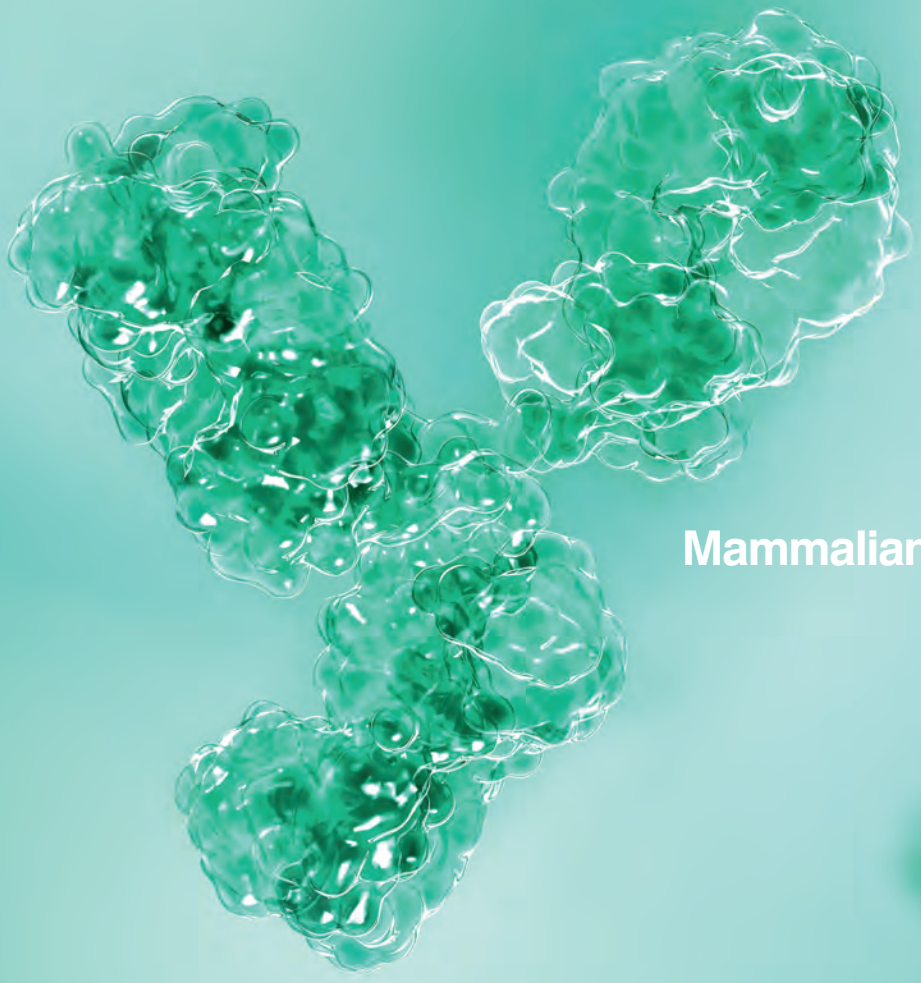
FUJIFILM

Diosynth biotechnologies



# Apollo™

ADVANCED MAMMALIAN EXPRESSION

## Mammalian Expression System

Partners for *Life*

Advancing tomorrow's medicines

# The Biologics and Gene Therapies CDMO partner for life

# Good science, experience and a quality driven approach

## Cell Line/Strain Development

As your partner, we help expedite this process by bringing our years of experience and our expression platform technologies for microbial expression, pAVEway™; and platforms and solutions for mammalian expression, Saturn™ and Apollo™ X.

## Process Development

At FUJIFILM Diosynth Biotechnologies our Process Development philosophy is driven by designing processes for a wide range of expression systems that result in having phase appropriate product controls that will result in successful process execution during cGMP manufacturing.

## cGMP Contract Manufacturing

We offer our partners highly flexible clinical and commercial cGMP facilities for the production, by microbial fermentation and cell culture, of biologics and advanced therapies.

