



DAISEP MABXPURE: INNOVATIVE STRATEGIES FOR ENHANCING HCP CLEARANCE IN CLARIFICATION AND DOWNSTREAM PROCESSING OF MABS

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INTRODUCTION

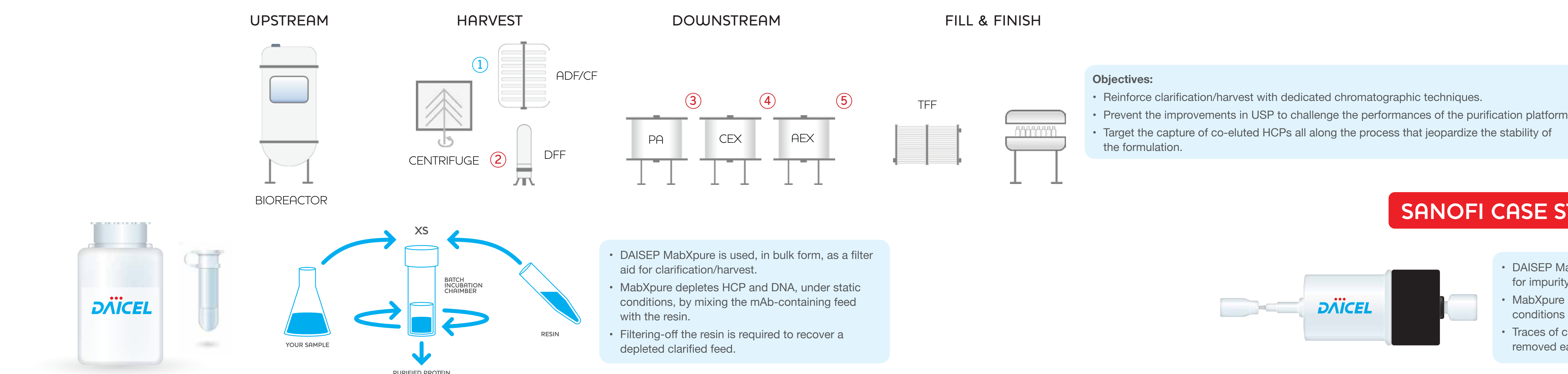
In recent years, biopharmaceutical manufacturing has shown significant improvements in antibody production, with ever-increasing titers generally associated with higher cell densities. These increases in productivity induces higher levels of process-related impurities like host cell proteins (HCP), DNA, HMW fragments or lipids and consequently shifts the production bottleneck to the downstream steps (clarification, chromatography, and filtration). **In such context, centrifugation and filtration techniques have reached their limit and will not be able to provide enough protection to the downstream purification platform.**

TECHNOLOGY

DAISEP MabXpure™, an innovative flow-through single-use technology (SUT) combines multimodal depletion mechanisms (Size Exclusion and Anion Exchange) to improve bioburden depletion performances. MabXpure can be used as a single device technology or within a platform frame. The technology can be used as a filter aid, by mixing the resin with very low ratio feed/media, or as a polishing cartridge, when prepacked, without compromising the antibody yield (>90%). As a flow-through technology, MabXpure removes up to 2 LRV for DNA and 1 LRV for HCP under static or dynamic conditions.

The flexibility of MabXpure is unrivaled. As a filter aid, it allows the combination of centrifuge and depth filtration via alluvial filtration, as a prepacked cartridge, it is used as a Protein A guard column or as ion exchange DSP step combination. MabXpure improves overall bioburden depletion and the co-eluted impurities profile before formulation.

