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Theme Alert

Sector Healthcare

Company

Clarity Pharmaceuticals (CU6)

The COBRA strikes…with a lot of venom

Recommendation OVERWEIGHT

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Announcement Highlights

Clarity have released results from their Phase II COBRA trial, evaluating their ^{64}Cu-SAR-bisPSMA PET agent in prostate cancer (PCa) patients with suspected Biochemical Recurrence (BCR). There were three key takeaways from the top-line result that investors should be cognisant of; 1) ^{64}Cu-SAR-bisPSMA is able to detect BCR PCa with high sensitivity at a delayed timepoint (24-hours post) revealing further lesions (not feasible with other PSMA PET agents), consistent with data demonstrated in PROPELLER trial; 2) sensitivity of ^{64}Cu-SAR-bisPSMA creates new questions in regards to the current standard of truth (SoT) reference– that being biopsy and existing approved PSMA PET agents; and 3) the path to market for ^{64}Cu-SAR-bisPSMA could look different to our initial expectations with delayed scanning in BCR patients potentially an initial niche for them to target in this indication (still paired with initial staging as per previous expectations, currently being assessed in the CLARIFY trial).

Wilsons' View

Initial analysis

COBRA trial design. The COBRA trial recruited 52 participants with suspected BCR based on rising PSA post definitive therapy (radical prostatectomy, radiation therapy/brachytherapy /cryotherapy) with a negative or equivocal finding on conventional imaging. Participants received a single 200MBq dose of ^{64}Cu-SAR-bisPSMA and were evaluated at two timepoints (1-4hrs post injection and 24 hours post injection). In addition to safety, primary efficacy endpoints were patient-level correct detection rate (CDR, defined as the proportion of true positive participants out of all scanned participants) and region-level positive predictive value (PPV, defined as the proportion of true positive regions out of all positive regions on the ^{64}Cu-SAR-bisPSMA PET scan with corresponding evaluable SoT).

Detection rate of ^{64}Cu-SAR-bisPSMA comparison difficult vs SOC. The detection rate in the COBRA trial was premised on the proportion of true positive participants on Day 0 and Day 1 post-scan ^{64}Cu-SAR-bisPSMA (^{64}Cu). After patients were scanned with ^{64}Cu, the trial was designed to assess true positive detection rate via SoT comparison (composite of SOC imaging which includes PSMA scans, PSA levels and biopsy where possible/appropriate). As ^{64}Cu identified a large number of lesions that were not visible with SOC PSMA scans (^{18}F, ^{68}Ga agents) (60% and 80% on Day 1 and 2 respectively), which was not expected, it was not medically ethical to verify all of these lesions with biopsy. As such, and as per pre-specified protocol, if a lesion identified on the ^{64}Cu scan was not biopsied and it was also not present on follow-up SOC imaging, it was considered as false positive in the analysis by default. Clarity have set themselves an exceedingly tough bar.

Primary outcome measures. Safety: overall, there were minimal safety issues; a single resolved Grade 2 AE only. Efficacy. The CDR range across the central readers on Day 0 was 21.4–28.6%, increasing to 28.6–38.1% on Day 1. The region-level PPV on Day 0 range was 39.1–44.8% and on Day 1 was 32.7–43.3%. The specificity of PC detection in the pelvic lymph nodes, a common site of PCa metastases, was high across all readers on both days (Day 0: 93.8–96.9%; Day 1: 81.3–87.9%). The CDR and PPV, in particular were impacted by the higher than expected lesion detection rate, whereby the ^{64}Cu scans were classified as false positives (unless a biopsy was available). As a reminder, comparison to PYLARIFY's CONDOR and POSLUMA's SPOTLIGHT trial are difficult here, given the SOC imaging utilised was CT, MRI and bone scintigraphy (alongside histopathology). Given these confounding elements the low CDR and PPVs are easily misinterpreted (noting POSLUMA CDR was 51-54%, and PPV was 46-60%, with PPV failing to meet pre-specified threshold), however highlight the challenges that Clarity may face in selecting a SoT benchmark.

What does all of this mean? The absolute degree of difference in lesion detection by current SOC and ^{64}Cu-SAR-bisPSMA is unexpected, however the Day 1 delayed scan ability and higher uptake of Clarity's agent into lesions do provide points of differentiation. The challenge that uniquely faces Clarity is how to definitively prove true positives when there is a new SOC scan involved (that was absent in the prior trials to support PYLARIFY, ILLUCCIX etc) with an agent apparently superseding SoT specificity (noting the negative biopsy – true positive lesion example provided).

Earnings implications

Forecasts under review. Results from the COBRA trial pose a different pathway to market from previous expectations with regards to BCR indication (expectations were that they would follow LNTH, TLX etc.). Given the insights provided from the results today, and the anticipated changes in Phase III trial design, further analysis of the potential for Clarity to receive a) accelerated approval, b) more selective initial target BCR patient population (aka those with unmet need; rising PSA levels, Day 1 imaging priority), c) elongated trial/ commercialisation timeframes (for broader BCR patient population), and d) a mixture of the above, needs to be conducted. Noting that we do not expect this to deleteriously impact CU6's overall opportunity, and remain bullish on prospects with all of their pipeline agents including ^{64}Cu-SAR-bisPSMA, noting this does not impact the pathway for the initial staging indication for the agent (CLARIFY trial underway now).

Investment view

Maintain OVERWEIGHT. Our last published risked PT for Clarity Pharmaceuticals was $2.78/sh which is under review.

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