## Quality

This is at the heart of everything we do. Quality drives the development and the successful production of your biologics and advanced therapy products from beginning to end, with propriety statistical design tools like RAPTA™ for Laboratory Process Characterization (LPC).

Apollo™X
ADVANCED MAMMALIAN EXPRESSION

# An accelerated cell line for life

Efficient and high-quality cell line and process development is the critical first step in the development of a robust manufacturing process for expression of a therapeutic protein.

FUJIFILM Diosynth Biotechnologies has used directed evolution to identify host cell lines with optimum biomanufacturing potential. These new cell lines, combined with a proprietary host cell culture medium and a new Cyto-Mine® workflow, have removed a previous bottleneck in cell line development. The new Apollo™X advanced expression systems offers reduced timelines, from transfection to research cell banks, without compromising quality.

The benefits of the latest Apollo™X Mammalian Expression Platform are:

## Expression Vector

- DHFR based selection system
- Proprietary leader sequence developed for efficient secretion
- High productivities achieved without the need for amplification
- Codon optimization utilized
- Double gene vector for mAbs

## Optimized Host Cell Line

- CHO DG44 derived
- Adapted to chemically- defined medium and suspension culture
- Selected for superior growth and productivity characteristics by directed evolution
- Fully characterized cGMP cell bank available
- Full cell line history available