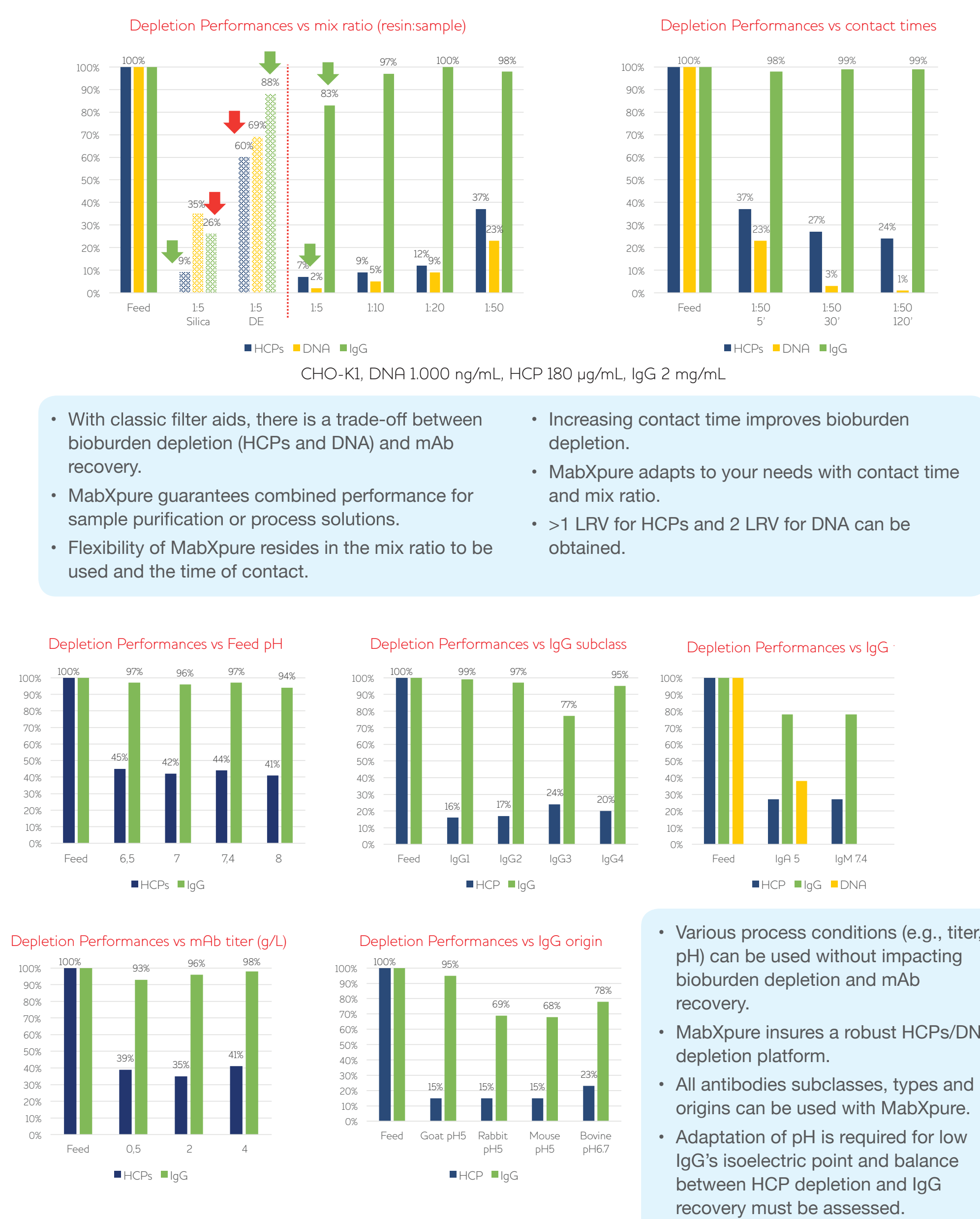
PROCESS SCHEME OF MABXPURE IMPLEMENTATION



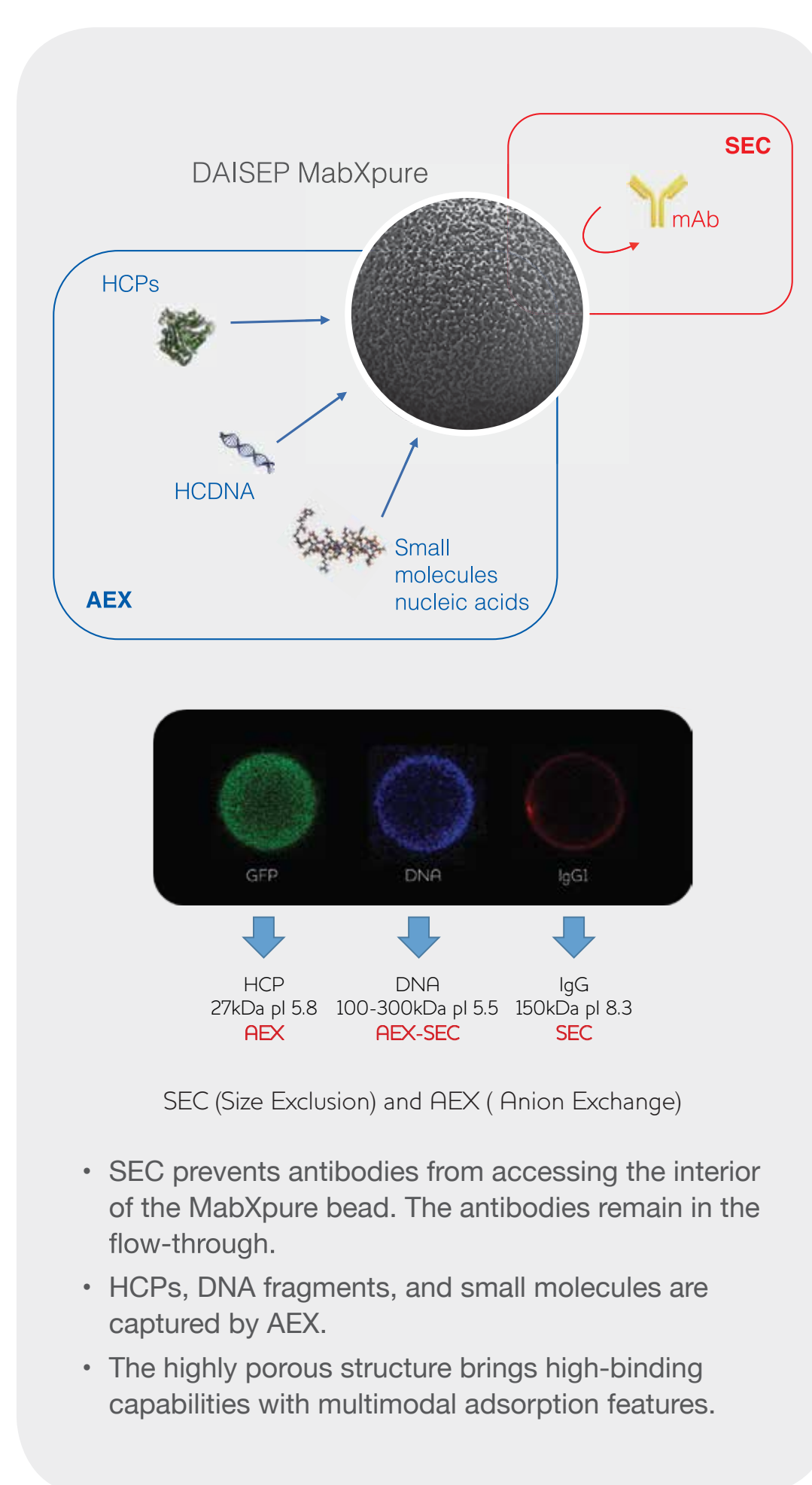
SANOFI CASE STUDY

- DAISEP MabXpure FT is a pre-filled filter cartridge used for impurity capture and polishing purposes.
- MabXpure FT depletes HCP and DNA under dynamic conditions from a mAb-containing feed.
- Traces of co-eluted HCPs and remaining DNA can be removed easily under flow-through conditions.

