Supplementary Material 1 Early-access designations in the US, EU, Japan and China

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| Country/ Regulatory body | Regulatory pathway (Year of introduction) | Implication | Qualifying criteria | Example cell/gene therapy product that used this designation |
| Serious life-threatening disease | Orphan patient population | Unmet medical need | Superior to existing treatment | Pediatric indications | Regenerative Medicine |
| US FDA | Priority review (1992) | Review decision within 6 months$2.7million FDA user fee + $2.4 million usual user fee [1] | √ |  |  | √ |  |  | Novartis: Kymriah;Exelixis: Cabometyx;Eisai: Lenvatinib |
| Accelerated approval (1992) | Approval based on effect on a predictive surrogate endpoint or an intermediate clinical endpoint [2] | √ |  |  | √ |  |  | Pfizer: bosutinib |
| Fast track (1998) | Option for rolling NDA/BLA submission [2] | √ |  | √ |  |  |  | Renova: RT-100 AC6 gene transfer (Ad5.hAC6);DNAtrix therapeutics: DNX-2401 |
| Breakthrough therapy (2012) | NDA/BLA data submitted as they are accumulated (rolling review); Most reviewed in 60 days or less, limited types of submissions require 90 days (FDA) [2] | √ |  |  | √ |  |  | Juno & Celgene: JCAR017Adaptimmune & GSK: NY-ESO-1c259TBluebird & Celgene: bb2121 |
| Expedited access pathway (2015) | For de novo requests, determination in less than 120 days; Reduces premarket data requirements [2] | √ |  | √ |  |  |  | Avita: Recell |
| Orphan drug designation (1983) | Approval in 6 months [2] |  | √ |  |  |  |  | Atara Bio: ATA129Astellas Pharmaceuticals: ASP2215 |
| Rare Pediatric Disease Priority Review (2014) | Sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. [2] | √ | √ |  |  |  |  | Enzyvant: RVT-802 |
| RMAT designation (2017) | Increased meeting opportunities with FDA (like Breakthrough therapy); Priority review (initial assessment of the BLA reduced from 10 months to 6 months) [2] | √ |  | √ |  |  | √ | Kiadis Pharma: ATIR101;Asteria: AST-OPC1 |
| EU EMA | Accelerated assessment (2004) [3] | Reduce review timeframe from 210 days to up to 150 days |  |  | √ |  |  |  | Alynylam Pharmaceuticals: patisiran |
| Orphan drug designation (2000) [3] | Fee reduction; Eligible for conditional marketing authorisation; 10 year market exclusivity | √ | √ |  |  |  |  | Edison Pharmaceuticals: EPI-743Astellas Pharmaceuticals: ASP2215 |
| Marketing authorization under exceptional circumstances (2005) [3] | Authorization without comprehensive data on efficacy and safety |  | √ |  |  |  |  |  |
| Conditional marketing authorization (2006) [3] | Earlier authorization based on less complete clinical data | √ | √ | √ |  |  |  |  |
| Adaptive pathway (2015) [3] | Scientific advice by authority, compassionate use, conditional approval mechanism |  | √ | √ |  |  |  | Atara Bio: ATA129 |
| PRIME(2016)[3] | Identify potential for accelerated assessment earlier in development; More scientific advice and support; Early rapporteur appointment; Dedicated contact person within EMA. |  |  | √ |  |  |  | Juno & Celgene: JCAR017Adaptimmune & GSK: NY-ESO-1c259TBluebird & Celgene: bb2121 |
| Japan PDMA | Priority review[4] | 9 months instead of 12 months | √ |  |  |  |  |  | Glecaprevir/Pibrentasvir (G/P), AbbVie |
| Orphan designation (1993) [4] | Administrative and scientific advices, preferential protocol assistance, grant aid for research expenses, authorization for tax deduction, reduction of application fee, extension of re-examination period |  | √ | √ |  |  |  | Edison Pharmaceuticals: EPI-743 |
| Conditional & Time-limited approval (2014) [4] | Earlier authorization based on less complete clinical data | √ |  | √ |  |  | √ |  |
| SAKIGAKE Forerunner review assignment (2015)[5] | Eligible for rolling review; Shorten consultation on clinical trials time from 2 months to 1 month; Review time from 12 months to 6 months [6] | √ |  |  | √ |  |  | Ono pharmaceutical & Bristol-Myers Squibb: Opdivo;Astellas Pharmaceuticals: ASP2215 |
| China | Accelerated and conditional approval (Draft issued in 2017)[7] | Grant conditional approval for meds that treat life-threatening conditions where significant unmet medical needs exist, if early- or mid-stage data can predict the drugs’ clinical benefits; cover orphan meds already approved in foreign countries, even those without any trial data from China. | √ | √ | √ |  |  |  |  |

References:

1 Ridley DB. Priorities for the priority review voucher. *American Journal of Tropical Medicine and Hygiene* 96(1), 14–15 (2017).

2 Raggio M. Overview of FDA Expedited Programs with a Focus on Breakthrough Therapy. (2015).

3 McBlane JW. Regulatory landscape for cell therapy - EU view. *Biologicals* 43(5), 433–436 (2015).

4 Jokura Y, Yano K, Yamato M. Comparison of the new Japanese legislation for expedited approval of regenerative medicine products with the existing systems in the USA and European Union. *Journal of Tissue Engineering and Regenerative Medicine* 12(2), e1056–e1062 (2018).

5 MHLW. Strategy of SAKIGAKE-the Ministry of Health, Labour and Welfare. 20 (2014).

6 Maruyama Y. “Regulation of Regenerative Medicine in Japan” (2017). https://www.pmda.go.jp/files/000219466.pdf.

7 CFDA. “总局关于征求《关于鼓励药品医疗器械创新加快新药医疗器械上市审评审批的相关政策》（征求意见稿）意见的公告（2017年第52号）(Translation: Encouraging Innovation and Accelerating the Review and Approval of New Drugs and Medical Devices (Draft for comment))” (2017). http://www.sfda.gov.cn/WS01/CL0087/172567.html (Archived by WebCite® at http://www.webcitation.org/73nSO5868).