy in anxiety, spasticity, and insomnia, though their use is limited due to poor tolerance, sedation, and drug interactions, which is believed to be due to a relative lack of GABA-A subtype selectivity. Preclinical work indicates that the sedative, ataxic, and dependence effects of benzodiazepines are mediated by the  $\alpha$ 1 subtype (sleep drugs such as Ambien activate the  $\alpha$ 1 subunit). Agonism at the  $\alpha$ 2 and  $\alpha$ 3 subtypes is believed to be associated with anxiolytic, analgesic, and spasmolytic activities, whereas  $\alpha$ 5 subtype activity is believed to have cognitive effects.

GABA

Benzodiazepines
Flumazenil
Zolpidem

Barbiturates
Intracellular

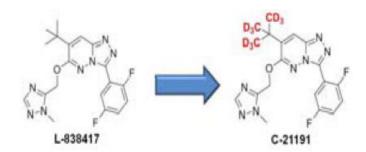
Intracellular

Exhibit 5: The GABA-A Receptor and Binding Sites of Various Therapeutics

Source: Katzung BG, Masters SB, Trevor AJ: Basic & Clinical Pharmacology, 11th Edition.

**CTP-354 Background.** Concert is developing CTP-354 as a subtype-selective GABA-A modulator for spasticity, neuropathic pain, and anxiety disorders. CTP-354 is an analog of L-838417, a compound that was developed as part of Merck's research effort towards subtype-selective GABA-A anxiolytics with reduced sedation and ataxia. The Merck compound was targeted by Concert for deuterium substitution because of its promising pharmacology: L-838417 demonstrated an attractive subtype-selective GABA-A profile, with partial agonism at  $\alpha$ 2,  $\alpha$ 3, and  $\alpha$ 5 subtypes, and antagonism at  $\alpha$ 1. However L-838417 possessed a poor preclinical pharmacokinetic profile and despite considerable preclinical work, was not advanced materially into the clinic.

Exhibit 6: Concert's Deuterated GABA-A Modulator CTP-354 (C-21191)



Source: Liu, et al. C-21191: Deuterated Subtype-Selective GABAA Modulator for Spasticity and Neuropathic Pain, Neuroscience 2011.

Concert developed the deuterated CTP-354 to overcome the poor pharmacokinetics of L-838417 by incorporating nine deuterium atoms in place of hydrogen at key positions. (Exhibit 6) With Concert's selective incorporation of deuterium, the pharmacokinetics with CTP-354 have been dramatically improved (Exhibit 7 below). With the material improvement in the pharmacokinetics of the compound, Concert now has been able to move CTP-354 into the clinic and plans to develop it in multiple indications. Importantly, deuterium substitution does not change the intrinsic pharmacology of CTP-354. Both L-838417 and CTP-354 have demonstrated the expected binding to the benzodiazepine site of the GABA receptor with no significant off target activities.

CTP-354 L-838417

Time (hr)

Exhibit 7: Improved PK of Deuterated CTP-354 vs. L-838417 (Rat data)

Source: Liu, et al. C-21191: Deuterated Subtype-Selective GABAA Modulator for Spasticity and Neuropathic Pain, Neuroscience 2011.

More specifically, CTP-354 has been shown to lack agonist activity at the GABA-A  $\alpha$ 1-receptor subtype, which should confer a lack of sedation with the compound, but it also has potent partial agonist activity at other key GABA-A receptor subtypes as noted above with L-838417. Importantly, as Concert looks to expand CTP-354's profile, in addition to having anxiolytic activity and strong muscle relaxant effects, L-838417 has also been reported to be efficacious in preclinical models of inflammatory and neuropathic pain, further expanding the potential for such a compound beyond anxiety. CTP-354's broader profile is shaping up well, for in preclinical models, it has been able to maintain the desirable pharmacology of benzodiazepines with no apparent sedation at therapeutic doses, and CTP-354 has also demonstrated efficacy in a preclinical model of neuropathic pain.

Axial Sagittal Coronal

Scan 1
Baseline

Scan 2
5 hours

Scan 3
24 hours

Exhibit 8: CTP-354 Brain Receptor Occupancy

Source: Concert Pharmaceuticals corporate presentation March 2014.

CTP-354 Clinical Development. Concert has moved CTP-354 into the clinic where it has shown promising activity. The single ascending dose studies have shown a long plasma half-life, long enough for once-daily dosing with no serious adverse-events seen. The molecule has high and sustained brain receptor occupancy (Exhibit 8), a key characteristic for these compounds. No sedation, ataxia, or adverse effects have been observed at the 20mg dose that yield 60% receptor occupancy at 24 hours. Concert has modeled that the 6mg dose should achieve this level of receptor occupancy. Importantly, CTP-354 appears less sedating at higher GABA-A receptor occupancy levels than benzodiazepines. (Exhibit 9 below.)

No sedation or other AEs 79% Receptor Occupancy 75% 63% 50% 5-Hour GABA 25% 25% 16% <10% 0% CTP-354 20 mg CTP-354 CTP-354 40 mg 60 mg 0.5 mg 20 ma 30 mg 30 µg/kg 2 mg 4 mg Compound (Single Dose)

Exhibit 9: CTP-354 Appears Less Sedating At Higher Receptor Occupancy Than BZDs

Source: Concert Pharmaceuticals corporate presentation March 2014.

Additional CTP-354 Considerations. Phase 1 results in a single ascending dose trial in 71 healthy volunteers in doses ranging from 0.15mg to 60mg show that a maximum tolerated dose was not reached, despite receptor occupancy saturation. Importantly, the long plasma half life supports once-daily dosing multiple ascending dose trial is underway; the study is expected to enroll up to 62 healthy volunteers. Dosing will be at 2mg and 6mg over 10 days, and due to a partial clinical hold, dosing is limited to the 6mg level for now—Concert is conducting studies designed to permit increased doses, and that could be complete by late 2014/2015. Phase 2 trials in the spasticity indication are to begin in 2H14, and they could progress fairly rapidly. With a profile that is showing a lack of sedation, combined with activity not only in spasticity, but in anxiety and potentially pain (neuropathic) settings, we believe the competitive positioning of CTP-354 is shaping up as quite promising.

Spasticity Description/Background. Spasticity is characterized by involuntary muscle spasm; it can result from a wide range of disorders, including multiple sclerosis (MS), spinal cord injury, cerebral palsy, amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), stroke, and hereditary spastic paraplegia. Symptoms can range from mild muscle tightness to more severe symptoms, including the painful inability to move limbs that can result in disability and diminished quality of life. The American Association of Neurological Surgeons estimated in 2006 that there were 12 million patients suffering from spasticity, including about 80% of people with MS. Of the estimated 400,000 patients with MS in the US, Concert estimates that at least 34% (140,000 patients), suffer from moderate to severe spasticity. Regarding spasticity associated with spinal cord injury, approximately 270,000 people in the US suffer from that condition (with 12,000 new incidences annually) according to Concert. 65% to 78% of those spinal cord injury patients experience some degree of spasticity, and Concert estimates that 28% to 46% of those (80,000 to 120,000 patients) suffer from problematic spasticity and could be candidates for therapy. (Exhibit 10)

**Exhibit 10: CTP-354 Initial Spasticity Target Markets** 

	US Disease Prevalence	% Treatable Spasticity*	Treatable Population
MS	400,000	34+%	140,000
SCI	270,000	28-46%	80,000-120,000

Source: Concert Pharmaceuticals corporate presentation March 2014.

Treatment of spasticity is through exercise, physical therapy, pharmacologic therapy, or surgery. Pharmacologic therapies considered include: baclofen (Lioresal) a GABA-B agonist, and tizanidine (Zanaflex) an  $\alpha$ 2 adrenergic agonist. Drowsiness and sedation are seen with both, and hypotension and multiple drug/drug interactions are seen with Zanaflex. Other therapeutics that may be considered include botulinum toxin (Botox) which is injected into the

affected muscles, and a cannabis extract containing dronabinol and cannabidiol (Sativex) is also under development for spasticity associated with MS and is approved in the EU.

CTP-354 Economics to Concert for Spasticity, Anxiety, and Possibly Other Indications. Regarding CTP-354's use in spasticity, due to the familiarity with the GABA-A receptor-related mechanism, and the compound's potential once-daily profile, we assume a penetration of 1/3 of the addressable market for MS and spinal cord injury, or just over 79,000 patients treated at peak in the US. We assume \$5,000 per patient per year at peak, resulting in peak revenue for CTP-354 of \$400 million in the US for this indication. For EU/international revenue, we assume slightly greater patient numbers, though lower pricing, and arrive at roughly the same figures. We model a partner for international rights for \$40 million upfront and \$300 million in milestones, and 15% to 25% royalties on international sales of the product, to be signed post Phase 2 data. We assume a 2019 launch, and in addition, we also assume additional indications for anxiety, and in various pain settings (the compound appears active in models of neuropathic pain). Collectively, these additional larger indications could add over \$1 billion in revenue in total, providing revenue totals in excess of \$2 billion. Given the safety work that still needs to be accomplished, we assign a relatively high discount of 40% per annum, given the well-validated GABA-A receptor target mechanism. Taken together, we estimate the fully-taxed, risk weighted economics of CTP-354 to Concert at \$8.01 per CNCE share (Exhibit 11). We note that as Concert ticks off the development items, and its risk profile is reduced, the potential for a material increase in this program's NPV to Concert exists.