MABXPURE AS FILTER AID (STATIC PERFORMANCE)



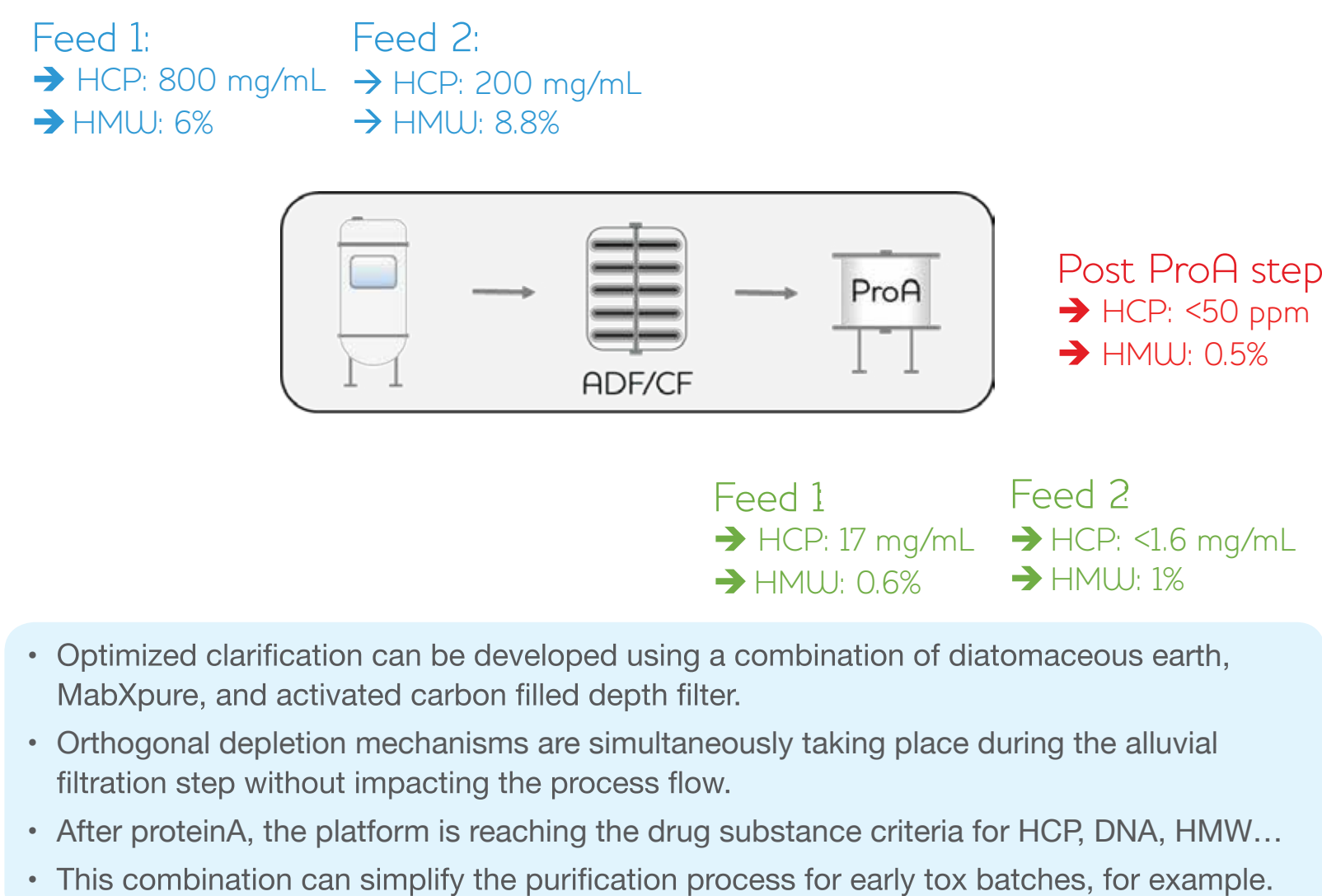
MECHANISM OF INTERACTION & DEPLETION



