CAR-T therapies have demonstrated some of the highest cure rates in history for late-stage cancer patients. However, they are plagued with controversy because of their early toxicity profile, manufacturing and cost. Hopefully, technology is evolving fast and safety protocols are reducing mortality. We see the next 12 months as data rich and believe investor confidence in this market will increase. Our take is that 2018 will lead to considerably more colour on the improved efficacy and safety of CAR-T. The first two CAR-T cell therapies, namely Novartis’ Kymriah and Kite’s Yescarta, have been approved for the treatment of ALL and DLBCL respectively, paving the way for additional new entrants. 2018 may be a good entry point for two further CAR-T approvals in DLBCL, such as Novartis’ CTL019 and Juno’s JCAR017. We are re-initiating Cellectis and Celyad.

- Tumours use many strategies to evade the host immune response, including downregulation or weak immunogenicity of target antigens and creation of an immune-suppressive tumour environment. T-cells play a key role in cell-mediated immunity and, recently, strategies to genetically modify T-cells either through altering the T cell receptor (TCR) specificity or through introducing antibody-like recognition in chimeric antigen receptors (CARs) have made substantial advances. As we believe TCRs are riskier owing to fatal off-target toxicities and too early stage compared with CAR-T, we focused this report on CAR-T cell therapy.

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- T cells engineered to express CARs by gene transfer technology specifically recognize their target antigen in a simplified manner (antibody scFv-based, MHC independent), resulting in T cell activation. Starting with today’s murine containing scFv containing products, future CAR products should feature fully human scFv, optimized to particular T-cell subsets, suicide/control switches and logic gates as well as an armamentarium of strategies that allow T-cells to thrive in a hostile tumour environment. Autologous T-cells are the cornerstone of present cell-based cancer immunotherapies, but allogeneic cell sources, possibly including stem cell-derived “off-the-shelf” T-cells, are likely to play an important role in the future.

- Cellectis – NEUTRAL FV EUR23: Seems affected by several issues: 1/UCART19 clinical program is progressing slowly and demonstrated disappointed preliminary clinical results; 2/ CD123 might be a dangerous target to use for CAR-T cell therapy; 3/GMP manufacturing problems might explain in part the delays that the company accumulates; 4/Other pre-clinical projects focus on Multiple Myeloma, which in our view is not a strategic indication to address, and these CAR-T product candidates are still too early stage to be included in our valuation model; 5/Lack of clinical data in 2018.

- Celyad – BUY FV EUR58: Seems to have everything it takes to succeed.1/Celyad has a very differentiated approach with its autologous NKG2D CART, addressing both liquid (AML), and solid (colorectal) cancers; 2/Celyad is developing both autologous and allogeneic CAR-T cell therapies; 3/Despite its earlier development stage, Celyad has a robust patent estate validated by two structuring deals related to its allogeneic platform. Also, this robust allogeneic IP could be leveraged with further licensing agreements with CAR-T players interested in developing allogeneic CAR-T product candidates; 4/Has its own manufacturing infrastructure.

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Opinion recommending not to trade in a stock short-term, neither as a BUYER or a SELLER, due to a specific set of factors. This view is intended to be temporary. It may reflect different situations, in particular those where a fair value shows no significant potential or where an upcoming binary event constitutes a high-risk that is difficult to quantify. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

Negative opinion for a stock where we expect an unfavourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential downside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

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