Exhibit 11: CTP-354 - NPV Calculation to Concert (2014 - 2030)

	2	014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	20
CTP-354 - Spasticity, Anxiety		-					35,000	250,000	450,000	700,000	975,000	1,225,000	1,425,000	1,675,000	1,875,000	2,125,000	2,225,000	2,325,0
US Sales		-	-	-	-	-	25,000	175,000	275,000	425,000	600,000	750,000	850,000	1,000,000	1,100,000	1,250,000	1,250,000	1,250,
Int'l Sales		-	-	-	-	-	10,000	75,000	175,000	275,000	375,000	475,000	575,000	675,000	775,000	875,000	975,000	1,075,
ntl Royalty Rate (15%-25%)			0%	0%	0%	0%	15%	15%	15%	15%	20%	20%	20%	25%	25%	25%	25%	
ntl Royalty		-	-	-	-	-	1,500	11,250	26,250	41,250	75,000	95,000	115,000	168,750	193,750	218,750	243,750	268
Jpfront/Milestones		-	40,000	-	10,000	10,000	50,000	-	-	-	-	-	25,000	-	-	-	-	100
otal Revenue to Concert			40,000		10,000	10,000	76,500	186,250	301,250	466,250	675,000	845,000	990,000	1,168,750	1,293,750	1,468,750	1,493,750	1,618
INCE Expenses																		
COGS (US only)		-	-	-	-	-	1,250	8,750	13,750	21,250	30,000	37,500	42,500	50,000	55,000	62,500	62,500	6
COGS pct		5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	
SG&A		-	-	-	1,000	1,000	40,000	55,000	60,000	65,000	70,000	80,000	80,000	85,000	85,000	85,000	90,000	9
R&D		5000	10,000	12,000	12,000	12,500	12,500	10,000	10,000	10,000	10,000	5,000	5,000	-	-	-	-	
Total Expense	5	,000	10,000	12,000	13,000	13,500	53,750	73,750	83,750	96,250	110,000	122,500	127,500	135,000	140,000	147,500	152,500	15
let to Concert	(5	,000)	30,000	(12,000)	(3,000)	(3,500)	22,750	112,500	217,500	370,000	565,000	722,500	862,500	1,033,750	1,153,750	1,321,250	1,341,250	1,46
NPV/year	-48	319.5	21538.2	-6622.4	-1273.5	-1142.9	3868.2	13650.5	18850.8	22905.7	24984.0	22799.4	19440.9	16643.5	13268.2	10843.2	7862.4	6
Discount Rate		15%	30%	30%	30%	30%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	
ax rate used		0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	
IPV Taxed (effective rate)	\$ (4	,820) \$	21,538 \$	(6,622) \$	(1,274) \$	(1,143) \$	3,868 \$	13,651 \$	12,253 \$	14,889 \$	16,240 \$	14,820 \$	12,637	\$ 10,818	\$ 8,624	\$ 7,048	\$ 5,111	\$
Total Value	\$198	985																
IPV Per Share		1.54																
otal Value taxed	\$ 138	,160																
IPV/share taxed		8.01																

Source: ROTH Capital Partners Pharmaceuticals Research.

#### CTP-499 - Potentially First-in-Class Therapy for Diabetic Kidney Disease

**Diabetic Kidney Disease Background**. Diabetic kidney disease is a condition where the ability of a person's kidney to filter blood is materially impaired, which 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). Concert is developing CTP-499 as an add-on to the standard of care to slow progression towards kidney failure. Type 2 diabetic kidney disease is a multifactorial disease involving inflammatory, oxidative and fibrotic processes. Phosphodiesterases (PDEs) is a family of enzymes that regulates the pathways involved in these processes.

**CTP-499 Background.** CTP-499 is a deuterated analog of 1-(S)-5-hydroxyhexyl-3,7-dimethylxanthine (HDX), which is an active metabolite of pentoxifylline (Trental); it has been deuterated to improve the compound's metabolic stability and allow greater exposure to pharmacologically active metabolites of pentoxifylline. Pentoxifylline, which is

a broad spectrum phosphodiesterases (PDE) inhibitor, was approved over three decades ago for the treatment of intermittent claudication (lower limb pain resulting from obstructed arteries), and through multiple complex mechanisms has been characterized as having a role in reducing inflammatory and fibrotic processes and has specifically been shown to reduce TNF $\alpha$  production. PDEs are enzymes that are believed to play an important role in the progression and worsening of type 2 diabetic kidney disease, and pentoxifylline has been reported in several clinical studies to have beneficial effects on proteinurea and renal function decline (Lin, et al. American Journal of Kidney Disease 2008; Perkins RM, American Journal of Kidney Disease 2009; Navarro, et al. Journal of the American Society of Nephrology, 2005)

CTP-499 Description. CTP-499 is also a novel, oral multi-subtype selective inhibitor of phosphodiesterases (PDEs). In preclinical studies, CTP-499 has been shown to inhibit PDEs 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 some detail below), where it has demonstrated encouraging results. We expect the compound to continue in development for diabetic kidney disease, with Concert potentially engaging a development partner for future studies. The antiinflammatory and antifibrotic effects of the parent drug of CTP-499, pentoxifylline, have suggested a role for it in reducing the consequences of hepatic fibrosis and even cirrhosis in various settings. For instance, pentoxyfilline has been studied in multiple settings, such as alcoholic cirrhosis, fibrosis due to radiation, and is being evaluated in more severe settings of non-alcholic fatty liver disease, such non-alcoholic steatohepatitis (NASH). Given its similar PDE inhibition mechanism, these additional hepatic settings, in particular NASH, could be an interesting long term course of development for CTP-499 in addition to diabetic kidney disease.

CTP-499 in Diabetic Kidney Disease: Phase 2 Trial Specifics. The Phase 2 trial currently completing for CTP-499 has three parts. Part 1 is a double-blind, parallel, two-arm study evaluating the safety and efficacy of 600 mg of CTP-499 bid vs. placebo for 24 weeks. This part enrolled 182 patients in was completed in 2013. Part 2 is a blinded 24week extension in which all who completed Part 1 were eligible to continue on CTP-499 or placebo. 143 patients were enrolled in this part and have completed dosing. 124 of the 143 patients completed Part 2 of the trial. Concert has preliminary analyses of 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, but has not finished the full analysis of the Part 2 data.

Final top line results for the first 48 weeks of the trial is expected 1H14. In part 3, all patients who completed Part 2 can receive 600 mg CTP-499 twice daily in a 48 week open-label extension study. At the end of 2013, 102 patients had enrolled in the open label extension. The objective of the study is to characterize the safety and efficacy of CTP-499 in CKD setting, and the primary endpoint was the measurement of changes in urine albumin to creatinine ratio or UACR. Key secondary endpoints included changes in serum creatinine and eGFR. Enrollment criteria include UACR >=200mg/g in men and 300 mg/g in women, and eGFR of 23 to 89 mL/min/1.73 m2, indicating mild to moderately severe type 2 diabetes, among other criteria.

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, though there were multiple reasons to be encouraged by 499's performance in the study. These include:

- 1) This trial was not powered for statistical significance with respect to serum creatinine or eGFR, and results were nearly significant on serum creatinine levels and there was a positive trend in eGFR levels at 48 weeks:
- 2) 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, though in a post-hoc analysis;
- 3) 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;
- 4) 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.

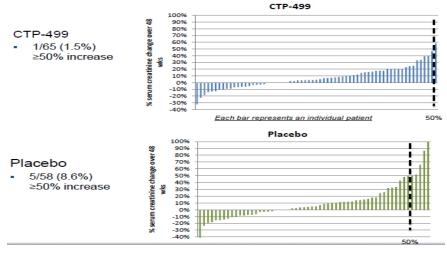
(mg/dL) (mg/dL) 2.0 2.0 CTP-499 p=0.0568Serum Creatinine Serum Creatinine 1.9 Worsening 1.8 1.8 -SMean (SE) LSMean (SE) 1.5 48 20 36 40 44 PBO78 75 61 58 CTP-499 82 81 81 79 78 70 65 Mean serum creatinine level increase over 48 weeks CTP-499: 0.13 mg/dL Placebo: 0.21 mg/dL

Exhibit 12: CTP-499 - Preliminary Analysis Shows Trend Against Serum Creatinine Increases

Source: Concert corporate presentation March 2014.

**Specific Phase 2 Results.** Concert's preliminary 48 week analyses suggest that the serum creatinine of those receiving CTP-499 rose less than those of patients who received placebo. 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 12). The lower value in the case of CTP-499 represents a 38% improvement as compared placebo and may indicate a slower decline of kidney function in patients taking CTP-499. The statistical analysis in this trial was a rigorous analysis (two-tailed), however, a less rigorous but common (one-tailed) analysis would have shown significance for CTP-499. Also, 14% taking placebo, experienced a 30% or greater decline in eGFR, compared with 6.2% (p = 0.11) for CTP-499, and 5.2% of patients experienced a 40% or greater decline in eGFR, compared with 1.5% receiving CTP-499.