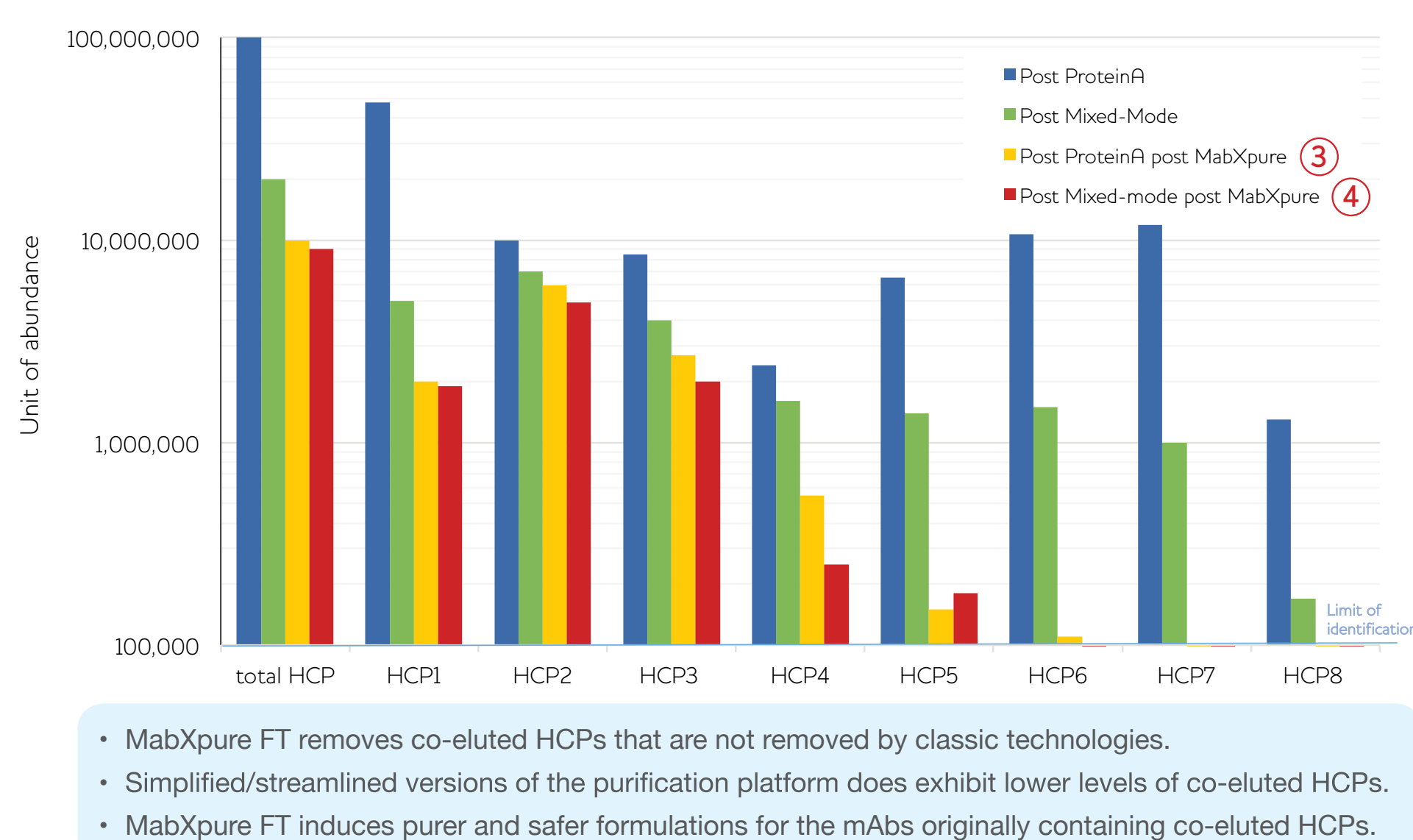
MABXPURE AS FILTER CARTRIDGE (DYNAMIC PERFORMANCE)