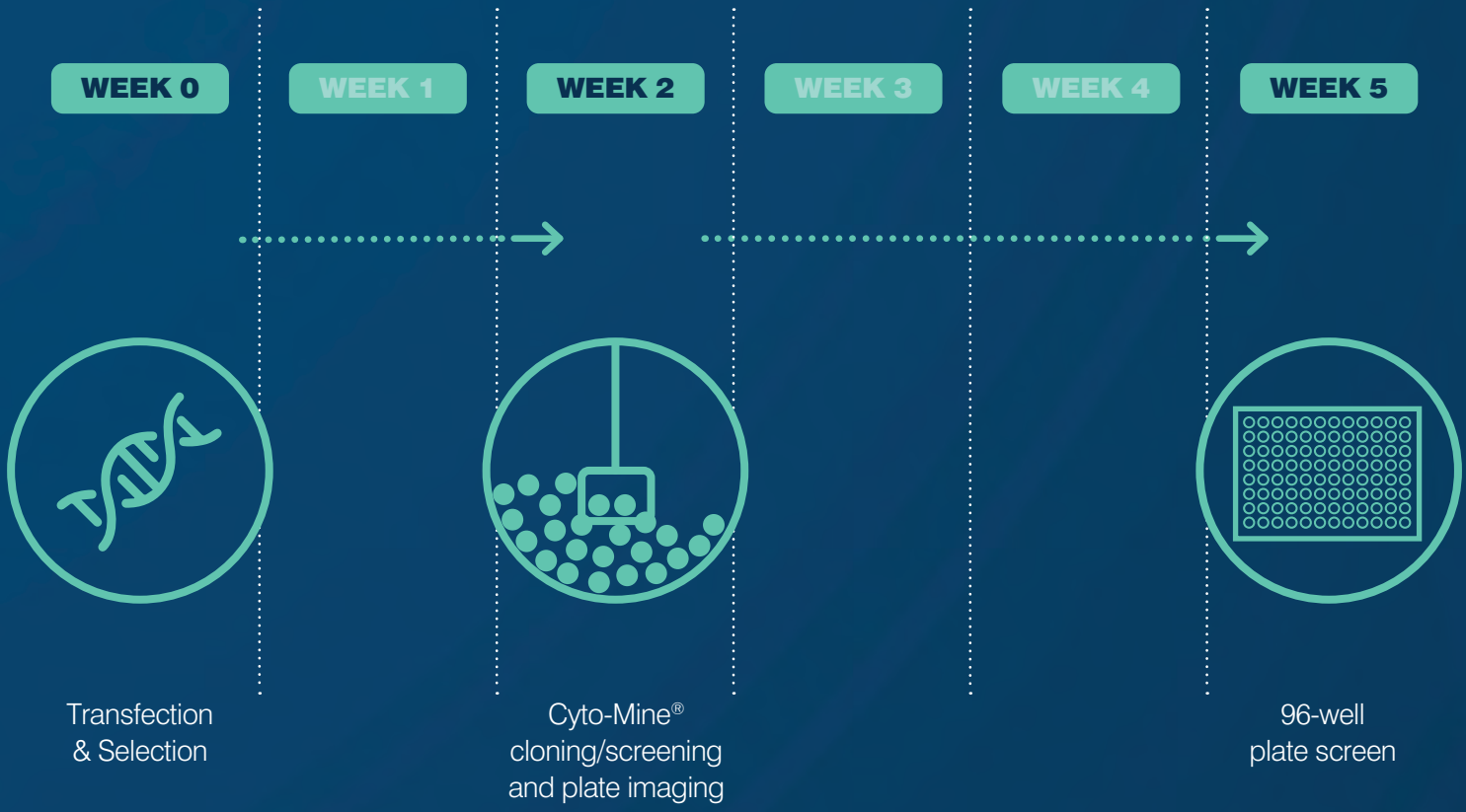
## Improved Platform CLD Processs

- ACF media and reagents
- Robust cloning strategy: High probability of monoclonality
- State-of-the-art screening strategies
- Achieved >10 g/L using platform conditions
- 10 weeks from transfection to research cell bank production