Exhibit 13: CPT-499 Appears to Protect Against Large Increases in Serum Creatinine



Source: Concert corporate presentation March 2014.

**Results Point Toward Phase 3 Trial Design.** Importantly, 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. 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. This new Phase 3 endpoint has recently been

granted in a Special Protocol Assessment (SPA) between Nephrogenex and FDA. This endpoint migration comes as 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 endpoints mentioned above, which could be in reach of CTP-499, has the potential to result in licensing of CTP-499.

Exhibit 14: CTP-499 – NPV Calculation to Concert

:	:		-					2022E	2023E	2024E	2025E	2026E				
-	-			-	-	105,000	325,000	600,000	825,000		1,200,000	1,375,000	1,525,000	1,675,000	1,825,000	1,975
-			-	-	-	70,000	250,000	425,000	550,000	650,000	725,000	800,000	850,000	900,000	950,000	1,000
	-	-	-	-	-	35,000	75,000	175,000	275,000	375,000	475,000	575,000	675,000	775,000	875,000	975
	0%	0%	0%	0%	0%	15%	15%	15%	20%	20%	20%	25%	25%	25%	25%	
-	-	-	-	-	-		11,250	26,250	55,000		95,000	143,750	168,750	193,750		243
-	25,000	-	-	10,000	50,000	25,000	-	-	-	100,000	-	-	-	-	100,000	
-	25,000	-	-	10,000	50,000	100,250	261,250	451,250	605,000	825,000	820,000	943,750	1,018,750	1,093,750	1,268,750	1,243
-	-	-	-	-		3,500	12,500	21,250	27,500	32,500	36,250	40,000	42,500	45,000	47,500	51
5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	
-	-	-	1,000	1,000	35,000	50,000	60,000	65,000	65,000	70,000	80,000	80,000	80,000	80,000	80,000	80
5000	10,000	15,000	15,000	15,000	15,000	10,000	10,000	10,000	10,000	5,000	5,000	-	-	-	-	
5,000	10,000	15,000	16,000	16,000	50,000	63,500	82,500	96,250	102,500	107,500	121,250	120,000	122,500	125,000	127,500	13
(5,000)	15,000	(15,000)	(16,000)	(6,000)	-	36,750	178,750	355,000	502,500	717,500	698,750	823,750	896,250	968,750	1,141,250	1,113
96.0	461.0	827.0	1192.0	1557.0	1922.0	2288.0	2653.0	3018.0	3383.0	3749.0	4114.0	4479.0	4844.0	5210.0	5575.0	5
0.3	1.3	2.3	3.3	4.3	5.3	6.3	7.3	8.3	9.3	10.3	11.3	12.3	13.3	14.3	15.3	
-4853.2	10267.8	-9047.3	-7720.3	-2316.1	0.0	4459.2	15492.3	21977.1	22220.3	22641.6	15749.9	13262.5	10306.9	7950.3	6690.0	4
12%	35%	25%	25%	25%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	
0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	
(4,853) \$	10,268 \$	(9,047) \$	(7,720) \$	(2,316) \$	- \$	4,459 \$	10,070 \$	14,285 \$	14,443 \$	14,717 \$	10,237 \$	8,621	6,700	5,168	\$ 4,348	\$
	5% - 5000 5,000 (5,000) 96.0 0.3 -4853.2 12%	5% 5% 5000 10,000 5,000 10,000 (5,000) 15,000 96.0 461.0 0.3 1.3 -4853.2 10267.8 12% 35% 0% 0%	5% 5% 5% 5000 10,000 15,000 5,000 10,000 15,000 (5,000) 15,000 (15,000) 96.0 461.0 827.0 0.3 1.3 2.3 -4853.2 10267.8 -9047.3 12% 35% 25% 0% 0% 0%	5% 5% 5% 5% 5% 5% 5000 10,000 15,000 15,000 16,000 16,000 16,000 10,000 13,000 16,000	- 25,000 - 10,000 - 25,000 - 10,000 - 5% 5% 5% 5% 5% 5% 5% - 1,000 1,000 - 1,000 15,000 15,000 15,000 - 10,000 15,000 16,000 16,000 - 16,000 15,000 16,000 (6,000) - 15,000 15,000 (15,000) (16,000) - 15,000 15,000 (15,000) (20,000) - 20,000 15,000 (15,000) (20,000) - 20,000 15,000 (20,000) - 20,000 15,000 (20,000) - 20,000 1	- 25,000 - 10,000 50,000  - 25,000 - 10,000 50,000  - 5% 5% 5% 5% 5% 5% 5% 5% 5%  5000 10,000 15,000 16,000 16,000 16,000 16,000  (5,000) 15,000 (15,000) (16,000) (6,000) -  96.0 461.0 827.0 1192.0 1557.0 1922.0 0.3 1.3 2.3 3.3 4.3 5.3  -4853.2 10267.8 -9847.3 -7720.3 -2316.1 0.0  12% 35% 25% 25% 25% 40%  0% 0% 0% 0% 0% 0% 0%	- 25,000 10,000 50,000 25,000 25,000 - 25,000 - 10,000 50,000 25,000 - 25,000 - 25,000 - 25,000 - 25,000 - 10,000 50,000 100,250 3,500 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5%	- 25,000 - 10,000 50,000 25,000 100,250 261,250 - 25,000 - 10,000 50,000 50,000 100,250 261,250 - 25,000 - 10,000 50,000 100,250 261,250 - 3,500 10,000 10,000 10,000 10,000 10,000 10,000 15,0	- 25,000 - 10,000 50,000 25,000 11,250 261,250 451,250 - 25,000 - 3,000 10,000 50,000 100,250 261,250 451,250 - 3,000 10,000 10,000 10,000 10,000 10,000 10,000 15,000 10,000 15,000 10,000 15,000 10,000 15,000 10,000 15,000 10,000 15,000 10,	- 25,000 - 10,000 50,000 100,250 261,250 451,250 605,000 - 25,000 100,250 261,250 451,250 605,000 - 25,000 100,250 261,250 451,250 605,000 - 3,000 100,250 261,250 27,500 10,000 15,000 15,000 10,000 15,000 15,000 15,000 15,000 15,000 15,000 10,000	- 25,000 10,000 50,000 25,000 11,250 26,250 55,000 75,000 - 25,000 100,000 50,000 25,000 10,0250 261,250 451,250 605,000 825,000	- 25,000 - 10,000 50,000 50,000 100,250 261,250 451,250 605,000 75,000 95,000 - 25,000 100,000 - 100,000 50,000 100,250 261,250 451,250 605,000 825,000 820,000 - 25,000 10,000 50,000 100,250 261,250 451,250 605,000 825,000 820,000 - 3,500 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5%	- 25,000 10,000 50,000 100,250 261,250 451,250 65,000 820,000 943,750 - 25,000 10,000 50,000 100,250 261,250 451,250 605,000 825,000 820,000 943,750 3,500 12,500 21,250 27,500 32,500 36,250 40,000 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5	- 25,000 - 10,000 50,000 25,000 10,250 261,250 451,250 605,000 820,000 820,000 943,750 1,018,750	- 25,000 10,000 50,000 25,000 10,250 261,250 451,250 605,000 825,000 820,000 943,750 1,018,750 1,033,750 - 25,000 10,000 50,000 100,250 261,250 451,250 605,000 825,000 820,000 943,750 1,018,750 1,033,750 1,	- 25,000 - 10,000 50,000 50,000 100,250 261,250 451,250 605,000 820,000 820,000 943,750 1,018,750 1,033,750 1,288,750 1,000,000 - 25,000 100,000 - 25,000 100,000 100,250 261,250 451,250 605,000 820,000 820,000 943,750 1,018,750 1,033,750 1,288,750 1,000,000 100,

Source: ROTH Capital Partners Pharmaceuticals Research.

CTP-499 Economics to Concert. As significant Phase 3 trials are contemplated with CTP-499, we expect the molecule to ultimately be partnered, potentially in international markets. We note that the more robust analysis of its Phase 2 study bodes well for CTP-499's Phase 3 consideration and for licensing. We assume international licensing could occur in 2H14 after Concert's discussions with FDA at end of Phase 2, and that could be a validating event for the CTP-499 program. For revenue modeling purposes, since CTP-499 is being partnered at a much later stage than the other compounds, but does not have an existing brand that it would be extending, we expect deal terms slightly north of the Jazz and Avanir deals, somewhat in line with that of Celegene, though with a higher royalty and more modest milestones due to regulatory success. The potential for such a compound in the setting is quite material, as there are over one million diabetics in the US with macroalbuminuria. If successful, 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 \$5.12 per CNCE share. (Exhibit 14)

**Diabetic Kidney Disease Statistics.** Diabetic kidney disease is a condition in which the kidneys' ability to filter blood is impaired. Approximately 26 million in the US in 2010 had diabetes and 90% to 95% were type 2. Diabetic kidney disease is now the nation's leading cause of dialysis, kidney transplant, and death from kidney failure. Numerous medical organizations point to type 2 diabetes is the leading cause of chronic kidney disease, including end stage renal disease, its most severe stage. Patients with both type 2 diabetes and chronic kidney disease have a markedly increased mortality compared to type 2 diabetics without chronic kidney disease (+270% according to the NHANES Survey in 2011). There are between 900k and 1.8 million type 2 diabetics with macroalbuminuria in the US; these patients have greatly elevated risks for both progression to end-stage renal disease. And according to Concert, the transition of a patient to dialysis increases patient cost by ~\$60,000 per year.