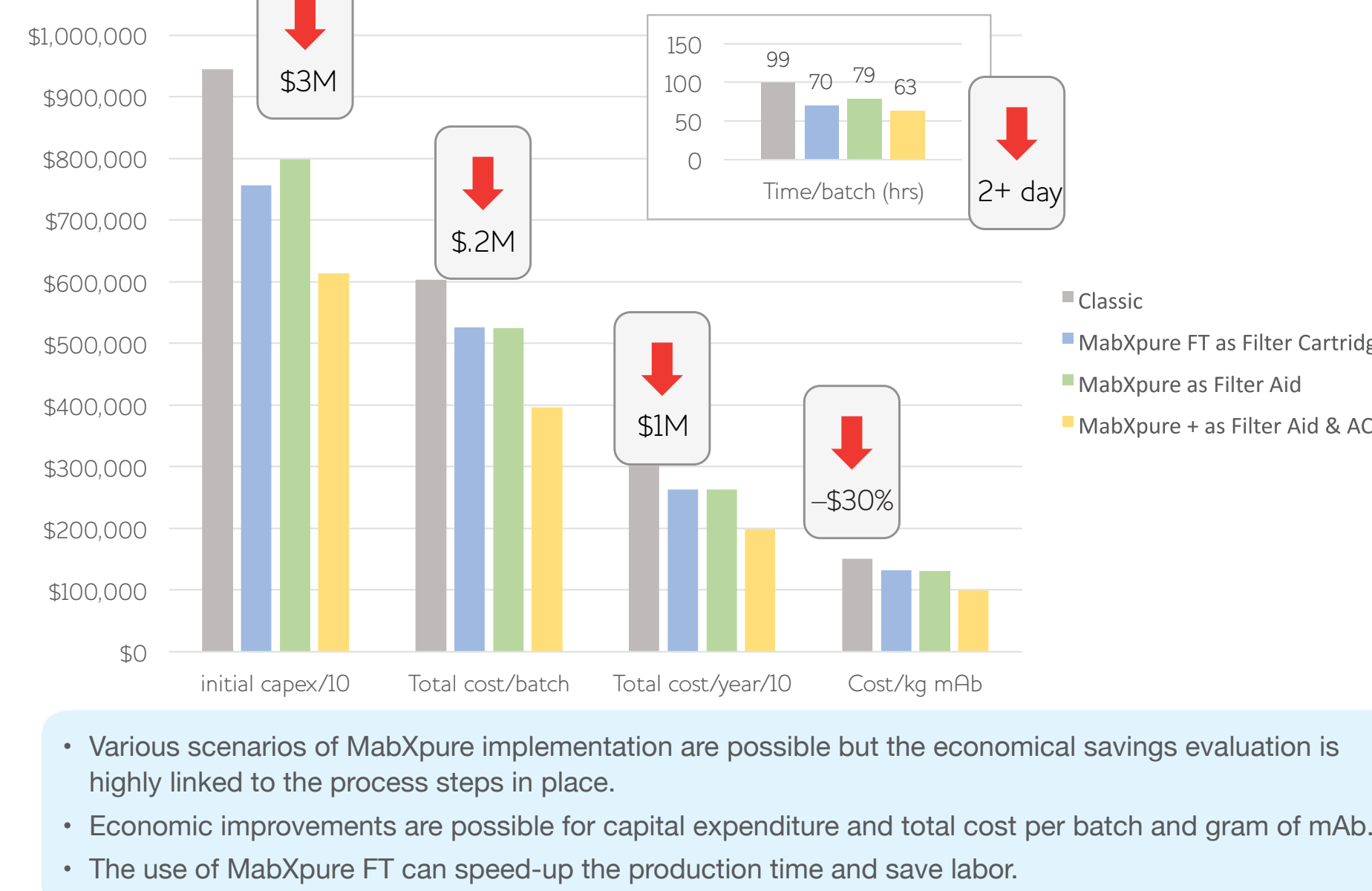
OPTIMIZED CLARIFICATION PLATFORM



SANOFI CASE STUDY CO-ELUTED HCP DEPLETION PERFORMANCES



COGS



CONCLUSION

DAISEP MabXpure is a new, innovative, flow-through, single-use HCPs and DNA depletion technology. The use of MabXpure as a filter aid, in static mode, fits naturally within a process where depth filters are used (alluvial filtration). Ideally, MabXpure's conditions of use are optimal with high mix ratios and short contact times for sample preparation, or lower mix ratios and higher contact times for

in-process applications. In its pre-filled resin filter cartridge (RFC) design, the MabXpure FT fits very easily within a purification platform process where streamlined conditions are expected (flow-through).

MabXpure has a very high capability for depleting host cell proteins and DNA, with extremely high mAb recovery (>95%). Less intrusive

to the product, it allows the removal of up to 1 LRV of HCPs, 2 LRV of DNA depending on the mode of action, and reduces co-eluted HCPs species. MabXpure can supplement, complement, or replace the pre-existing DSP unit operations.

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