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: JCAR017  Adaptimmune & GSK: NY-ESO-1c259T  Bluebird & 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: ATA129  Astellas 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-743  Astellas 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: JCAR017  Adaptimmune & GSK: NY-ESO-1c259T  Bluebird & 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. | √ | √ | √ |  |  |  |  |

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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).

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