# Concert's Material Partnerships - Avanir, Jazz, and Celgene

#### Avanir – AVP-786, A Deuterated Neudexta

**Avanir Deal Backgound.** In February 2012, Concert inked a license agreement with Avanir Pharmaceuticals for worldwide rights to develop and commercialize Concert's deuterated dextromethorphan, now known as AVP-786 (or D-DM). The agreement includes the rights to multiple D-DM compounds, and Avanir has overall responsibility for research, development and commercialization of AVP-786. AVP-786 includes one of the D-DM analogs licensed to Avanir, and is a combination of a deuterium-substituted dextromethorphan analog and an ultra-low dose of quinidine. The deuteration allows for an ultra low-dose of quinidine to be included in AVP-786, an advantage over Avanir's existing franchise Neudexta.

Exhibit 15: Dextromethorphan: Multiple Receptor Activity in the CNS

### DEXTROMETHORPHAN **NMDA** Serotonin Receptor Reuptake Antagonist Inhibitor Low affinity (Ki = 1500 nM)<sup>1,2</sup> (Ki = 40 nM)Sigma-1 Norepinephrine Receptor Reuptake Agonist Inhibitor $(Ki = 200 nM)^{3-5}$ (Ki = 240 nM for inhibition of uptake; 13 µM for inhibition of binding)6

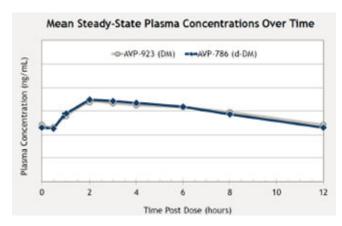
DM Binds to Key Receptors in the CNS

Source: Avanir Corporate presentation, March 2014.

**Neudexta and AVP-786 Rationale.** AVP-786 is a deuterated version of dextromethorphan hydrobromide, the primary active ingredient in Neudexta, which is being currently launched by Avanir for the treatment of pseudobulbar affect (PBA). PBA occurs secondary to a variety of unrelated neurological conditions, and is characterized by involuntary, sudden, and frequent episodes of laughing and/or crying; its episodes occur out of proportion or are not similary to the person's emotional state. Dextromethorphan acts on sigma-1 and NMDA receptors and is an inhibitor of serotonin and norepinephrine (Exhibit 15), but Neudexta also includes quinidine sulfate as a metabolic inhibitor, enabling therapeutic dextromethorphan concentrations. With AVP-786, incorporation of deuterium into specific positions of the dextromethorphan molecule strengthens the chemical bonds and reduces susceptibility to enzyme cleavage and first pass metabolism without altering dextromethorphan's pharmacology, according to Avanir. Having lower levels of quinidine reduces chances for a patient to experience QTc prolongation, and AVP-786 contains much less quinidine than Neudexta.

AVP-786 and AVP-923: Beneficial Development. Avanir is developing AVP-786 for the treatment of neurologic and psychiatric disorders, and expects to enroll patients in a study with AVP-786 in treatment-resistant major depressive disorder in 2H14. The start of this trial triggers a milestone of \$2 million to Concert. In addition, it should be noted that Avanir will enroll patients in a Phase II trial to investigate the use of its related compound AVP-923 for the treatment of levodopa induced dyskinesia (LID) in patients with Parkinson's disease (PD). This is meaningful because Avanir has FDA acceptance that it may apply results from AVP-923 to the AVP-786 program, potentially significantly truncating its development timeline in multiple indications.

Exhibit 16: AVP-786 Has Similar Pharmacokinetics Compared to AVP-723



Source: Concert Pharmaceuticals corporate presentation Feb 2014.

**AVP-786 Key Data.** In February 2013, Avanir reported positive results from a Phase 1 double-blind crossover clinical trial of AVP-786 where AVP-786, with a reduced dose of quinidine compared to AVP-923, demonstrated a PK profile similar to AVP-923 with comparable safety and tolerability (Exhibit 16 above). In October 2013, Avanir reported plans to advance AVP-786 into a Phase 2 clinical trial in the second half of 2014 for treatment-resistant major depressive disorder in patients with insufficient response to conventional anti-depressants, based on data generated by AVP-923 in patients with PBA and depression noted in Exhibit 17 below.

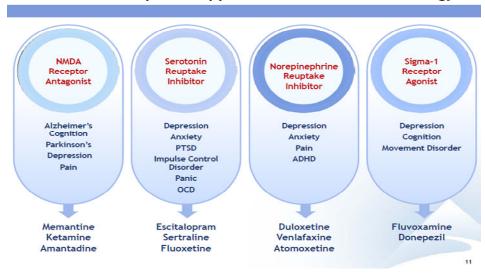
Exhibit 17: Avanir's AVP-923 in Depression in Pseudobulbar Affect Patients

Endpoint	AVP-923 30/10	AVP-923 20/10	Placebo	P Value (30/10 vs. Placebo) (20/10 vs. Placebo)
	(n=50)	(n=55)	(n=52)	
BDI-II	-3.36	-2.3	-1.1	0.065 0.378

Source: Avanir Corporate presentation, March 2014.

Exhibit 18: Dextromethorphan: Potential Broad Activity

#### Potential Therapeutic Applications of DM Pharmacology



Source: Avanir Corporate presentation, March 2014.

Avanir Deal Economics to Concert. Concert received a \$2 million upfront payment for the initial deal, and during 2013, it also recognized a \$2 million milestone payment based on positive data from Avanir's Phase 1 clinical trial of AVP-786. Concert is eligible to earn up to \$4 million in development milestones, up to \$37 million in regulatory milestones and up to \$125 million in sales milestones. The next potential milestone Concert could receive is \$2 million for initiation of dosing in a Phase 2 or Phase 3 clinical trial for AVP-786, which we believe could occur in 2H14 as Avanir begins the Phase 2 study in treatment-resistant depressive disorder. Concert is also to receive royalties ranging from the mid-single digits to low double digits on worldwide net product sales, which extends to the longer of specified patent expiration or 10 years following commercial launch. As AVP-786 appears key to Avanir's long term plans and potential success, we expect a continued rollout of news flow on the various indications being pursued. (Exhibit 18 above, Exhibit 19.) We remind that positive events for AVP-923 should also be positive for AVP-786.

AVP-923

Pseudobulbar Affect
Agitation (Alzheimer's)
Dyskinesia (Parkinson's)

AVP-786

Treatment-Resistant Depression
Neuropathic Pain

Investigator Programs

AVP-923

Treatment-Resistant Depression
Behavior Symptoms (Autism)
Bulbar Function (ALS)

Exhibit 19: Avanir: Big Plans for AVP-786, AVP-923: Both Beneficial to Concert

Source: Avanir Corporate presentation, March 2014.

**AVP-786 Opportunity/Economics to Concert.** The reduction of quinidine in AVP-786 may free the dextromethorphan asset to be developed in many settings, and Avanir is doing just that, with plans to examine the Concert drug in treatment-resistant depression and neuropathic pain settings (Exhibit 19), among others. All this development should ultimately be beneficial to Concert, as the royalties and milestones accrue. There is also ongoing work with AVP-923 that should benefit AVP-786 as well, in multiple other settings, including agitation in Alzheimer's, Parkinson's dyskensia, among others. Collectively, success in these indications should also accrue over to AVP-786, so we model its peak revenue in excess of \$1 billion. All in, with revenue and milestones noted above, we estimate AVP-736's fully taxed, risk weighted NPV is \$3.85 per CNCE share to Concert. (Exhibit 20)