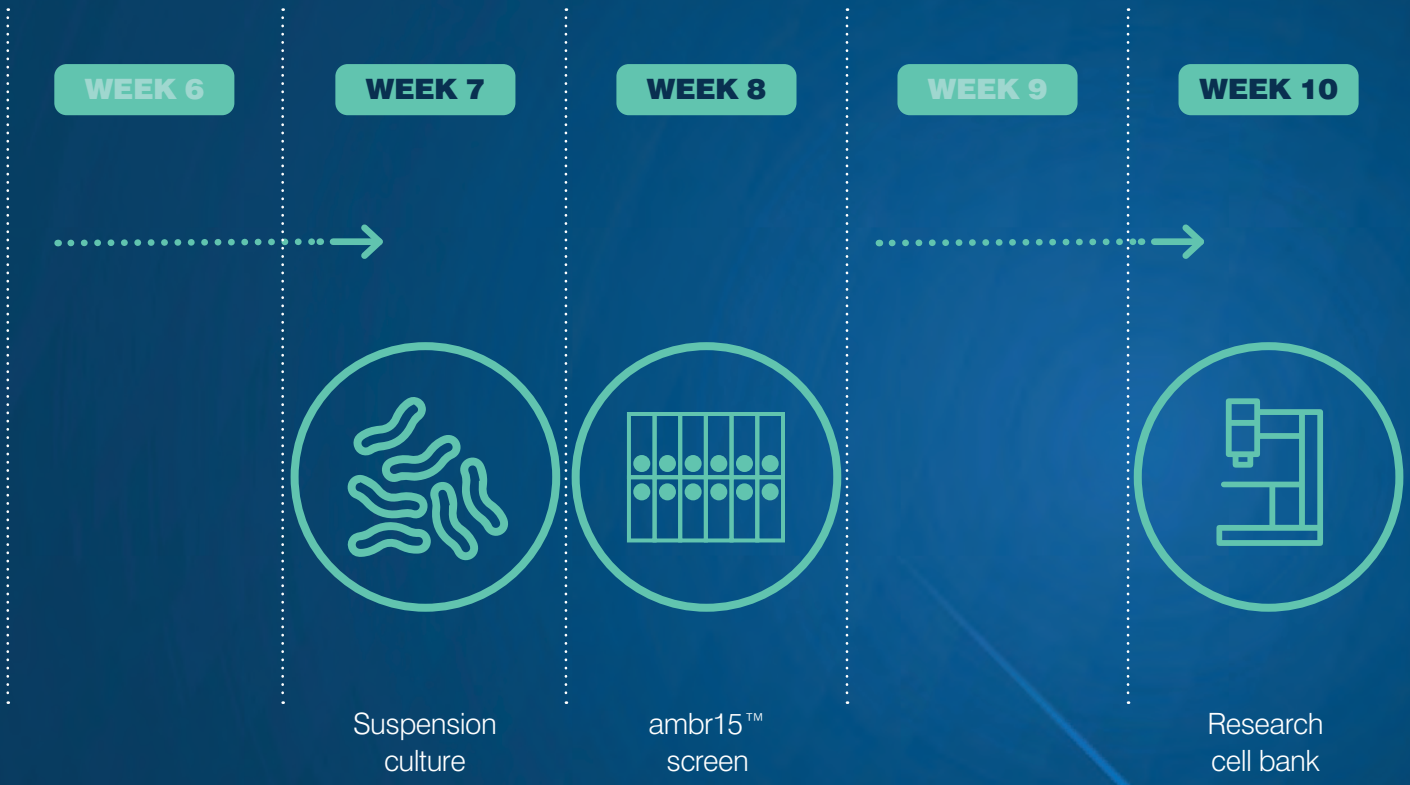
## Platform Media, Feeds and Process

- Proprietary Apollo™X basal medium developed by FUJIFILM
- Used throughout gene to cGMP manufacture
- Chemically defined and protein free
- Superior bioprocess characteristics including growth, titer and product quality
- Recombinant cell lines screened in ambr15 using new basal medium and an improved process

# Apollo™ X now delivers: transfection to RCB in 10 weeks



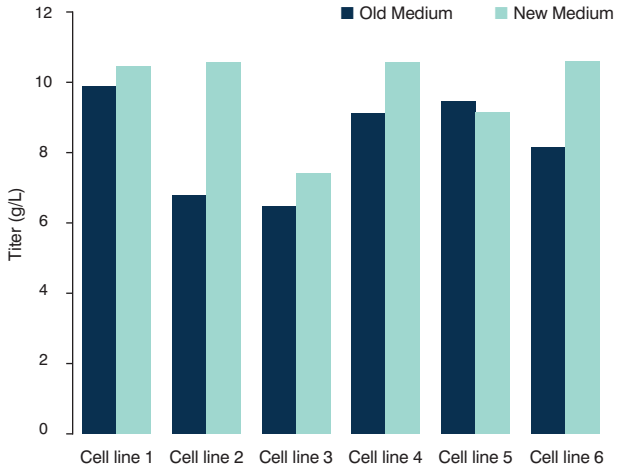

CLD timelines now reduced from ~25 weeks to ~10 weeks through the integration of a new host cell line with superior growth and productivity characteristics **> 10 g/L clonal cell lines after 10 weeks**


WEEK 6
WEEK 7
WEEK 8
WEEK 9
WEEK 10
Suspension culture
ambr15™ screen
Research cell bank


100
80
60
40

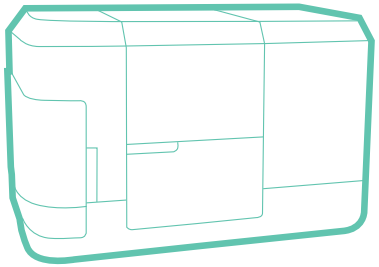
# Titer improvement through the introduction of a new basal medium

- New proprietary medium, specific for Apollo™X, developed in-house by FUJIFILM
- Ability to achieve high titers whilst controlling peak cell density and maintaining high cell viability.
- Recombinant cell lines from PoC work screened in ambr® 15 using new basal medium and improved process:




# Maintaining a robust cloning strategy with one round of cloning

- Using new technology with a qualified plate imaging procedure
- Sphere Fluidics Cyto-Mine® Platform