Exhibit 20: AVP-786 NPV Calculation to Concert

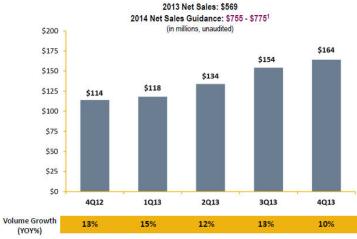
	 2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	20
Avanir - AVP-786	-	-		-	-	67,500	170,000	295,000	430,000	565,000	692,500	820,000	947,500	1,060,000	1,165,000	1,270,000	1,375
US Sales	-	-	-	-	-	40,000	105,000	170,000	235,000	300,000	365,000	430,000	495,000	560,000	625,000	690,000	755
Int'l Sales	-	-	-	-	-	27,500	65,000	125,000	195,000	265,000	327,500	390,000	452,500	500,000	540,000	580,000	620
Royalty Rate	-	-	-	-	5%	5%	5%	7.5%	7.5%	7.5%	10%	10%	10%	12%	12%	12%	
Royalty	-	-	-	-	-	3,375	8,500	22,125	32,250	42,375	69,250	82,000	94,750	127,200	139,800	152,400	165
filestones	2,000	2,000		-	10,000	27,000	-	10,000	-	-	50,000	-	-	-	-	65,000	
otal Revenue to Concert	2,000	2,000		-	10,000	30,375	8,500	32,125	32,250	42,375	119,250	82,000	94,750	127,200	139,800	217,400	16
let to Concert	2,000	2,000		-	10,000	30,375	8,500	32,125	32,250	42,375	119,250	82,000	94,750	127,200	139,800	217,400	16
Days to End	96.0	461.0	827.0	1192.0	1557.0	1922.0	2288.0	2653.0	3018.0	3383.0	3749.0	4114.0	4479.0	4844.0	5210.0	5575.0	
ears to end	0.3	1.3	2.3	3.3	4.3	5.3	6.3	7.3	8.3	9.3	10.3	11.3	12.3	13.3	14.3	15.3	
IPV/year	1927.8	1588.6	0.0	0.0	3860.2	9380.2	2098.6	6345.3	5096.0	5356.7	12052.4	6630.1	6128.8	6582.2	5783.8	7195.5	
iscount Rate	15%	20%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	
ax rate used	0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	
PV Taxed (effective rate)	\$ 1,928 \$	1,589 \$	- \$	- \$	3,860 \$	9,380 \$	2,099 \$	4,124 \$	3,312 \$	3,482 \$	7,834 \$	4,310 \$	3,984 \$	4,278 \$	3,759	\$ 4,677	\$
Total Value	\$91,953																
NPV Per Share	\$5.33																
otal Value taxed	\$66,369																
NPV/share taxed	\$3.85																

Source: ROTH Capital Partners Pharmaceuticals Research.

### Jazz Pharmaceuticals – JZP-386: Toward A Better Xyrem

Jazz Deal Backgound. In February 2013, Concert signed a license agreement with Jazz Pharmaceuticals providing Jazz with the worldwide rights to Concert's deuterated sodium oxybate (D-SXB) compounds. Jazz has responsibility for ongoing development activities, though Concert is providing development support services through a single Phase 1 clinical trial. JZP-386, is a product candidate containing a deuterated analog of sodium oxybate for potential use in patients with narcolepsy. Sodium oxybate is the active ingredient in the marketed drug Xyrem, which is being successfully marketed by Jazz, with the product achieving revenue of nearly \$570 million during 2013.

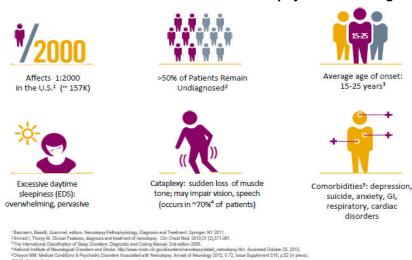
Exhibit 22: Jazz Pharmaceuticals's Xyrem Franchise – A Major Success



Source: Jazz Pharmaceuticals Corporate Presentation March 2014.

**Jazz Deal Economics to Concert.** Concert received a \$4.0 million upfront payment from Jazz, and could earn up to \$8 million in development milestones, up to \$35 million in regulatory milestones, and up to \$70 million in sales-based milestones. The next milestone could be \$4 million for the completion of a Phase 1 clinical trial in the EU. In addition, Concert is to receive royalties at mid-single digits to low double digits, on a country-by-country and licensed product-by-licensed product basis, on worldwide net product sales of licensed products.

Exhibit 21: Jazz Pharmaceuticals's Narcolepsy Focus: A Large Orphan Opportunity



Source: Jazz Pharmaceuticals Corporate Presentation March 2014.

The JZP-386 Opportunity. Xyrem (sodium oxybate) is an oral solution is indicated for the treatment of cataplexy and excessive daytime sleepiness (EDS) in patients with narcolepsy. Xyrem is the only product approved by the FDA for the treatment of cataplexy and EDS in narcolepsy and was first approved in 2002. As noted above, growth with the therapy has been quite robust, with the product generating revenue of \$569 million and growth of 50% in 2013. JZP-386 is a deuterated analog of sodium oxybate being developed for potential use in patients with narcolepsy. In vivo testing with JZP-386 demonstrated an extended pharmacokinetic profile compared to Xyrem, providing JZP-386 with the potential for reducing the middle-of-the-night dosing that is required for Xyrem.

In December 2013, an Investigational Medicinal Product Dossier (IMPD), the basis for initiating clinical trials in the EU, was filed for JZP-386, signaling Jazz's enthusiasm for the project. Jazz Pharmaceuticals has reported that it expects a Phase 1 clinical trial of JZP-386 to commence in 2014, with completion of enrollment and reporting of initial data also expected in 2014. With JZP-378's potential to replace and improved Xyrem, potentially expanding the original brand materially, given the growth of the Xyrem brand, we model its peak revenue in excess of \$1 billion. All in, with relatively low development risks assumed with the program, and revenue and milestones noted above, we estimate the NPV is \$2.73 to Concert. (Exhibit 23)

Exhibit 23: JZP-386 NPV Calculation to Concert

	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	203
Jazz JZP-386 - sleep indications	-	-		-		55,000	170,000	272,500	375,000	477,500	580,000	682,500	785,000	887,500	990,000	1,092,500	1,195,00
US Sales	-	-		-	-	45,000	105,000	170,000	235,000	300,000	365,000	430,000	495,000	560,000	625,000	690,000	755,00
Int'l Sales	-	-	-	-	-	10,000	65,000	102,500	140,000	177,500	215,000	252,500	290,000	327,500	365,000	402,500	440,0
Royalty Rate		-	-		-	5%	5%	7.5%	7.5%	7.5%	10%	10%	10%	12%	12%	12%	12
Royalty	-	-	-	-	-	2,750	8,500	20,438	28,125	35,813	58,000	68,250	78,500	106,500	118,800	131,100	143,4
Milestones	-	2,000		2,000	4,000	35,000	-	-	-	-	20,000	-	-	-	-	20,000	
Total Revenue to Concert	-	2,000		2,000	4,000	37,750	8,500	20,438	28,125	35,813	78,000	68,250	78,500	106,500	118,800	151,100	143,40
Net to Concert		2,000		2,000	4,000	37,750	8,500	20,438	28,125	35,813	78,000	68,250	78,500	106,500	118,800	151,100	143,40
Days to End	96.0	461.0	827.0	1192.0	1557.0	1922.0	2288.0	2653.0	3018.0	3383.0	3749.0	4114.0	4479.0	4844.0	5210.0	5575.0	5940
Years to end	0.3	1.3	2.3	3.3	4.3	5.3	6.3	7.3	8.3	9.3	10.3	11.3	12.3	13.3	14.3	15.3	16
NPV/year	0.0	1676.4	0.0	1102.7	1837.8	11657.7	2098.6	4036.8	4444.2	4527.1	7883.3	5518.3	3137.9	3274.8	2808.0	2747.2	200
Discount Rate	15%	15%	20%	20%	20%	25%	25%	25%	25%	25%	25%	25%	30%	30%	30%	30%	30
Tax rate used	0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35
NPV Taxed (effective rate) \$	- \$	1,676 \$	- \$	1,103 \$	1,838 \$	11,658 \$	2,099 \$	2,624 \$	2,889 \$	2,943 \$	5,124 \$	3,587 \$	2,040 \$	2,129 \$	1,825 \$	1,786	\$ 1,30
Total Value	\$62,669																
NPV Per Share	\$3.63																
Total Value taxed	\$47,165																
NPV/share taxed	\$2.73																

Source: ROTH Capital Partners Pharmaceuticals Research.

## The Celgene/Concert Deal

In April 2013 Concert entered into a development and license agreement with Celgene for the development and commercialization of deuterated compounds that are deuterated analogs of certain nondeuterated compounds targeting cancer or inflammation. Unfortunately, these specifics of these compounds have yet to be disclosed. What has been disclosed it that the collaboration will initially focus on one program, CTP-730, but could involve up to four programs in total. Oversight of each of the four programs is conducted by a separate joint steering committee.

Milestones associated with the total deal Celgene deal total up to \$1.4 billion, as the deal terms also include three other potential assets. We believe the milestones total of \$1.4 billion point to its significance. In terms of inflammatory indications, 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. CPT-730 is expected to enter the clinic this year, and Phase 1 results could be achieved by year end.

Celgene's deuterated CTP-730 is nearing Phase 1 development for inflammatory diseases; though the specific target and parent molecule of CTP-730 has not been disclosed, For the initial program, CTP-730, Concert granted Celgene an exclusive worldwide license to develop, manufacture and commercialize products that contain deuterated analogs of a selected non-deuterated compound (not disclosed) and several close chemical derivatives thereof. Concert is responsible for conducting research and early development activities of the first program. This includes the

completion of single and multiple ascending dose Phase 1 clinical trials and any mutually agreed upon additional Phase 1 clinical trials approved by a joint steering committee for the collaboration.

Concert also granted Celgene licenses with respect to two additional programs and an option with respect to a third additional program. Concert and Celgene have agreed on the non-deuterated (parent) compounds for each of the two additional license programs. With respect those two, Celgene is restricted from utilizing its research, development and commercialization rights unless Celgene pays Concert a license exercise fee within seven years of the effective date of the initial agreement. For the option program, Celgene may select the non-deuterated compound at a later time, which will be limited to a compound for which Celgene possesses exclusive rights.

**Celgene Economics – Considerable.** The Initial Celgene Program Milestones - Concert received a \$35 million non-refundable upfront payment from Celgene for the initial agreement. In addition, regarding CTP-730 Concert is eligible to earn up to \$23 million in development milestone payments, up to \$247.5 million in regulatory milestone payments and up to \$50.0 million in sales based milestone payments related to products within the initial program. The next milestone payment the Company might be entitled to receive under the initial program is \$8 million related to the completion of a Phase 1 clinical trial.

The Two Additional Celgene Licences Milestones - If Celgene exercises its rights with respect to either of the two additional license programs, Concert will receive a license exercise fee of \$30 million and will also be eligible to receive up to \$23 million in development milestone payments and up to \$247.5 million in regulatory milestone payments. With respect to one of the additional license programs, the Company is eligible to receive up to \$100 million in sales-based milestones, and with the other additional license program, Concert can receive up to \$50 million in sales-based milestones.

The Option Program Milestone Structure - If Celgene exercises its option with respect to the option program, Concert will receive an exercise fee of \$10 million and will be eligible to earn up to \$23 million in development milestone payments, and up to \$247.5 million in regulatory milestone payments.

Exhibit 24: CTP-730 - NPV Calculation to Concert

	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030
Celgene - CTP-730 - Inflam.	-				-	35,000	170,000	272,500	375,000	477,500	580,000	682,500	785,000	887,500	990,000	1,092,500	1,195,00
US Sales	-	-	-	-	-	25,000	105,000	170,000	235,000	300,000	365,000	430,000	495,000	560,000	625,000	690,000	755,00
Int'l Sales	-	-	-	-	-	10,000	65,000	102,500	140,000	177,500	215,000	252,500	290,000	327,500	365,000	402,500	440,00
Royalty Rate		-			0%	5%	5%	7.5%	7.5%	7.5%	10%	10%	10%	12%	12%	12%	125
Royalty	-	-	-	-	-	1,750	8,500	20,438	28,125	35,813	58,000	68,250	78,500	106,500	118,800	131,100	143,40
Milestones		8,000		15,000	100,000	147,500	-	-	-	-	15,000	-	-		-	35,000	
Total Revenue to Concert		8,000		15,000	100,000	149,250	8,500	20,438	28,125	35,813	73,000	68,250	78,500	106,500	118,800	166,100	143,40
CNCE Expenses																	
COGS (US only)	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	
COGS pct	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	09
SG&A					-	-	-	-	-	-	-	-	-	-	-	-	
R&D	2000	2000	0	0	-	-	-	-	-	-	-	-	-	-	-	-	
Total Expense	2,000	2,000	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Net to Concert	(2,000)	6,000		15,000	100,000	149,250	8,500	20,438	28,125	35,813	73,000	68,250	78,500	106,500	118,800	166,100	143,40
Days to End	96.0	461.0	827.0	1192.0	1557.0	1922.0	2288.0	2653.0	3018.0	3383.0	3749.0	4114.0	4479.0	4844.0	5210.0	5575.0	5940
Years to end	0.3	1.3	2.3	3.3	4.3	5.3	6.3	7.3	8.3	9.3	10.3	11.3	12.3	13.3	14.3	15.3	16
NPV/year	-1927.8	4526.4	0.0	7237.8	23804.2	25377.0	1031.4	1771.3	1741.1	1583.6	2303.6	1538.4	1263.9	1224.8	975.0	973.7	600
Discount Rate	15%	25%	25%	25%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40
Tax rate used	0%	0%	0%	0%	0%	0%	0%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35
NPV Taxed (effective rate)	\$ (1,928) \$	4,526 \$	- \$	7,238	\$ 23,804	\$ 25,377 \$	1,031 \$	1,151 \$	1,132 \$	1,029 \$	1,497 \$	1,000 \$	822 \$	796 \$	634 \$	633	\$ 39
Total Value NPV Per Share	\$75,078 \$4.35																
Total Value taxed	\$69,818 \$4.05																

Source: ROTH Capital Partners Pharmaceuticals Research.

Royalties, Valuation Calculations. In addition, Celgene is required to pay Concert royalties on net sales of each licensed product ranging from the mid-single digits to low double digits (we estimate 13%), on worldwide net product sales of licensed products. Despite not knowing the specifics of the compounds in development we believe these represent significant programs for Celegene, for instance, Celgene mentions in its presentations about a once-daily version of Otezla, which could be a deuterated version, of that promising franchise, which is ready to launch in psoriasis and psoriatic arthritis in 2014. Given the magnitude of the program, we assume potential collective of over \$1B for CTP-730, and estimate its risk-weighted net present value to concert at \$4.05 NPV. (Exhibit 24) In addition,

though the calculation is not specifically disclosed in an exhibit, we risk weight the cumulative royalties and milestones of the two additional programs and the option program collectively at \$0.54 per CNCE share.

### **Concert's Other Proprietary Opportunities – Behind the Curtain**

**Deuterated Ivacaftor Analogs** – As mentioned above, Concert has a large number of deuterated assets in its stable, that have the potential to mature fairly rapidly. For instance, with Vertex's ivacaftor (Kalydeco) which is currently approved for cystic fibrosis, deuteration at the major site of biotransformation stabilized its metabolism in human in vitro models and greatly improved the pharmacokinetic properties of the deuterated analogs in dogs (Exhibit 25). Further studies of the analogs are warranted to evaluate the potential of deuterated ivacaftor to be a more convenient, or potentially more effective CFTR potentiator. Though we currently initially assign only modest value to these efforts--we collectively value them at \$0.97 per CNCE share--we fully expect to be considering greater value for these programs in the future.

#### **Exhibit 25: Ivacaftor amd Deuterated Ivacaftor Analogs**

Source: Nguyen, S. et al. Deuterated Analogs of Ivacaftor Have Improved Metabolism and Pharmacokinetic Properties. ISSX International Meeting 2013.

# Appendix 1: Concert's Patent Portfolio – Displaying Pipeline Breadth

D-Agomelatine No. 7,608,737	D-Iloperidone No. 8,198,305	<u>D-Vandetanib</u> : No. 8,609,673
<u>D-Almorexant</u>	<u>D-Maraviroc</u>	F-Tadalafil
No. 8,084,464	No. 7,932,235	No. 7,863,274
D-Apremilast	D- Mibefradil	<u>D-HDX</u>
No. 8,124,646	No. 8,513,434	No. 8,263,601
No. 8,404,737	No. 8,575,361	
		D-Sitagliptin
D-Atazanavir	D-Morpholine Derivatives Process	No. 7,820,666
No. 8,158,805	No. 8,354,557	
No. 8,258,309		D-Sodium Oxybate
, ,	<u>D-Mosapride</u>	No. 8,461,197
<u>D-Bosentan</u>	No. 7,528,131	110. 0, 101, 107
No. 8,071,596		D-Udenafil
No. 8,080,549	D-Niacin	No. 8,552,008
110. 0,000,010	No. 8,471,034	No. 0,332,000
<u>D-Cilostazol</u>	110. 0,47 1,004	D. Vieriuiree
No. 8,349,817	D. Dorovetine	D-Vicriviroc
No. 8,357,674	<u>D-Paroxetine</u> No. 7,678,914	No. 8,367,674
140. 0,007,074		
	No. 8,450,492	D-GABA modulators
<u>D-Darunavir</u>	No. 8,450,492	D- L838417
	No. 8,450,492  D- Praziquantel	<i>D- L838417</i> No. 8,003,646
<u>D-Darunavir</u> No. 8,592,487	No. 8,450,492	<i>D- L838417</i> No. 8,003,646 No. 8,399,467
D-Darunavir No. 8,592,487  D-Dasatinib	No. 8,450,492  D- Praziquantel	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA
<u>D-Darunavir</u> No. 8,592,487	No. 8,450,492  D- Praziquantel	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815
D-Darunavir No. 8,592,487  D-Dasatinib	No. 8,450,492 <u>D- Praziquantel</u> No. 8,563,554	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA
D-Darunavir No. 8,592,487  D-Dasatinib	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815
<u>D-Darunavir</u> No. 8,592,487 <u>D-Dasatinib</u> No.8,338,425	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin	No. 8,450,492  D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin No.: 8,575,221	D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine No. 7,943,620	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738 D-Gefitinib No. 7,855,204
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin	D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine No. 7,943,620  D-Rimonabant	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738  D-Gefitinib No. 7,855,204  D-Silodosin
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin No.: 8,575,221  D-Elvitegravir	D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine No. 7,943,620	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738  D-Gefitinib No. 7,855,204  D-Silodosin
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin No.: 8,575,221  D-Elvitegravir	D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine No. 7,943,620  D-Rimonabant No. 7,514,068	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738  D-Gefitinib No. 7,855,204  D-Silodosin No. 8,013,007
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin No.: 8,575,221  D-Elvitegravir No. 7,994,194  D-Erlotinib	D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine No. 7,943,620  D-Rimonabant No. 7,514,068  D-Rivaroxaban	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738  D-Gefitinib No. 7,855,204  D-Silodosin No. 8,013,007
D-Darunavir No. 8,592,487  D-Dasatinib No.8,338,425  D-Dextromethorphan No. 8,541,436 No. 8,188,110 No. 7,973,049  D-Dimethylcurcumin No.: 8,575,221  D-Elvitegravir No. 7,994,194	D- Praziquantel No. 8,563,554  D-Raltegravir No. 7,687,509 No. 8,318,754  D-Regorafenib No. 8,410,082  D-Ranolazine No. 7,943,620  D-Rimonabant No. 7,514,068	D- L838417 No. 8,003,646 No. 8,399,467 D-Alpha5IA No. 8,557,815 D-NS11394 No. 8,278,460 d-TPA-023 No. 8,501,738  D-Gefitinib No. 7,855,204  D-Silodosin No. 8,013,007