**STEP 1**

**Encapsulate**

Encapsulate up to 200,000 single cells (or 40 million cells in pools)

**STEP 2**

**Assay**

Screen cell populations by antigen specificity or immunoglobulin productivity

**STEP 3**

**Sort**

Sort based on fluorescence intensity to find positive 'hit' cells or highest producers

**STEP 4**

**Image & Dispense cells**

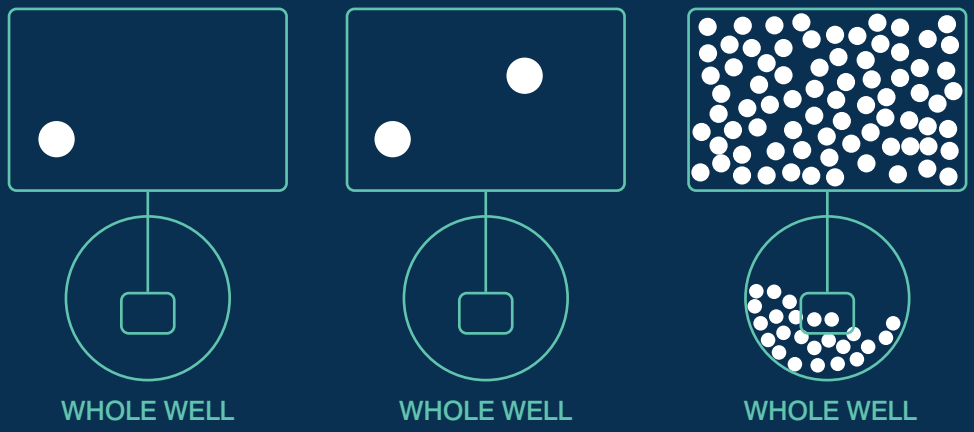
Image single cells during dispensing into 96- or 384- well plates to record monoclonality

# Multi-step approach providing visual evidence of Monoclonality

## Cell Metric® Plate imaging

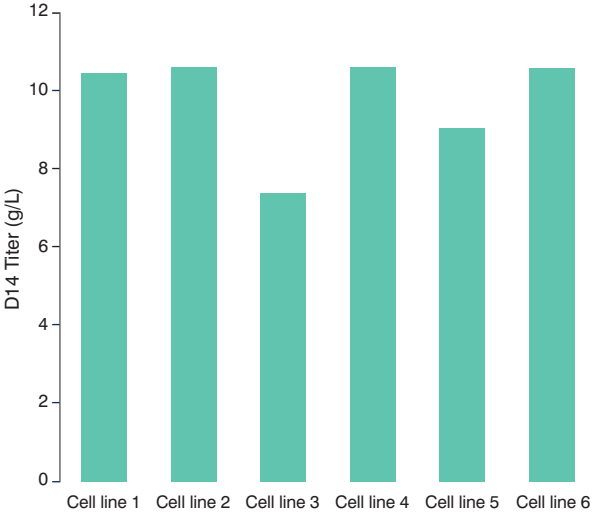
- Imaging is provided at pre-deposition, Day 0, Day 1 and Day 14 are performed
- Once colonies are visible, images are analysed to identify wells where colonies are derived from single cell
- Cross-checking Cyto-Mine® data to verify monoclonality

### WELL TIMELINE

# Performance: cell lines in shaken, fedbatch multi-well plate and ambr15™ screens

- State-of-the-art multi-well plate and micro bioreactor systems are utilized to screen cell lines in an environment that is closer to that of a production bioreactor
- Operated in fed-batch mode with cells in suspension culture
- Enables improved and early prediction of the 'best' cell lines to progress
- High probability of success
- Large number of high titer cell lines




| mAb | Average Titer Improvement |
|---|---|
| mAb1 | 2.0 x |
| mAb2 | 1.9 x |
| mAb3 | 1.4 x |
| mAb4 | 2.1 x |
| **Average** | **1.9 x** |

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