#### **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 \$25.27 per CNCE share, representing the lion's share of our \$28 CNCE shares target (Exhibit 3).

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. 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. 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, we value the program at \$5.12 per CNCE share. Other less mature proprietary products are much more modest opportunities at this point and valued at \$0.97 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 \$3.85 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 materially opportunity, generating a \$2.73 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 \$4.05 NPV, by our calculation. The remainder of the Celgene assets are estimated at \$0.54, and net cash, NOLs and the drag of general corporate expense totals \$2.70 per CNCE share, yielding the \$27.97 total, driving our \$28 CNCE shares 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 is drug development, Concert is subject to the very 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 severely 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 molecules may take material time and resources to complete clinical development, if they are able to do so at all. In addition, the company may seek one or more collaborators for the 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 that it is able to enter into one with beneficial terms. Despite multiple collaborators, these development programs have major investor interest and their progress may not continue, if at all. It 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. Because these programs are 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. 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.** No deuterated drug has ever been successfully commercialized, to the best of our knowledge. There may be specific risks to gaining the approval of these types of agents from regulatory authorities, though these do not appear to have not emerged as yet. In addition the company may also incur manufacturing challenges, or the costs that they may be required to incur for the manufacture of any product candidate that receives marketing approval may be substantial.

#### **COMPANY DESCRIPTION**

Concert Pharmaceuticals create novel medicines that address medically important needs by applying its DCE Platform (Deuterated Chemical Entity Platform) to compounds with well-characterized pharmacological activity. This approach may enable drug discovery and clinical development that is more efficient and less expensive than conventional small molecule drug research and development. The company was co-founded in 2006 by Richard Aldrich, Roger Tung and Christoph Westphal, and is located in the historic town of Lexington, Massachusetts.

# **CONCERT PHARMACEUTICALS, INC**

NCERT PHARMACEUTICAI	LS, INC.								Comp	any No	ote - A	pril 1, 2
	2011A	2012A	2013A	1Q14E	2Q14E	3Q14E	4Q14E	2014e	2015E	2016E	2017E	2018E
Concert Pharmaceuticals, Inc.												
Product Revenue	\$ - \$	•	•	•	•	Φ.	•	•	Φ.	•	•	
CTP-354 Total - US	0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	0
- International	0	0	0	0	0	0	0	0	0	0	0	0
CTP-499 Total - US	\$ - \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$ 0	- \$	- 0
- International	0	0	0	0	0	0	0	0	0	0	0	0
Other/Collab revenue	0	0	0	0	0	0	0	0	0	0 \$	- \$	-
Total Proprietary Sales Revenue	0	0	0	0	0	0	0	0	0	0	0	0
Milestone & Royalty Revenue												
Total Royalties from Partners	0	0	0	-	•	-	-	0	-	-	•	-
Upfront, Milestones Payments	\$ 5,500 \$	1,500 \$	2,000 \$	- \$	- \$	2,000 \$	2,000 \$	4,000 \$	25,000 \$	13,000 \$	40,000 \$	
Total Upfront, Milestones Payments	5,500	1,500	2,000	-	-	2,000	2,000	4,000	25,000	13,000	40,000	147,000
License and Development Revenue	13,967	11,349	23,408	2,500	2,500	2,500	2,500 \$	10,000	8,500	8,500	9,000	9,000
Total Concert Revenue	\$19,467	\$12,849	\$25,408	\$2,500	\$2,500	\$4,500	\$4,500	\$14,000	\$33,500	\$21,500	\$49,000	\$156,000
Expenses:				**		**	•		**		**	••
COGS R&D	\$0 23,436	\$0 24,193	\$0 21,790	\$0 5,750	\$0 6,000	\$0 6,500	\$0 6,750 \$	\$0 25,000	\$0 26,500	\$0 30,000	\$0 30,000	\$0 35,000
SG&A Total Expenses	7,377 \$30,813	7,266 31,459	8,028 29,818	2,100 \$7,850	2,200 \$8,200	2,500 \$9,000	2,700 \$ \$9,450 \$	9,500 34,500	10,000 \$36,500	10,200 \$40,200	13,000 \$43,000	15,000 \$50,000
Operating Income	(11,346)	(18,610)	(4,410)	(5,350)	(5,700)	(4,500)	(4,950) \$	(20,500)	(3,000)	(18,700)	6,000	106,000
Operating Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Interest Income	44	22	20	0	50	100	100 \$	250	400	275	200	800
Interest Expense Other Income (Expense)	(18)	(1,856) 0	(1,666) 0	0	0	0	0 \$ 0 \$	-	(100) 0	(200) 0	(200) 0	(200) 0
Other financing income (expense) Total Other Income, net	0 26	0 (1,834)	(1.646)	0	0 50	100	0 \$	250	300	0 75	0	600
Pretax Income	(11,320)	(20,444)	(1,646)	(5,350)	(5,650)	(4,400)	(4,850) \$	(20,250)	(2,700)	(18,625)	6,000	106,600
Pretax Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Effective Taxes Tax Rate	0.0%	0.0%	0.0%	0.0%	- 0.0%	- 0.0%	0.0%	0.0%	0.0%	- 0.0%	420 7.0%	9,061 <i>8.5%</i>
Fully Taxed rate	(4,302)	(7,769)	(2,301)	(2,033)	(2,147)	(1,672)	(1,843) \$	(7,695)	(1,026)	(7,078)	2,280	40,508
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)	-	-	-	- (1.070) 4	-	- (2 = 22)	-	-	-
Net Income (Loss) - Effective taxed	(12,389)	(20,832)	(6,452)	(5,350)	(5,650)	(4,400)	(4,850) \$	(20,250)	(2,700)	(18,625)	5,580	97,539
Income - Fully taxed  Margin	(7,018) NM	(12,675) NM	(3,755) NM	(3,317) NM	(3,503) NM	(2,728) NM	(3,007) \$ NM	(12,555) NM	(1,674) NM	(11,548) NM	3,720 NM	66,092 NM
Other Comprehensive Income (Loss)	16	(5)	0	-	-	-	-	0	-	-	-	-
Comprehensive Income (Loss)	(11,304)	(20,449)	(6,056)	(5,350)	(5,650)	(4,400)	(4,850) \$	(20,250)	(2,700)	(18,625)	6,000	106,600
EPS (ex-charges; eff. taxed)	(\$9.66)	(\$16.15)	(\$4.99)	(\$0.32)	(\$0.34)	(\$0.26)	(\$0.29)	(\$1.21)	(\$0.16)	(\$1.08)	\$0.31	\$5.33
EPS (ex-charges; fully-taxed) EPSS (comprehensice Income (eff taxes)	(\$5.47) (\$8.81)	(\$9.83) (\$15.85)	(\$2.91) (\$4.69)	(\$0.20) (\$0.32)	(\$0.21) (\$0.34)	(\$0.16) (\$0.26)	(\$0.18) (\$0.29)	(\$0.75) (\$1.21)	(\$0.10) (\$0.16)	(\$0.67) (\$1.08)	<b>\$0.20</b> \$0.32	<b>\$3.55</b> \$5.73
Shares O/S (000), Basic			1,292		16,750	16,750		16,750	17,100		18,200	18,300
Shares O/S (000), Diluted	1,283 1,283	1,290 1,290	1,292	16,700 16,700	16,750	16,750	16,800 16,800	16,750	17,100	17,200 17,200	18,500	18,600
				(% of sales)								
Cost of Sales (product sales) Gross	0.0% NM	0.0% NM	0.0% NM	0.0% NM	0.0% NM	0.0% NM	0.0% NM	0.0% NM	0.0% NM	NM NM	NM NM	NM NM
R & D S G & A	NM 31.0%	NM 31.0%	NM 31.0%	NM 31.0%	NM 31.0%	NM 31.0%	NM 31.0%	NM 31.0%	79.1% 31.0%	139.5% 31.0%	61.2% 31.0%	22.4% 31.0%
Total	158.3%	244.8%	117.4%	314.0%	328.0%	200.0%	210.0%	246.4%	109.0%	187.0%	87.8%	32.1%
Revenue				ear Growth		N:18.4	N 18 4	A18.4	100.00/	0F 00/	107.00/	010 40/
Revenue Operating Income	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	139.3% NM	-35.8% NM	127.9% NM	218.4% NM
Pretax Income Income	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM
EPS (ex-charges) EPS (ex-charges; fully-taxed)	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM	NM NM
=: = (=n orangoo; rany tanoa)	14101	14141	. 4141	. 4141	. 4141	. 4141	. 4141	14141	1 4141	14141	1 4141	14141

Source: Concert Pharmaceuticals, Inc. SEC documents and ROTH Capital Partners estimates.

Contact Information: Robert Hazlett, Senior Research Analyst, ROTH Capital Partners, 646-358-1912.

# **CONCERT PHARMACEUTICALS, INC.**

MACEUTICALS, INC.						COII	ipany iv
	12/31/2011A	12/31/2012A	12/31/2013E	12/31/2014E	12/31/2015E	12/31/2016E	12/31/2017E
BALANCE SHEET							
ASSETS	***	A7.5	40.0	<b>#</b> 00.0	0447.0	01015	0107.7
Cash & equivalents	\$22.9	\$7.5	\$9.6	\$62.0	\$117.0	\$101.5	\$107.7
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	\$5.0	\$3.2	\$7.4
Prepaid & other current assets	\$0.9	\$1.2	\$1.5	\$0.1	\$0.3	\$0.2	\$0.5
Total Current Assets	\$44.1	\$28.9	\$34.5	\$87.3	\$145.4	\$128.0	\$138.6
Property & Equipment, net, other	\$4.4	\$3.5	\$2.6	\$2.6	\$2.6	\$2.6	\$2.6
Long term investment	\$0.0	\$0.0	\$1.3	\$1.3	\$1.3	\$1.3	\$1.3
Other Assets	\$0.8	\$0.8	\$3.0	\$3.0	\$3.0	\$3.0	\$3.0
Total Assets	\$49.4	\$33.1	\$41.3	\$94.1	\$152.3	\$134.8	\$145.4
LIABILITIES & S.E.							
Accounts payable	\$1.6	\$0.8	\$3.8	\$1.4	\$3.4	\$3.2	\$7.4
Accrued expenses	\$1.5	\$2.0	\$3.2	\$3.4	\$3.7	\$4.0	\$4.3
Deferred short-term revenue	\$6.9	\$0.0	\$3.5	\$3.4 \$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	\$5.4	\$2.8	\$6.7	\$4.3	\$0.0
Total Current Liabilities	\$10.3	\$7.9	\$16.2	\$8.9	\$14.1	\$11.8	\$12.0
Leasehold improvement loan, net of current	\$0.9	\$0.6	\$0.3	\$2.0	\$2.0	\$2.0	\$2.0
Deferred lease incentive	\$1.4	\$0.9	\$0.3	\$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	\$0.4	\$0.5	\$0.5	\$0.5	\$0.5
Note Payable/Long-term Liabilities	\$7.1	\$14.9	\$9.0	\$9.0	\$9.0	\$9.0	\$9.0
Total liabilities	\$24.7	\$28.0	\$26.3	\$24.4	\$29.6	\$27.3	\$27.5
Total Shareholders Equity	\$24.7	\$5.2	\$15.1	\$69.7	\$122.7	\$107.5	\$118.0
Depreciation	\$49.4	\$33.1	\$41.3	\$94.1	\$152.3	\$134.8	\$145.4
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	12/31/2011A	12/31/2012A	12/31/2013E	12/31/2014E	12/31/2015E	12/31/2016E	12/31/2017E
CASH FLOW STATEMENT							
Cash Flow from Operating Activities  Net income (loss)	(11.3)	(\$20.4)	(6.1)	(20.3)	(2.7)	(18.6)	6.0
Other adjustments	0.0	\$0.0	0.0	0.0	52.0	(12.0)	(12.0)
Depreciation & Amortization	1.6	\$1.5	1.0	1.1	1.2	1.4	2.0
Noncash compensation expense	0.9	\$0.9	0.9	1.0	1.5	2.0	2.5
Other non-cash financing expense	0.8	\$0.4	0.0	0.0	0.0	0.0	0.0
Amortization of financing costs, warrant	(0.5)	(\$0.1)	0.0	0.0	0.0	0.0	0.0
Accounts receivable	1.0	\$0.5	(0.0)	(1.8)	(2.9)	1.8	(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)	(0.2)	1.4	(0.2)	0.1	(0.3)
Other assets	(0.1)	\$0.0	0.0	0.0	0.0	0.0	0.0
Accounts payable and accrued expenses	0.7	(\$0.3)	3.1	(2.2)	2.2	0.2	4.4
Other operating activities (deferred rent)	(11.2)	(\$8.4)	(2.3)	(2.6)	3.9	(2.4)	(4.3)
Cash Flow from Operating Activities	(18.1)	(26.4)	(3.5)	(23.3)	55.0	(27.5)	(5.8)
Cash Flow from Investing Activities							
Maturities of Investments	64	\$37.7	35	0	0	0	0
Purchase of investments	(41)	(\$38.4)	(38)	0	0	0	0
Capital Expenditures, net	(0.3)	(\$0.5)	0.0	0.0	0.0	12.0	12.0
Other	-	\$0.0	(0.3)	-	-	-	-
	22.9	(1.2)	(3.33)	0.00	0.00	12.00	12.00
Cash Flow from Financing Activities							
Issuance of loan payable, net	7.3	\$12.5	0	0	0	0	0
Principle pmts of loan payaable	0.0	\$0.0	(3)	0	0	0	0
Repayment of leasehold impt loan	(0.3)	(\$0.3)	(0)	0	0	0	0
	0.0	\$0.0	0	88.0	0.0	0.0	0.0
Proceeds from iss. of common stock (net)							
Proceeds/Retirement of Debt, Other	0.0	\$0.0	0	0.0	0.0	0.0	0.0
			(3.3)	0.0 <b>88.0</b>	0.0	0.0	
Proceeds/Retirement of Debt, Other  Cash Flow from Financing Activities	7.0	\$0.0 12.2	(3.3)	88.0	0.0	0.0	0.0
Proceeds/Retirement of Debt, Other	0.0	\$0.0					0.0 0.0 101.5 6.2

Source: Concert Pharmeceuticals Inc. SEC documents and ROTH Capital Partners estimates.

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Regulation Analyst Certification ("Reg AC"): The research analyst primarily responsible for the content of this report certifies the following under Reg AC: I hereby certify that all views expressed in this report accurately reflect my personal views about the subject company or companies and its or their securities. I also certify that no part of my compensation was, is or will be, directly or indirectly, related to the specific recommendations or views expressed in this report.

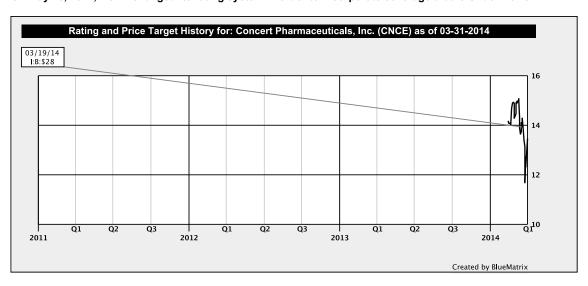
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On September 28, 2010, ROTH changed its rating system in order to replace the Hold rating with Neutral. On May 26, 2011, ROTH changed its rating system in order to incorporate coverage that is Under Review.



Each box on the Rating and Price Target History chart above represents a date on which an analyst made a change to a rating or price target, except for the first box, which may only represent the first note written during the past three years. **Distribution Ratings/IB Services** shows the number of companies in each rating category from which Roth or an affiliate received compensation for investment banking services in the past 12 month.

#### **Distribution of IB Services Firmwide**

IB Serv./Past 12 Mos. as of 04/01/14

Rating	Count	Percent	Count	Percent
Buy [B]	186	78.81	106	56.99
Neutral [N]	31	13.14	11	35.48
Sell [S]	1	0.42	0	0
Under Review [UR]	17	7.20	6	35.29

Our rating system attempts to incorporate industry, company and/or overall market risk and volatility. Consequently, at any given point in time, our investment rating on a stock and its implied price movement may not correspond to the stated 12-month price target.

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**Neutral:** A rating, which at the time it is instituted and or reiterated, that indicates an expectation of a total return between negative 10% and 10% over the next 12 months.

**Sell:** A rating, which at the time it is instituted and or reiterated, that indicates an expectation that the price will depreciate by more than 10% over the next 12 months.

**Under Review [UR]:** A rating, which at the time it is instituted and or reiterated, indicates the temporary removal of the prior rating, price target and estimates for the security. Prior rating, price target and estimates should no longer be relied upon for UR-rated securities.

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